1. Welcome & Apologies & Declarations of Interest

Present
Public Health Consultant, NHS Bristol (Chair)
Interface pharmacist, NHS Bristol
Interface pharmacist, NHS Bristol
HoMM, NHS Bristol
Service Development Manager, NHS Bristol
HoMM, NHS North Somerset
Formulary Pharmacist, North Bristol NHS Trust
GP (Old School Surgery), NHS Bristol
HoMM, NHS South Gloucestershire (part of meeting)
North Bristol NHS Trust D&TC Chair (until 12.15pm)
Clinical Effectiveness Research Lead, NHS Bristol
Formulary Pharmacist, AWP
Principal Pharmacist, University Hospitals NHS Foundation Trust Bristol (UHB)

Apologies
GP, North Somerset
GP, Bristol
Consultant Neurologist, NBT
Deputy Chief Pharmacist, Weston Area Healthcare Trust

Declarations of Interest
None

The meeting was quorate (until 12.15pm)

2. Minutes from December Meeting

The minutes from the Joint Formulary Group (JFG) meeting on the 5th December 2012 had been circulated by NB following the meeting and comments requested within 2 weeks. No comments had been received and therefore the minutes were agreed as accurate.

Matters arising from December Meeting

a. Joint Formulary Process and NICE Guidance

Following publication of the NICE guidance on ‘Developing and updating local formularies’ (December 2012) NB had attended a workshop in London run by NICE. NB was able to gain insight into how other areas work and areas that the BNSSG formulary needs to improve. It was evident though that BNSSG are further ahead than many PCTs / Acute Trusts in terms of a formulary and also are dealing with a larger stakeholder group than most other delegates (i.e. 3 PCTs and 3 Acute Trusts). The recommendations within this guidance will be used as the basis for reviewing the current JFG process and ensuring that they are robust.

VH raised the issue of how the JFG would feed into the wider context of commissioning, especially CAF after 1st April 2013. However, there is also the issue of how commissioning feeds into the JFG. Public Health have offered to undertake a project including the commissioning of new drugs. This
project will need to be aligned with the work that has already been undertaken by the PCTs in terms of establishing new governance routes for the approval of drug spend within the CCGs. The differences in the processes that were undertaken by CAF and those that are being undertaken by JFG will need to be mapped. The BNSSG partnership board agreed at the 22nd January 2013 meeting that the starting point for all new drug requests will be the JFG.

The future of the BNSSG Drugs and Therapeutic committee was raised but there has been no discussion / thoughts about this committee not continuing to function.

CB raised the issue of continued GP attendance at these meetings. It has been proposed that the HoMMs will be the clinical lead for prescribing for the CCGs and as such are able to co opt GPs to the JFG so, at present, the GPs attendance will continue but that new representatives should be considered in terms of resilience and future planning.

The non NICE PbR excluded drugs budget will come under the Medicines Management teams from April 2013. Horizon scanning for new drugs will need to be undertaken and a business case submitted to the CCGs for the funding of these drugs.

**Action:**
1. NB to arrange meeting to discuss NICE formulary guidance. **Part of April meeting of the JFG to be used to map current processes.**

b. Tolvaptan - update from NBT

NBT confirmed that they have directorate sign off for this application that was put forward at the last meeting by UHB. They intended to use it as per the Formulary stipulations.

UHB had submitted an appeal to VH relating to the decision made at the 5th December 2012 in terms of restricting the use of this drug to acute patients only under the care of consultant endocrinologist only. The decision to reject its use in the chronic patient environment was made on the basis that we were informed that the SMC were due to be looking at this use. However it has since been confirmed that the SMC are not considering this drug. Therefore the JFG will revisit the decision made at the next meeting in terms of chronic usage and it’s usage in oncology patients.

**Action:**
1. NB to amend JF website to reflect NBT’s use of this drug
2. VH to forward appeal email to NB on the appeal
3. NB to add to the agenda for next meeting

c. Minocycline

At the last meeting, a request from primary care was put forward to consider making this non-formulary. This is currently on the formulary as TLS blue with no restrictions. It was suggested that it should be made non-formulary on the basis that:

> ‘Although minocycline has various indications, it is used primarily as one of a number of oral antibiotics available for the treatment of acne. Unlike some other drugs in its class e.g. tetracycline and oxytetracycline, it is available as a once-daily treatment and need not be taken on an empty stomach. However, there are concerns regarding its place in therapy:

- There is no clear evidence that minocycline is more effective or better tolerated than other tetracyclines.
- There are safety concerns specific to minocycline – a Cochrane review identified these.
• **Alternative once-daily treatments e.g. doxycycline and lymecycline are available.**

• **Minocycline has a relatively high acquisition cost.** *(Ref – NPC Key Therapeutic Topics April 2012)*

Secondary care have reported back wishing minocycline to remain on the formulary as it is useful in the antibiotic armamentarium for treating a wide range of infections such as joint infections and MRSA.

It was agreed that the drug to remain on the formulary but a line to state that it is NON-Formulary for acne in primary care.

*Action: NB to amend website*

3. **NICE New Technology Appraisals published**

It was noted that four new TAs had been published with a positive FAD, two with a negative FAD and two that had a terminated appraisal. The positive TAs will be added to the joint formulary website within 90 days.

4. **New Drug Requests (NDRs)**

- **Methylnaltrexone**
  - Approved - TLS blue on the advice of palliative care team

- **Dapagliflozin**
  - Rejected - await NICE TA

- **Alteplase and Dornase Alfa**
  - Clinically Approved – TLS Red, however final decision deferred until funding stream identified and agreed

- **MagTab**
  - Approved for use by Renal Consultant only - TLS Red. Review in 6 months

- **Urocit K**
  - Approved for use by Renal Consultant only in patients for the treatment of distal renal tubular acidosis and hypocitraturia - TLS Red.

- **Botox**
  - Rejected

- **Suboxone**
  - Reject currently - more evidence required to support decreased divergence

- **Aflibercept**
  - Reject currently - more trial evidence is required to support sequential use of aflibercept

- **Doublebase Dayleve Gel**
  - Await e consideration – JF Pharmacist suggests this should be included in the formulary.

- **Ranolazine**
  - Await e consideration – JF Pharmacist suggests this should be included in the formulary for NBT (currently on the formulary as UHB only)

  a. **Methylnaltrexone**
Please see NDR application form for full details.

This NDR had been jointly submitted by Dr RM and Dr AS. Dr SK (Locum consultant UHB) attended the meeting to present this application.

This application was for the inclusion of methylnaltrexone for the treatment of opioid induced constipation in advanced illness patients who are receiving palliative care when response to usually laxative therapy has not been sufficient.

NICE are currently reviewing this [bowel function - methylnaltrexone (ID2)] and the expected date of publication in November 2013. The SMC also recommended restricted use in Scotland in 2008.

The London New Drugs Group considered it in July 2008. The review stated that approximately half the patients responded to the drug in the trials, with bowel movements occurring within 4 hours. The predominant cause of constipation in the non-responders may be due to drugs or the disease process. If it were possible to use this and avoid switching to other expensive opiates the cost could be curtailed. There is a risk that it could be over used and therefore guidelines are needed.

A Cochrane review in 2011 states that ‘subcutaneous methylnaltrexone is effective in inducing laxation in palliative care patients with opioid-induced constipation and where conventional laxatives have failed. However, the safety of this product is not fully evaluated. Large, rigorous, independent trials are needed.’

Data available from 3 phase III RCTS of moderate quality strongly suggests an efficacy of methylnaltrexone in causing laxation within four hours and up to 24 hours compared with placebo in half the patients. The main criticisms of the trials are that they did not seek to optimise previous laxatives before moving to methylnaltrexone.

It appears to be a useful agent but there needs to be a clear pathway in order that it does not get overused. Its advantage is that it is subcutaneous and can be used for patients unable to tolerate the oral / rectal route. Its use would be short term to overcome constipation induced nausea and then the patient would resume their usual laxatives.

Predominant use would be during inpatient stays, for patients under the care of the palliative care team. If required on discharge it is mostly likely that the patients would already be requiring input from district nurses who could administer it.

The drug has been licensed for a number of years and has been used at UHB following discussion with pharmacy department and now having gained some experience of this drug have submitted an application as they have identified a small niche group for its use.

The estimated number of patients is 10 a year at UHB and this may rise to 20 across BNSSG but there is unlikely to be a cumulative effect.

Use in primary care would also be necessary and thus a TLS status of red would not be appropriate thus TLS blue on the advice of palliative care team.

NBT opinion has been sought – they are unlikely to use this drug but would like the option to use it if the need arises. Directorate sign off had been obtained.

The committee agreed that this drug could be used as a rescue therapy for a small cohort of patients where the oral route / rectal route is not appropriate on the advice of specialist Palliative Care. A treatment pathway needs to be developed to show when it should be used.
(i.e. not first line). If NICE were to publish a negative appraisal later this year, then this drug would need to be decommissioned and therefore removed from the formulary.

**Finance:** In tariff  
NBT – Signed off  
UHB – await division sign off  
WHAT – await divisional sign off  
Primary Care – approved

**Action:**
1. KG to inform applicant and the need for a treatment pathway  
2. NB to add to the JF website TLS blue on the advice of the palliative care team once financial sign off achieve.

b. Dapagliflozin

Please see NDR application form for full details.

This NDR had been submitted by Dr DF, Christchurch Family Medical Centre, NHS South Gloucestershire.

This application was for the inclusion of dapagliflozin to improve the glycaemic control in type 2 diabetics. This is a novel agent which received its marketing authorisation in November 2012. It is licensed as a monotherapy and “add on” combination therapy. It is the first SGLT2 inhibitor on the market.

It is on the NICE technical appraisal programme and the ACD (Feb 13) has been published which states that NICE are minded not to recommended however, it is necessary to await the FAD (due June 13). CSAS have questioned the cost effectiveness of dapagliflozin and also the credibility on reproducibility of the economic model. There is limited data in the use in patients aged 65 - 75. The safety profile differs from other oral diabetic agents – the most common adverse events were urinary tract and genital infections.

The committee agreed to await the FAD due to the concerns raised by CSAS /NICE in terms of cost effectiveness. If there is a positive FAD, then this drug will be dealt with through the NICE College and added to the formulary. If there was a negative FAD then the drug would not be added to the formulary.

**Finance:**  
NBT – await NICE decision  
UHB – await NICE decision  
WHAT – await NICE decision  
Primary Care – await NICE decision  

**Action:** None - await NICE

c. Alteplase and Dornase Alpha

Please see NDR application form for full details.
This NDR had been submitted by Dr NM, Respiratory Consultant NBT and he attended the meeting to present the application.

This application was for the inclusion of Alteplase and Dornase Alfa to facilitate the draining of infected pleural collections via intrapleural administration. Both of these drugs are not licensed for this indication and also not licensed for administration via the intrapleural route either.

Current practice for the treatment of infected pleural collections is to drain first line. If it doesn’t resolve, a CT scan is required and if the collection is shown to be small and the CRP is ok, the patient would be treated conservatively. If the collection is large and the CRP is raised, more intervention is needed. The only option currently is surgery. Some of these patients are not fit for surgery and are therefore left with no other treatment option.

Evidence for this use is based on one published trial in the NEJM in 2011, of which Dr Maskell is the second author. The results of this 4 arm study showed that there was a synergistic effect when these two drugs were used - pleural infection and effusion decreased and there was a reduced need for surgery. The study also showed that those patients who were given DNAse alone, there was a significant negative effect on outcome. Dr Maskell has previously published a trial which showed that streptokinase alone had no beneficial effect on outcomes. There is a lack of data on significant side effects due the small number of trial patients (50 for this arm in this study) but there was no greater haemorrhaging into the chest drain. Funding is currently being sought for the next phase of the trial, MIST III.

This is the only trial to be published and there is no published data to suggest which provides better outcomes - surgery or the use of these drugs, however this trial shows that the drug combination is certainly an option for those patients that aren’t fit for surgery as it can reduce the need for surgery.

The combination is currently being used around the world with patient data being collected (approximately 120 people, with approx 60 being based in the UK) and it is hoped that this will be published next year.

It has been used on 12 - 15 patients within Bristol who were unfit for surgery. Its use would be restricted to the pleural service only. A decision to use these drugs depends on if the patient had large number of co morbidities, if they can tolerate surgery and their preference. The protocols / SOP have been taken from the New England Journal. If surgery is subsequently required then the patient has to wait 12 hours before this can be undertaken.

As the decision to use these drugs is usually an immediate / same day decision then exceptional funding / individual patient funding route is not appropriate. The drug costs in the region of £1600 per course of treatment which may be offset by a reduction in referrals for thoracic surgery and a reduction in bed days. It is estimated to save 4 inpatient bed days per patients. However the use of intrapleural alteplase is associated with a top up tariff of £830.00 i.e. an increased income for secondary care but a cost to the PCT (CCG).

Long term outcomes - data is again limited but there is a minimum 3 month follow up with x ray and lung function tests.

There was discussion as to how these drugs would be funded i.e. PbR excluded or In-tariff. They both appear on the PbR excluded list, however these are both being used outside of their license. Therefore there was debate as to whether they would still be classified as PbR excluded or not. Post meeting note: It has since been clarified that as the drugs are PbR excluded, whatever indication they are being used for, they are still recharged via this route. Therefore the funding decision is down to the PCTs (CCGs). Agreement therefore needs to be sought from
the CCG for financial support before this use can be added to the formulary.

The committee agreed that although the trial data was limited, effort was being made to gain more evidence to support the use of these drugs. For those patients for whom surgery was not an option then this drug does provide a benefit.

Clinically, the use of these drugs was accepted by the committee for those patients who were not fit for surgery or where a delay to surgery would be detrimental to the patient. The committee recommended the inclusion of these drugs in the formulary pending identification of the correct funding route and the need to look at the wider implications of funding. Local polices to manage the risk associated with the use of unlicensed drugs via the intrapleural route will need to be in place. TLS Red NBT pleural services only.

Finance
NBT – NA
UHB – NA
WHAT – NA
Primary Care – NA
CCG – Await financial sign off

Action:
1. TW to inform applicant and confirm funding stream
2. NB to add to formulary TLS Red NBT pleural services only once funding stream agreed.

MagTab

Please see NDR application form for full details.

This NDR had been submitted by Dr CT Renal Consultant NBT who attended the meeting to present the application.

This application was for the inclusion of MagTab for the use in the treatment of hypomagnesaemia caused by Gitelman syndrome and other metabolic disturbances. This is a niche group of patients with a low magnesium level due to a congenital renal condition. People suffering from Gitelmins syndrome present with symptoms which are identical to those of patients on thiazide diuretics. MagTab is not licensed for these indications. If it is agreed to add MagTab to the formulary then this would be the fourth magnesium supplement on the formulary and could potentially lead to confusion / risk of errors. It is suggested that it could replace one of the other magnesium supplement on the formulary – Magnesium Glycerophosphate. TW confirmed that at this stage, this would not be possible, as although this is also unlicensed, it is accepted practice that Mg Glycerophosphate is used, and it is referenced in the BNF. Magnesium Oxide and Magnesium Hydroxide are also used at NBT.

Anecdotal evidence suggests that MagTab is better tolerated (less diarrhoea) and that the dose can be reduced by a third leading to cost savings as it is the same price as magnesium glycerophosphate. However, these are only observational findings and the mechanism by which it is better tolerated is unknown. There are unlikely to be any large scale trials as the number of patients are small however a rare disease register is being compiled which may increase information available.

As there is a very limited evidence base, then local experience will be necessary to establish if the use of this drug does lead to cost savings.
The committee agreed to add this drug to the formulary for use by renal consultants only (not restricted to Gitelman syndrome) to allow time to gain local experience and to establish cost savings (reduction in dosage in existing patients) as there was only anecdotal evidence. This decision will be reviewed in 6 months to assess usage/reduction in dose. TLS Red Renal Consultants only.

Finance: Renal services are commissioned via specialised commissioning however this drug is in tariff

NBT – await directorate sign off
UHB – NA
WAHT – NA
Primary Care – NA

Action Points
1. TW to inform applicant
2. NB to update the formulary once financial approval received

e. Urocit K

Please see NDR application form for full details.

This NDR had been submitted by Dr CT, Renal Consultant NBT who attended the meeting to present the application

This application was for the inclusion of Urocit K (potassium citrate) to the formulary for
a) the treatment of distal renal tubular acidosis
b) treatment of hypocitraturia
c) prevention of recurrent calcium oxalate kidney or uric acid kidney stone formation.

This preparation is not licensed in the UK but is available in the United States for the management of renal tubular acidosis. The monthly cost is to Acute hospitals £240.00 (2 tablets tds) per patient.

Potassium Citrate BP liquid has a history of poor compliance due to the taste (only approximately 30% compliance) and there is on going national supply problem with Effercitrate which is an alternative preparation that is better tolerated.

Urocit K reduces the formation of kidney stones and thus the need for further intervention. However, it takes several years before it is known if there is a reduction in stone formation and therefore difficult to define the cohort of patients who have "recurrent stones".

For the prevention of recurrent calcium oxalate kidney or uric acid kidney stone formation there is a theoretical case for the use of Urocit K but there are other option available (e.g. sodium bicarbonate) and the cost implications do not justify it’s use.

There is a need for an alternative palatable potassium containing product on the formulary whilst effercitrate is unobtainable. For the first two indications, there are no other palatable alternatives, and therefore it can be justified to add this to the formulary for these patients. However in the third indication, Sodium Bicarbonate may also be used. Urocit K has a theoretical advantage over Urocit K, however there is an increased cost associated with using Urocit K in these patients.

The committee agreed to add Urocit K to the formulary, second line, for the treatment of distal renal tubular acidosis and hypocitraturia in patients unable to tolerate Potassium Citrate BP
liquid, Renal Consultant only. However, since this drug is a unlicensed special then the cost in the community would far exceed the price quoted in the application and thus the prescribing would remain the responsibility of the acute trust with a pass through payment being made to the PCT / CCGs. Usage of this drug to be reviewed in 1 year. The use of Urocin K for the prevention of recurrent calcium oxalate kidney or uric acid kidney stone formation was rejected on the grounds of cost as a palatable alternative was available.

**Finance:**

   - NBT – directorate sign off agreed
   - UHB – NA
   - WHAT – NA
   - Primary Care – NA

**Action:**

1. TW to inform applicant
2. NB to add to formulary TLS Red Renal Consultant only second line to potassium citrate BP liquid

f. **Botox**

The meeting was no longer quorate when this application was discussed and e approval is necessary.

Please see NDR application form for full details.

This NDR was submitted by SL Directorate of Plastic Surgery who was not present at the meeting.

This application was for the inclusion Botulinum toxin type A for the treatment on Raynaud’s disease of the hand. This drug would be used in less than 10 patients a year and is an off label use of the drug.

The cost for Botox for the treatment of Raynuad’s disease of the hand is in the region of £240 for 100 unit per hand and this is administered as an out patient. Current therapy for this condition is Iloprost infusion which costs £479 - 799 plus vat and is associated with a 5 day inpatient stay. Although iloprost is an unlicensed product, there is a large evidence base around it use.

The evidence for the use of Botox is only based on case reports between 2004 and 2010 for which there were positive outcomes. There have been no RCTs.

There are other commissioning polices within BNSSG which have been produced as the result of applications to use this drug and any decision made on this application should be consistent with these.

Discussion with the rheumatologists in relation to this application is also necessary as they also treat this condition.

The committee rejected the inclusion Botulinum toxin type A for the treatment on Raynaud’s disease of the hand to the joint formulary as the benefits presented were only theoretical and based on case reports. There is a need for a large randomised control trial and the committee noted a trial recruiting currently in the States. The committee also noted the need for a Botulinum Toxin review for all indications within BNSSG.
Finance: N/A as application rejected
NBT – NA
UHB – NA
WAHT – NA
Primary Care – NA

Action:
1. TW to inform applicant and to gauge the opinion of the rheumatologists over its use / this application
2. TW to initiate Botox review within BNSSG.

g. Suboxone AWP

The meeting was no longer quorate when this application was discussed and e approval is necessary.

Please see NDR application form for full details.

This NDR was submitted by Dr FL, AWP and presented by BS.

This application was for inclusion of Suboxone (buprenorphine and naloxone) to the formulary for substitution treatment for opioid drug dependence.

It is already on the AWP formulary but not the BNSSG formulary. It is more expensive than generic buprenorphine. It is stated that by using Suboxone this reduces the risk of divergence, there is less risk of injecting due to the presence of the naloxone and as a result of this it has a lower street value.

The SMC and AWMSG reported over 5 years ago, and stated that it should be available to patients but restricted to those patients in whom methadone is unsuitable and where buprenorphine is suitable.

According to NICE, methadone should be first line therapy in patients, and buprenorphine used only if this is unsuitable. The advantage of Suboxone is that it reduces the abuse potential and also it can lead to a possible reduction in the need for supervised dosing. There are no RCTs that provide the evidence to support this. There is a large cost differential between methadone, buprenorphine and Suboxone, with Suboxone being almost double the cost of buprenorphine. It is difficult to define a cohort of patients who do not need supervised consumption.

The estimated number of patients would be 100 a year.

The committee agreed to reject the application as the benefits of this drug are theoretical and it is difficult to justify the acquisition costs. APW to supply further evidence on the risk of divergence. SM to obtained the number receiving supervised buprenorphine from the Shared Care Monitoring Group and how effective buprenorphine is / its place in therapy across BNSSG.

Finance: N/A as application rejected
NBT – NA
UHB – NA
WAHT – NA
Primary Care – NA
Action:
1. BS to inform application
2. SM to obtain number receiving supervised buprenorphine from the shared care monitoring group

h. Aflibercept

The meeting was no longer quorate.

Please see NDR application form for full details.

This NDR was submitted by AR Consultant Ophthalmologist UHB who attended the meeting to present the application

This application was for the inclusion of aflibercept for the treatment of neovascular age related macular degeneration (wet AMD), second line following failure of Lucentis treatment.

Aflibercept is currently on the NICE TA work plan but this is for first line treatment.

The cost of aflibercept is very similar to Lucentis but cost savings would be achieved as the drug has a less frequent dosing schedule thus saving on drug costs (lower mean number of doses needed in the first year of treatment) and out patient appointment costs and also there is a possible reduction in infection rates.

All trials of aflibercept have been first line treatment and head to head trials with Lucentis have been undertaken. The VIEW trial in the UK and Europe has shown that aflibercept is non inferior to Lucentis. Safety outcomes are the same. There is only anecdotal evidence that aflibercept works in patients resistant (non responders) to Lucentis.

There are 1600 patients with wet AMD and approximately 10% are not ideal responders. Currently these patients would continue of Lucentis in accordance with NICE.

In terms of the use of aflibercept in anti-vascular endothelial growth factor refractory cases, there is limited evidence available to demonstrate the efficacy. There are papers (10) which show evidence of sequential use / switch to aflibercept but these were not submitted as part of the application. AR to be asked to forward these papers to the committee.

If aflibercept were to be used in these patients, funding would not be able to come from the NICE budget, but would need to be agreed by the CCGs.

The committee agreed to reject the application currently as no evidence was submitted on the sequential use of aflibercept and this was necessary before a decision could be made on second line use. The applicant is invited to resubmit with the appropriate evidence. To take to the CCG boards re funding and criteria for usage once clinical effectiveness / inclusion onto the formulary agreed.

Finance: NA as application rejected
NBT –
UHB –
WAHT –
Primary Care –
Action:
1. KG to inform applicant and the need to submit additional papers
2. NB to add to the agenda of the next JFG.
3. To be taken to the CCG board for approval for funding if accepted onto the formulary

i. Doublebase Dayleve Gel

This application was for discussion and any comments / acceptance to be returned to NB and SB by 26th March 2013.

Please see NDR application form for full details

This NDR was submitted by VA Dermatology Specialist Nurse South Glos Community Health Services NBT.

This application was for the Doublebase Dayleve Gel for the management of dry or chapped skin conditions which may also be itchy or inflamed. The advantage of Doublebase Dayleve Gel is that is a long lasting applied emollient gel and there is theoretical advantage that it provides longer lasting protection and requires less frequent administration. Doublebase gel is currently on the formulary and the dermatology nurse confirmed that the Dayleve product is useful for patients finding that normal Doublebase is not providing sufficient levels of emollient and that its inclusion to the formulary would result in a reduction of the prescribing of more expensive urea containing emollients.

The committee confirmed that the approval for this application would be via correspondence. The recommendation of the formulary pharmacist undertaking the critical appraisal is for the acceptance of this application.

Finance: in tariff
NBT –
UHB –
WAHT –
Primary Care – Agreed

Action:
1. E correspondence to be sent to Nicola Bruce and Sasha Beresford

j. Ranolazine

This application was for discussion and any comments / acceptance to be returned to NB and SB by 26th March 2013.

Please see NDR application form for full details

This NDR was submitted by Dr AS Consultant cardiologist NBT.

This application was for the inclusion of ranolazine for patients with symptomatic stable angina as add-on therapy in patients who are inadequately controlled or intolerant of first line anti-anginal therapies.

Within the application, it was suggested that the drug would be suitable for amber status – it is currently on the formulary for UHB only, TLS Red. A previous request by UHB for a change to an amber TLS had been rejected by the JFG at the 1st August meeting 2012 due to lack of familiarity of this drug in primary care. If this application is accepted it would remain as TLS Red.
The committee confirmed that the approval for this application would be by electronic correspondence. The recommendation of the formulary pharmacist undertaking the critical appraisal is for the acceptance of this application in line with UHB.

**Finance:** In tariff
NBT – await divisional sign off
UHB – NA
WAHT – NA
Primary Care – NA

**Action:**
1. E correspondence to be sent to NB and SB

5. Specialised Commissioning

a. Fingolimod

Please see NDR application form for full details

This NDR was submitted by Dr DC who attended the meeting to present the application.

This application was for the inclusion of Fingolimod (Gilenya®) for the treatment of 4 groups of patients with highly active relapsing remitting multiple sclerosis who were not covered by the NICE TA 254 published April 2012. The 4 groups are detailed below:

1. Those continuing to relapse and fail treatment, fulfilling section 1.1 of the NICE guidance but taking Copaxone a drug equally efficacious as the Interferon betas.
2. Patients with rapidly evolving MS who are not suitable for Natalizumab (Tysabri®) due to the high risk of progressive multifocal leucoencepalopathy (PML)
3. Patients on Natalizumab (Tysabri®) whom continue to relapse on Tysabri or develop neutralising antibodies.
4. Patients whom had been on Natalizumab (Tysabri®) for several years whom are JC positive and carry a high risk of PML

The use of fingolimod for non NICE patients had first been raised at the July 2012 BNSSG Drugs and Therapeutic committee meeting and was to be discussed at CAF, however the CAF meetings were subsequently cancelled.

This was the first time that this drug request had been considered by the JFG.

The use of Fingolimod in the groups above although not supported with significant evidence, seems logical. It does not seem equitable not to be able to offer Fingolimod to patients who have failed on glatiramer, yet those that have failed on interferon are offered Fingolimod and this is funded by the NICE budget. Those patients that are eligible for natalizumab under NICE but at risk of PML should be able to be offered Fingolimod as the risk of PML does not seem to exist with Fingolimod. And, those that fail on natalizumab, again should be able to be offered an alternative treatment. By using Fingolimod, the local health economy could potentially realise savings. The issue is which budget would fund these patients. If they are not being prescribed according to NICE, the NICE budget would not fund.
Post April 2013, the treatment of MS will be commissioned by Specialised Commissioning (National Commissioning Board) and not the CCG. The NCB had published a draft policy "Disease Modifying Therapies for MS" which limits the use of fingolimod to patients meeting NICE TA 254 criteria only. Dr Cottrell had fed back to the NCB on this draft policy and the omission of the groups identified above. At this time is not clear who would meet the drug costs if patients, who did not meet the NICE criteria, were given fingolimod i.e if Specialised Commissioning would take over paying for these patients or if this would be the responsibility of the CCG’s.

The Greater Manchester Neurosciences Medicines Management Group had considered these 4 groups of patients in May 2012 in light of the NICE publication and approved the use of fingolimod for these patients. This is also supported by the North of England Specialised Commissioning Group in September 2012.

There is no process currently in place within the PCTs for funding a small cohort of patients as exceptional funding (individual funding request) is not appropriate by the very nature of there being a cohort.

The drug company would supply the drug under the same conditions as the NICE PAS scheme for non NICE patients at a cost of £11,704.00 per annum.

Since the end of December 2012, funding has been agreed on an individual basis for those patients in group 4 who are clinically at risk and wish to change to fingolimod.

The committee could not agree to add fingolimod to the formulary for patients not meeting NICE criteria due the cost of the drug and the uncertainty of future funding. The funding of those patients clinically at risk in group 4 only will continue on a case by case basis. A paper to be written for the CCG board to consider the funding issues around the patients in the other groups. A pathway also needs to be developed for the use of copaxone, beta interferon and Fingolimod.

**Action:**

1. **TW to inform applicant**

2. **NB to write draft paper on the funding of the patients identified in groups 1 to 4 should Specialised Commissioning not agree to fund them.**

3. **NB/SM to write a paper for the CCG board to consider the funding**

**b. Ivacaftor**

For information - Specialised Commissioning Policy Statement: Ivacaftor for cystic fibrosis was published in December 2012. The supply of this drug will be free to the PCT’s until the end of March 2013 when commissioning responsibility will transfer to Specialised Commissioning.

**Action: NB to add to formulary TLS Red**

**c. Hizentra Subcutaneous IVIg**

Please see NDR application form for full details.

This NDR was submitted by Dr MG, Immunology NBT who was not present at the meeting.

This application was for the Hizentra (IVIg) in antibody deficient patients and is administered subcutaneously. It is currently on the formulary for use by UHB only. There is also an on going supply problem with Subcuvia for new patients.
The committee agreed to for NBT to use Hizentra in line with UHB but as the meeting was not quorate, e approval is necessary.

**Finance: PbR excluded funded by Specialised Commissioning**

*NBT – await divisional sign off*  
*UHB – NA*  
*WHAT – NA*  
*Primary Care – NA*

**Action:**
1. NB to remove ‘UHB only’ from Hizentra entry in the formulary once e approval and funding agreement received.

6. **Cancer drugs fund**

   a. **Ruxolitinib**

   Please see NDR application form for full details

   This NDR was submitted by Dr AW, Consultant Haematologist NBT who was not at the meeting.

   This application was for the inclusion of Ruxolitinib for the treatment of myelofibrosis. This is on the NICE TA work plan with an expected publication date of June 2013. Funding for patients within the South West had already been received form the Cancer Drugs Fund but as this drug was not currently on the BNSSG Joint Formulary a NDR is necessary to follow established governance processes - i.e. the clinical governance process around the use this drug had been followed.

   *The committee noted requests for the use of this drug would be forwarded to the cancer drugs fund as individual patient requests.*

   **Action: None**

7. **For information**

   a. **Ticagrelor SCP updated**

   This SCP had been updated and added to the JF website to reflect the change from amber to amber 1 months and now included UHB details

   **Action: None**

   b. **Eplerenone SCP Updated**

   This SCP had been updated to reflect the change in licensing.

   **Action: None**

8. **AOB**
Please note - provisional dates for additional JFG meetings have been arranged but a decision is still need to be made if these meetings are needed.

Tuesday 14th May 10am to 1pm Boardroom South Plaza
Tuesday 10th September 11am to 2pm Boardroom South Plaza
Wednesday 6th November 10am to 1pm Boardroom South Plaza
### 2012 / 13 Dates for Meetings

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Venue</th>
<th>Cut off for NDRs</th>
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<tbody>
<tr>
<td>Tuesday 9th April 2013</td>
<td>10.00 – 1.00pm</td>
<td>Boardroom South Plaza</td>
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<tr>
<td>Tuesday 4th June 2013</td>
<td>10.00 – 1.00pm</td>
<td>Boardroom Trust Headquarters Frenchay</td>
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<td>Tuesday 30th July 2013</td>
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<td>10.00 – 1.00pm</td>
<td>Seminar Room Southmead Pharmacy</td>
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<tr>
<td>Tuesday 10th December 2013</td>
<td>10.00 – 1.00pm</td>
<td>Boardroom South Plaza</td>
<td></td>
</tr>
</tbody>
</table>
1. Welcome & Apologies & Declarations of Interest

Present
- Interface pharmacist, NHS Bristol CCG
- Interface pharmacist, NHS Bristol CCG
- HoMM, NHS Bristol CCG (Chair)
- Service Development Manager, NHS Bristol CCG
- HoMM, NHS North Somerset CCG
- HoMM, NHS South Gloucestershire CCG
- Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust Bristol
- Formulary Pharmacist, AWP

Apologies
- GP, North Somerset
- GP, Bristol
- Consultant Neurologist, North Bristol NHS Trust
- Formulary Pharmacist, North Bristol NHS Trust
- GP, Bristol
- D&TC Chair, North Bristol NHS Trust
- Clinical Effectiveness Research Lead, Bristol City Council
- Public Health Consultant, Bristol City Council
- Chief Pharmacist, AWP
- Nurse Prescriber, Bristol
- Deputy Chief Pharmacist, Weston Area Health NHS Trust

Declarations of Interest
None

The meeting was not quorate and any decisions will require e approval sign off

2. Minutes from February Meeting

The minutes from the Joint Formulary Group (JFG) meeting on the 26th February 2013 had been circulated by NB following the meeting and comments requested within 2 weeks. No comments had been received and therefore the minutes were agreed as accurate.

Matters arising from February Meeting

a. Tolvaptan Appeal

Appeal received from UHB over decision made by JFG on Tolvaptan on 5th December 2012. JFG agreed that tolvaptan should be made available ‘for Consultant Endocrinologist use
only for the acute treatment of hyponatraemia secondary to syndrome of inappropriate anti-diuresis (SIADH) in those patients who are not responsive to fluid restriction / where the use of fluid restriction and / or demeclocycline is inappropriate or contraindicated whilst the underlying cause of SIADH is being investigated and corrected’. This decision was made on the following grounds

- The JFG were informed that there would be an imminent submission to the SMC for chronic use. The JFG agreed to await the SMC decision for this patient cohort and review the application in light of the SMC outcome.

Appeal sent to Chair by the applicant, received 6th February detailing following points:

1. There are no plans that the manufacturer will submit to SMC.
2. Endocrinology has no capacity to be cross referred oncology patients urgently for approval. Request Oncology consultant approval.
3. Acceptance of controlled semi-chronic usage.

Currently the JFG does not have an appeals process although the development of one is on the 13/14 work plan, see under AOB. However, it was agreed to deal with this issue in a timely manner and to review the application and the decision made.

The JFG discussed the details of the appeal and considered each point:

1. It has been confirmed that the SMC would not be producing a report due to lack of submission of data by the manufacturer. The JFG agreed that the lack of a SMC report would not affect their decision but this raised the unanswered question as to why the manufacturer did not submit any evidence.

2. The JFG acknowledged the lack of consultant endocrinologist cross cover with Oncology services and agreed Consultant Oncologist use of tolvaptan for the treatment of hyponatraemia secondary to syndrome of inappropriate anti-diuresis (SIADH) in those patients who are not responsive to fluid restriction / where the use of fluid restriction and / or demeclocycline is inappropriate or contraindicated whilst the underlying cause of SIADH is being investigated and corrected.

3. The JFG agreed that the evidence submitted was weak in terms of the routine funding of this drug for chronic usage. There have been no long term comparator trials with demeclocycline. The JFG upheld the decision not to routinely fund this drug for chronic usage. This decision does not preclude an individual funding request being submitted in which exceptionality would need to be established. The JFG would consider another application for chronic usage if further evidence on the use of tolvaptan in chronic patients was submitted.

Monitoring of the usage of this drug will be necessary and the data set needed to undertake this should soon be available.

Post meeting Note: Tolvaptan is PbR excluded for 13/14 and is commissioned by NHS England. The ‘Manual for prescribed specialised services’ also states that within Adult Specialist endocrinology services tolvaptan is commissioned by NHS England. However, the CCG commissions the ‘assessment on management of hyponatraemia and the syndrome of inappropriate antidiuretic hormone.’ Based on current advice from SCG, the responsible commissioner will pay for the drug, regardless of how it is used i.e. whether it is being used within a prescribed service or not.
Action:
1. VH to inform applicant
2. NB to update website once e approval received

b. Methylaltrexton - NICE terminated appraisal

The decision to use methylaltrexton was agreed in February 2013 however in March 2013 NICE published a terminated appraisal on this drug. TMC Pharma Services informed NICE in December 2012 that it would not be making an evidence submission for this appraisal. The manufacturer stated that it is holding the European marketing authorisation for methylaltrexton on a temporary basis while the product owner finds a permanent European partner, but timelines for this are not currently known. The JFG agreed that the reason for this terminated appraisal did not alter the decision that was made and for methylaltrexton to remain on the formulary for use on the advice of the palliative care team - TLS blue.

Action:
1. None - to remain of formulary TLS blue

c. Alteplase and Dornase Alfa

The NDR was submitted for discussion on the 26th February. The group accepted the use of these for the treatment of infected pleural collections, however clarification was required regarding the funding. Dornase alfa is PbR excluded, and NHS England commissions in line with the national Cystic Fibrosis policy. TW has confirmed to NB via email that the off license use of a PbR excluded drug was still accounted for as a PbR excluded drug. The use of Alteplase also attracts an additional tariff of £830.00. The financial approval for the use of these drugs will therefore need to be agreed by the individual CCGs boards and a business case will need to be submitted including a population based indication of the number of patients per year. Horizon scanning has not been undertaken for PbR excluded non-NICE, Non SCG budget for 2013-2014, therefore individual CCGs will need to agree in year funding. To ensure conformity on the business cases submitted to the three CCG boards a proforma will need to be developed along the lines of Implementation plan used by the TAG Review group (see New Drug Request process under section 8).

The JFG agreed that in 2013/14 all New Drug Requests should come to the JFG for a clinical decision and then if additional funding was required, i.e. not cost neutral, cost saving or would be funded through the primary care prescribing budget for which the HoMMs were budget holders, then a decision will be required from the individual CCG boards.

Action:
1. SBe to develop proforma along the lines of the NICE Implementation Plan currently used by the TAG Review Group
2. Proforma to be submitted to CCG Boards for financial approval for the use of Alteplase and Dornase Alfa
3. NB/SBe/TW to liaise with the applicant

d. Suboxone

The JFG on the 26th February had rejected this application but invited further submission of evidence and information - the JFG meeting was not quorate at this stage.
An email from TW, Consultant AWP, has since been forwarded to NB. He had confirmed that suboxone would not be used routinely, and also expressed concerned over the cost of suboxone, but did not define a cohort of patients for whom this drug would be used. The BNSSG Controlled Drug Local Intelligence Network (LIN) had not identified diversion of buprenorphine as a problem. The group believed that if the client is at risk of diversion then they should be receiving supervised consumption and not being given a supply of the medication.

The JFG was also informed that the applicant, FL, had now left AWP.

There would be a significant cost associated with the use of this drug. There are no RCTs that show that Suboxone is superior to buprenorphine or methadone in terms of efficacy or diversion. There is a lack of UK based data.

Suboxone is now on the AWP formulary and its use is to be reviewed in 12 months.

The JFG felt that the lack of evidence and the significant increase in cost associated with suboxone made it unsuitable for adding to the BNSSG formulary currently. The JFG would reconsider its use if AWP could define a specific cohort of patients and after they have more experience of its use.

**Action:**

1. BS to inform AWP
2. Use of suboxone at AWP to be reviewed in 12 months

e. E decisions from 26th February – For information

**Doublebase Dayleve gel** - NB had received a comment questioning the need for another emollient on the formulary. The JFG however agreed that the use of emollients was very patient focussed, the application was essentially cost neutral and the emollient section of the joint formulary needs to be reviewed with the help of dermatology nurses. The JFG agreed to add Doublebase Dayleve gel to the formulary.

**Action:**

1. NB to inform applicant and add Doublebase Dayleve gel to the formulary TLS Green

**Ranolazine** - no comments had been received by NB. The JFG therefore agreed for ranolazine to be added to the formulary for NBT as well as UHB,TLS Red.

**Action:**

1. TW to inform applicant and add Ranolazine to the formulary for NBT TLS Red

**Hizentra** - no comments had been received by NB. This drug will be funded by specialised commissioning from April 13. The JFG agreed for Hizentra to be added to the formulary TLS Red with a note that it is funded by specialised commissioning.

**Action:**

1. NB to inform applicant and add Hizentra to the formulary TLS Red

f. Fingolimod for patients not meeting the NICE TA 254 criteria

Specialised commissioning will honour any funding arrangements agreed before the 1st April.
2013 for individual patients within this cohort.

SM had been in email contact with Lynne Richie - Specialised Commissioning Pharmacist for the Wessex Area Team (AT). The Wessex AT will be managing individual funding requests (IFR) on behalf of the BNSSSG AT. LR had confirmed that they would not be considering cohorts of patients as the IFR process was about individuality. Cohorts would need to be considered by the Clinical Reference Groups and the Clinical Senates. A Neurology Clinical Reference Group in Bristol is planned to be set up soon. If more than 5 IFRs are received for the use of the same drug then this would trigger a review.

**Action:**
1. SM to email Dr Cotterell and to send him the link to the IFR forms which will need to be submitted.

g. Aflibercept
This application had been rejected at the 26th February 2013 as no evidence had been submitted on the sequential use of aflibercept following ranabizumab (Lucentis).

NB had recently received an email detailing further evidence about the sequential use of aflibercept. The JFG agreed that in order to be able to make a fully informed decision that this evidence needed to be reviewed and appraised by the clinical effectiveness pharmacist / public health colleagues and to be brought back to the next meeting. Funding of this drug would need to be agreed as minuted from the JFG meeting on the 26th February 2013 (see below) as Lucentis is funded through the NICE College budget. Following action agreed:
- PH clinical effectiveness review
- Application re-considered by JFG
- If approved by JFG to take to the CCG boards re funding and criteria for usage once Consideration as whether this is a service development is also necessary.

**Action:**
1. NB to add to the next JFG agenda

3. NICE New Technology Appraisals published

It was noted that four new TAs had been published (February - March 13) with 3 positive FADs, and 1 a terminated appraisal. The positive TAs will be added to the joint formulary website within 90 days.

4. New Drug Requests (NDRs)

**Plasmalyte**
Deferred to next meeting - no critical appraisal not submitted

a. Plasmalyte

This application was deferred to the next JFG meeting as no critical appraisal had been submitted.

**Action:**
1. None
5. Specialised Commissioning

a. Update

There is an ongoing need for the JFG to develop a relationship with Specialised Commissioning. Once the SCG pharmacist for the region is in post, this should improve.

Specialised Commissioning has published interim generic policies for direct commissioning effective from the 1st April 2013 - see link below. These policies will be of use (reference source) for commissioning within BNSSG
http://www.england.nhs.uk/ourwork/d-com/policies/

Specialised Commissioning has also updated / add clinical polices and commissioning statements

Action:
1. None

b. Cinryze

A NDR for Cinryze had been discussed and rejected at the JFG, May 2012 on the grounds that there was no evidence supporting its superiority over current agents and its increase in cost. “C1-esterase inhibitor” is on the list of drugs funded by Specialised Commissioning but does not list brands for this group. The JFG agreed that the use of this drug was now outside the remit of this group and the use of Cinryze needed to be agreed with Specialised Commissioning.

Action:
1. NB to email MQ to establish Specialised Commissioning’s position of the use of C1-esterase inhibitor drugs and which brands are commissioned

Post meeting note
Specialised commissioning have now issued a Clinical Commissioning Policy: Treatment of Acute Attacks in Hereditary Angioedema which states the product with the lowest procurement cost should be used unless otherwise clinically indicated (see link below)
http://www.england.nhs.uk/wp-content/uploads/2013/04/b09-p-b.pdf  This policy results in the need for the inclusion of cinryze in the BNSSG formulary as the procurement cost for this drug is potentially less for patients over 65kg than the other drugs.

Action:
1. NB to add Cinryze to the formulary

6. Shared Care Protocols

a. No SCP were discussed at this meeting due to time constraints and would be added to agenda of the next JFG

Action:
7. Joint Formulary Year End report and Compliance to NICE Guidance

Year End Report
NB had produced the draft JFG Year End Report, and this was discussed. Suggested additions to the report:

- Meeting frequency to be increased
- Decisions that require review after 6 / 12 months (as noted in the minutes of the meetings)
- Financial decision making / funding streams - decisions on cost saving, cost neutral, identified funding from acute trusts (PbR) or can be absorbed within the primary care prescribing budget can be agreed at the JFG meetings.

This report needs to be submitted to the individual CCG boards via the quality governance route to establish the remit of the JFG.

2013/14 - to record the type of funding decision - primary care, in tariff, CCG commissioned non NICE PbR excluded drugs.

For the financial year 2014/15 there is a need to undertake horizon scanning for the PbR excluded non-NICE non SCG (see AOB) and ensure that this is incorporated into the commissioning process.

SM to draft paper to go with the year end report to establish / obtain an indication on what information the CCG boards wish to receive e.g. reporting lines, annual report, minutes, involvement of the CSU, financial support for NICE College, CCG commissioned non NICE RbR excluded drugs budget, support for the commissioning round.

Action:
1. NB amend report and re circulate
2. MK to produce spreadsheet to record attendance against organisations
3. SM to draft paper for CCG boards to establish what information they wish to receive

Compliance to NICE Guidance on updating local formularies

The work of the JFG had been compared against the NICE guidance on the developing and updating of local formularies [http://www.nice.org.uk/media/94A/F8/GPG1Guidance.pdf](http://www.nice.org.uk/media/94A/F8/GPG1Guidance.pdf)
Areas indentified that need to be addressed will be reviewed during 2013/14 - Terms of Reference, appeals process, decision criteria, selection criteria.

8. Local Decision Making Process

Local Decision Making / LDM Diagram
The governance around the JFG still needs to be agreed by the CCG boards and how the JFG reports to the boards. The HoMMMs are the prescribing lead for the CCGs and therefore have
the authority to make decisions. It was agreed that the minutes should go to the clinical governance committees of the CCGs for information. North Somerset CCG already receives the minutes from the JFG for information.

The JFG has evolved over the last 18 months and the JFG agreed that this group should now become a stand alone group and not be a sub group of the BNSSG D&TC. This had been discussed at the BNSSG D&TC meeting on the 21st March 2013 but the decision will need to be formally minuted at the next BNSSG D&TC meeting.

CAF - still no decision on how this will be “absorbed” into the new structure(s) but all NDRs will go to the JFG first where there is the expertise to discuss all requests.

Action:
1. NB amend the LDM diagram
2. MK to add decision of the JFG to become a stand alone group to the BNSSG D&TC meeting agenda

Funding Streams

New Drug Requests need to have financial agreement from the correct funding stream before they can be added to the formulary. The JFG agreed the following funding streams available for the funding of formulary drugs.

- In-tariff drugs (i.e. secondary care) - the directorate or division is requested to sign these off.
- Drugs that are funded from the Primary Care prescribing budget and that are cost-neutral are agreed by the Heads of Medicines Management.
- Drugs that are should be funded via the Primary Care prescribing budget but have a significant cost implication should be taken further to the board, or a business case put forward after the JFG clinical approval.
- Drugs that have been approved for use by a NICE Technology appraisal are managed and funded via the NICE TAG group as previously stated.
- Drugs that now are commissioned via NHS England, Specialised Commissioning are not the remit of the JFG from April 2013-2014.
- Drugs that are PbR excluded and non-NICE approved and not commissioned via SCG should now be managed by discussion at the JFG first, and then if there is clinical agreement, a concise summary implementation plan will be written to take to the individual CCG Boards for consideration of financial approval.

New Drug Request (NDR) application process

NB / SBe to update the NDR application process and to include a business case / proforma to be completed for drugs that will need CCG financial approval in 13/14. The proforma to be based on the NICE College Implementation plan.

Criteria for assessment and prioritisation of new drug requests needs to be established and the NHS CB commissioning policy: ethical framework for priority setting and resource allocation should be used as a basis http://www.england.nhs.uk/wp-content/uploads/2013/04/cp-01.pdf

Terms of Reference
NB to update the ToR in light of the discussions / changes in reporting structure and circulate for comment prior to the next meeting

**Action:**
1. NB update ToR and circulate prior to next meeting

### 9. AOB

**Appeals process**
As identified in the review of the JGF against the NICE guidance on developing and updating local formularies an appeals process will need to be developed. An appeal can only be lodged if the applicant believes that the JFG did not follow the agreed process when arriving at a decision. The interim commissioning policy: Individual funding request NHSCB/CP/03 [http://www.england.nhs.uk/wp-content/uploads/2013/04/cp-03.pdf](http://www.england.nhs.uk/wp-content/uploads/2013/04/cp-03.pdf) and the interim commissioning policy: The management of individual funding requests NHSNCB/SOP/02 [http://www.england.nhs.uk/wp-content/uploads/2013/04/cp-04.pdf](http://www.england.nhs.uk/wp-content/uploads/2013/04/cp-04.pdf) should be used as a basis for the BNSSG appeals process.

**Horizon scanning (HS)**
Horizon scanning for 14/15 for CCG commissioned non NICE PbR excluded drugs. The acute trusts will need to be involved in the HS and it will be necessary to establish a mechanism for their engagement / involvement - this could be tied into the NICE College horizon scanning process which starts in the autumn (September / October).

**Additional JFG meetings**
Please note - the additional date for the November meeting is Wednesday 6th November and not Tuesday as stated on the agenda - Wednesday 6th November 10am to 1pm Boardroom South Plaza.

**Change of venues**
Please note - the change in venue for the 14th May and the 10th September meetings from that on the agenda.

**Public Health continued involvement in the JFG**
NB to meet with VH Tuesday 6th April 2013 to update her on progress and to establish the continuing involvement on public health in the JFG.

**Publishing minutes on the website**
The JFG discussed the publication of the minutes on the Joint Formulary website. Concerns were raised that the publication may lead to increased pressure from the Pharma industry when a NDR is rejected. NB has found the minutes from other Medicines Management groups useful in terms of how / why a decision was made. No decision was made by the JFG on the publication of the minutes on the website.
### 2013 Dates for Meetings

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs</th>
<th>Cut off for SCPs</th>
<th>Time</th>
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<tr>
<td>Tuesday 14th May</td>
<td>Additional Date</td>
<td>2nd April</td>
<td>23rd April</td>
<td>10.00 – 13.00 NBT, Southmead Pharmacy Seminar Room</td>
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<td>Tuesday 4th June</td>
<td>30th April</td>
<td>14th May</td>
<td>10.00 – 13.00 NBT, Board Room Trust Headquarters Frenchay</td>
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<tr>
<td>Tuesday 23rd July</td>
<td>Change of date and time</td>
<td>18th June</td>
<td>2nd July</td>
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<td>Tuesday 10th September</td>
<td>Additional Date</td>
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<td>20th August</td>
<td>10.00 – 13.00 NBT Georgian Room, Trust Headquarters, Frenchay</td>
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<td>3rd September</td>
<td>25th September</td>
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<td>Wednesday 6th November</td>
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<td>29th October</td>
<td>19th November</td>
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1. Welcome & Apologies & Declarations of Interest

Present
- Public Health Consultant, Bristol City Council (Chair)
- Interface pharmacist, NHS Bristol CCG
- Interface pharmacist, NHS Bristol CCG
- HoMM, NHS Bristol CCG
- Service Development Manager, NHS Bristol CCG
- Formulary Pharmacist, North Bristol NHS Trust
- HoMM, NHS North Somerset CCG
- HoMM, NHS South Gloucestershire CCG
- Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust Bristol
- Consultant Neurologist and representative from NBT D&TC, North Bristol NHS Trust
- Deputy Chief Pharmacist, Weston Area Health NHS Trust
- Clinical Effectiveness Research Lead, Bristol City Council

Apologies
- GP, North Somerset
- GP, Bristol
- GP, Bristol
- D&TC Chair, North Bristol NHS Trust
- Chief Pharmacist, AWP
- Nurse Prescriber, Bristol
- Formulary Pharmacist, AWP

Declarations of Interest
None

The meeting was not quorate and any decisions will require e approval sign off

2. Minutes from April 2013 Meeting

The minutes from the Joint Formulary Group (JFG) meeting on the 9th April 2013 had been circulated by NB following the meeting and comments requested within 2 weeks.

VH sought clarification on the yearend report 12/13 and what would happen to it i.e. where it was to be sent. The finance part of the report still needed to be amended to reflect that the HoMMs were able to approve drugs that affected the primary care prescribing budget without referral to the CCG boards.

SM (Bristol) would be sending the report to the Financial Governance Committee with a covering paper outlining the remit of the JFG and the financial decisions it would have the delegated authority to make.
MG (South Glos) was taking the report to the Clinical Operations Executive that afternoon (14th May 2014) which is a sub group of the CCG board. As MG was the clinical prescribing lead for South Glos there would be no South Glos GP representative at the JFG meetings however GP input was still necessary in the JF process.

DC (N Somerset) was taking the report to the Quality Assurance Group on Thursday 16th May and then to Clinical Leadership Group.

The minutes were approved.

Matters arising from April 2013 Meeting

a. **Tolvaptan**
   
   On 30th April 2013 the FDA published a warning that Tolvaptan should not be used for longer than 30 days in patients with underlying liver disease because it can cause liver injury, potentially leading to liver transplant or death - see [Safety Alerts for Human Medical Products > Samsca (Tolvaptan): Drug Safety Communication - FDA Limits Duration and Usage Due To Possible Liver Injury Leading to Organ Transplant or Death](https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm351018.htm).

   This warning supports the decision made by the JFG only to approve the use of Tolvaptan for 3 to 10 days. The applicant Dr Karen Bradley, UHBristol was aware of this advice.

   **Action:**
   1. None

b. **Retigabine**
   
   HF also raised that the FDA had issued a [Public Health warning](https://www.fda.gov/Drugs/DrugSafety/ucm350189.htm) for Retigabine stating that it can cause blue skin colouration and eye abnormalities. The manufacturers (GlaxoSmithKline UK) were no longer actively marketing this drug and the decision has been made within the Neurology department at NBT that no new patients would be commenced on this drug.

   Retigabine is currently only on the formulary for those patients in whom their symptoms have not been controlled with other anti-epileptics and only on the recommendation of a specialist, but this should now be changed in accordance with the above. The EMA should be reporting on this shortly.

   **Action:**
   1. e PACT search for prescribing of this drug within the community and refer patients back to secondary care
   2. NB to amend formulary – not to be initiated in any new patients.

   Post meeting note – there was no primary care prescribing of Retigabine within BNSSG in the last 12 months.

3. **NICE New Technology Appraisals published**

   There had been 4 positive TAs published in April 2013 – 2 which affect the CCGs (TA 279 and TA280) and 2 which affect Specialised Commissioning (TA 278 and TA 282)

   **TAs adopted into the BNSSG Joint Formulary (published December 2012)**
   
   TA 268 melanoma (stage III or IV) - ipilimumab
   
   TA 269 Melanoma (BRAF V600 mutation positive, unresectable metastatic) – vemurafenib
4. New Drug Requests (NDRs)

Alteplase and Dornase Alfa – re discussion
Clinically appropriate for inclusion into the formulary decision made 26th Feb 2013. Funding now clarified, await financial approval by NBT directorate and then add to formulary TLS Red cohort has detailed in JFG minutes of the 26th Feb 2013.

Aflibercept – re discussion
NDR rejected 26th Feb 2013. Review of further submitted evidence – still insufficient evidence to support use of Aflibercept refractory to lucentis.

Plasma-lyte 148
Approved NBT Theatres and Critical Care only TLS red

a. Alteplase and Dornase Alfa – re discussion

This application had been discussed on the 26th February 2013 and although the JFG considered the drugs to be clinically appropriate for inclusion in the Formulary funding of these drugs needed to be clarified and approved.

Dornase Alfa is part of a prescribed service (‘The NHS CB commissions the following drugs: dornase, tobramycin, colistimethate sodium, aztreonam lysine in line with the national CF Commissioning Policy.’) and paid for by Specialised Commissioning in year (2013/14) on the 80/20 split (if 80% of the drug is used as part of a prescribed service then SCG will pay for all the drug use.)

For 2013/14 Alteplase is now part of the stroke best practice tariff and is no longer PbR excluded for any other indications. Thus, this drug is in tariff for empyema admissions and there are HRG codes to cover its use e.g. ‘installation of substance into the intra pleural cavity.’

There is no Specialised Commissioning policy relating to the use of these drugs in this indication. If a policy is published in the future, and there was a decision not to fund these drugs for this indication then it would be necessary to decommission them / remove from formulary.

There is no financial risk to the CCGs in 2013/14 (see under Specialised Commissioning notes re 14/15 financial risk to the CCGs).

The JFG agreed to add to the Formulary for 13/14 once financial approval had been clarified / approved from NBT directorate. 14/15 – if the financial risk passes to the CCG then this decision will need to be reconsidered.

Action:
1. TW to confirm directorate sign off for the funding of these drugs.
2. NB to add to formulary once NBT approval obtained TLS Red for use as defined in the minutes of the JFG meeting 26th February 2013.

b. Aflibercept – re discussion

This application had been discussed at the JFG meeting on the 26th February 2013 when further information was requested on the sequential use of aflibercept following lucentis. This
had been submitted just before the JFG meeting on the 9th April 2013. The JFG had agreed that in order to be able to make a fully informed decision that this evidence needed to be reviewed and appraised by the clinical effectiveness pharmacist / public health colleagues and to be brought back to the next meeting (14th May 2013).

CM had reviewed the evidence and submitted a paper for this meeting. In the Clear IT-1 and 2 trials, none of the patients had received or failed lucentis and so this data could be discounted as it was not relevant for this indication. In terms of the other evidence submitted, they were almost exclusively retrospective case series and these series had all been reported in abstracts from one conference in 2012. Most series involved very short follow up (typically one month) and reported results after one injection only. Whilst overall improvements in some series were reported to be statistically significant, the clinical significance and impact on patients of any of these changes was unclear. Long term impact and effect of further treatment (either regular or on demand) is uncertain: maintenance of any initial response may not be sustained. There had been no peer review of the studies.

Further clarification on these issues had been sought by SBe, and an email had been received from the applicant, AR. The number of patients in the application was greater than the NICE costing template for lucentis for wet AMD but AR confirmed that this was only an estimate. There was some discussion around the term non-responders and how it would be better to classify these patients as frequent retreaters, rebounders, increasing exudation, and true non responders. He also confirmed that treatment would be stopped in accordance to NICE / RCOphth College guidance i.e. when vision falls below visual threshold for treatment or when there is permanent structural damage or fibrosis.


The NETAG group noted an emerging evidence base demonstrating the efficacy of aflibercept in AMD cases refractory to aVEGF therapies such as bevacizumab and ranibizumab. However the group considered this evidence to be of low quality and insufficient to confirm efficacy and safety in this patient group.

The JFG concluded that the use of aflibercept refractory to lucentis was not clinically appropriate as there is insufficient evidence to support its use. The JFG would reconsider the application if further evidence was submitted but this evidence must be prospective, longer term and have undergone peer review.

Action:
1. KG to inform applicant

c. Plasma-lyte 148

This application was submitted by Dr MT, Consultant Anaesthetist, NBT Critical Care and was presented to the JFG by AP Specialist ITU pharmacist.

For full details please see application form.

This request was for the inclusion of Plasma-lyte 148 as an IV fluid replacement. The rationale behind using Plasma-lyte 148 is to decrease the risk associated with the use of chloride based
IV solutions. The use of unbalanced chloride rich solutions is associated with increased acute kidney injury (AKI) and the need for renal replacement therapy (RRT). Plasma-lyte 148 is a balanced solution and is more appropriate for fluid resuscitation and can be used in patients with neurological injury. It contains more sodium than Hartmann's solution but less than sodium chloride.

Trials have occurred in Australia involving switching from sodium chloride 0.9% solutions to plasma-lyte 148. There are also other centres in the UK (London, Liverpool and Medway) who routinely use plasma-lyte 148.

Current practice within NBT is to use Hartmanns solution as the first IV bag for fluid resuscitation - they had moved away from sodium chloride about half way through 2012/13 due to the evidence that a chloride restrictive policy of fluid resuscitation may be beneficial to patients.

Plasma-lyte 148 is slightly more expensive than existing solutions. The manufacturer, Baxter, will price match the cost of Hartmanns but after 12 months the cost will rise by 20 – 30p a bag. If all NaCl bags used were changed to Plasma-lyte 148, there would be an increase annual spend of around £900, however in reality, it would be lower than this, as some patients would need to be continued with sodium chloride. After the price matching has finished, if all bags were continued to be plasma-lyte 148 there would be an additional annual spend of around £800.00. It is difficult to estimate a cost associated with the change due to the fact that NBT changed their fluid resus policy mid way through 2012-2013. It would be down to individual Consultant choice and patient needs as to what fluid is chosen, but would certainly be of use in neurological patients in place of Hartmanns.

There is a risk management issue that needs to be addressed in that there is a lack of compatibility data with drugs. Sodium chloride and dextrose will continue to be the preferred diluent for iv medications. There are also reports of false positive tests for aspergillus in some patients given plasma-lyte 148, and this will need to be discussed with micro.

The drug is in tariff.

UHB and Weston are not considering the use of plasma-lyte 148.

The JFG considered that the use of plasma-lyte 148 was clinically appropriate and should be included into the Formulary TLS Red, NBT only. Funding approval from NBT is required before it can be added to the website

**Action:**
1. **TW to confirm directorate sign off for the funding of these drugs.**
2. **NB to add to formulary once NBT approval obtained TLS Red.**

**NBT – await Directorate sign off re funding**
**UBT – NA**
**Weston – NA**
**Primary Care - NA**

5. **Shared Care Protocols**
a. Gentamicin via nebuliser (UHB/NBT) - management of chronic respiratory infections / colonisation (not including cystic fibrosis patients)

Shared care protocols (amber 3 months) had been agreed for the management of chronic respiratory infections / colonisation (not including cystic fibrosis patients) for colistimethate sodium (Oct 12) and tobramycin (Dec 12).

Comments had been received by CR (GP) prior to the meeting. These other SCPs were amber 3 months and this request for gentamicin was for amber 1 month. In the Duration of treatment section, it states a three month trial and the JFG agreed that, if approved, the SCP should be amber 3 months.

The use of Gentamicin via nebuliser is an unlicensed use of this drug and this needs to be reflected in the SCP, which is stated in Section 2, Route and Formulation.

The length of treatment needs to be clarified – e.g. is this long term, until secondary care say otherwise?

Section 3 needs amending slightly:

- Frequency of normal follow up
- If the eGFR is declining then the patient should remain under the care of the secondary care consultant until it stabilises.
- Periodic audiometry in patients at high risk of ototoxicity should be undertaken and managed by secondary care.

There are only a few patients in the community receiving this care and therefore GPs clinical knowledge will be limited. In order to in some way address this, a pathway detailing the use of antibiotics in patients with bronchiectasis needs to be developed before this SCP can be approved. The use of home care delivery was suggested – secondary care to look into the possibility of doing this.

SCP approved subject to amendments and the development of the pathway

**Action:**
1. NB to feedback to author
2. Secondary Care to investigate if this drug can be delivered via home care
3. Pathway to be produced to reflect the use of antibiotics in patients with bronchiectasis prior to SCP being published on the website

b. Mycophenolate and TLS change request from Red to Amber

An application had been received for a change in TLS status for mycophenolate from Red to Amber 3 months for conditions that require immune suppression (not for prevention of organ transplant.)

The use of this drug is unlicensed but its use is accepted practice. Mycophenolate is licensed of acute renal, cardiac or hepatic transplant rejection (in combination with ciclosporin and corticosteroids) under specialist supervision. The SCP has been written to cover 5 specialities. The specialities have agreed to common monitoring advice and FBC cut offs in line with those agreed by rheumatology. The author is also now liaising with the renal department to be
The reason for the application is to attempt to clarify the monthly monitoring of FBC’s and LFT’s – the majority being carried out by the GP with prescribing via the Trusts. Clinical responsibility lies with the prescriber. We are aware that the issue of blood monitoring of many of the DMARDs is a complicated one and that it is necessary to come to a solution. Currently, the monitoring of some of the DMARDs is covered by a Direct Enhanced Service (DES) which is adapted by the local community to form a Local Enhanced Service (LES). Under the LES the GPs are paid to undertake the monitoring of the DMARDs and it has been suggested that GPs would not undertake the monitoring and prescribing of mycophenolate without payment. There is a concern that these drugs and drugs not covered by the LES but still requiring monitoring are properly being monitored. It is necessary to clarify who will take the blood and who’s responsibility it is to review the results. Robust process around monthly monitoring will be necessary if mycophenolate is to become amber 3 months.

The need for monthly monitoring after 12 months on the drug was questioned with a suggestion that they could go to 3 monthly monitoring.

DC to take to the North Somerset Clinical Leadership Group to obtain a view on this application and how different mycophenolate is from methotrexate and azathioprine which are already monitored primary care.

Prior to the meeting, comments from a GP had been obtained. It was stated that there was not much experience of this drug in primary care. Also, a clause that is written in the azathioprine and methotrexate SCPs around monitoring should be added. And, it was felt that this could not be accepted as amber until it appeared on the LES alongside the other DMARDs and thus the GP would get payment for the additional work.

The JFG could not agree to the change from Red to Amber 3 months as greater understanding of how monitoring in the community would be undertaken and if payment would be necessary by GPs to undertake this monitoring and prescribing.

**Action:**

1. NB to feedback to author and to bring back to next meeting

6. Specialised Commissioning

a. Update

TW had been appointed to the role of pharmacist within the Local Area Team / Specialised Commissioning and would start on the 22nd July 2013. She will be based in South Plaza.

Financial risk to the CCGs – the 80/20 split for drugs will only apply in year (13/14). From April 2014, Specialised Commissioning will expect the Acute Trusts to invoice according to indication. Therefore, in terms of Alteplase and Dornase Alfa NDR, Dornase Alfa will not be funded by Specialised Commissioning for empyema admissions and the cost will fall to the CCGs from April 2014. This principle will also be applied to Individual Funding Requests (IFRs) that have been approved by SCG on the 80/20 split during 2013/14. Form April 2014, IFRs will have to be funded by CCGs from April 2014 if the indication is commissioned by the CCGs and not the SCG.
IFR requests from GPs are filtered by the CSU into CCGs or Specialised Commissioning and thus it would be possible to know what requests have been sent to Specialised Commissioning. However, the Acute Trusts send IFRs directly to the Wessex Area Team who deal with all IFRs on behalf of the Area Teams in the South West and therefore the number that maybe CCG commissioned from April 14 will be unknown.

In terms of IFRs there is a governance risk in year and a financial risk next year – HoMMs to consider if this should be added to the CCGs risk registers.

There will be no prior approval within the SCG.

Cancer Drugs Fund – there is no clinical governance screen of the application made to the CDF, the Acute Trusts apply directly using the Bluetech system.

Infliximab for pulmonary sarcoidosis – this is not commissioned by SCG currently however from April 2014 it will be commissioned by the SCG as it will be indication based and pulmonary sarcoidosis will be a prescribed service. The Clinical Reference Group (CRG) are developing a commissioning policy on this condition. A specialist pharmacist will now be part of each CRG whose decision / policies involves drugs. Chairs of the CRG – TW to circulate list.

Specialist Centres – a specification will be published in October 2013 and Acute Trust purporting to be a Specialist Centre will need to meet this specification and if they do not they cannot be classified as a Specialist Centre.

Rituximab (adult dermatology and rheumatology) is commissioned by the CCG where all other uses are SCG. Cytokine modulators (for paediatric use) are commissioned by the SCG where all other uses are CCG. These are the only to drugs where the commissioning is split between the two organisations (2013/14 only).

Clare Howard is continuing to lead on Medicines Optimisation for SCG.

Newly licensed drugs – within one month of the drug obtaining a licensed, the SCG will either make a commissioning decision / policy or an interim policy will be published.

Repatriation of drugs – still needs to be undertaken.

Block contracts – there are still block contracts e.g. HIV at NBT

Embedded pharmacist – SCG to fund pharmacist post within Hospitals (UHB only within the South West) to look for potential areas of cost savings / gain sharing and audit the use of SCG drugs.

**Action:**
1. TW to circulate notes and the names of the CRG chairs.

7. **Formulary Process**

   a. **BNSSG JFG Terms of Reference**
      There was insufficient time at the meeting to review the Terms of Reference
Action:
1. JFG to send feedback to NB

b. NDR Decision Pathway (for finance approval)
SM had developed a decision pathway to help the CCG’s financial committees to understand the funding routes for NDR and the need for the HoMMs to become the budget holders of the non-NICE, CCG commissioned, PbR excluded drugs budget. This process diagram does not give the full NDR process as this is not necessary for the CCG finance committees. Clarification was given on the process and amendments made.
Action:
1. MK to revise pathway and circulate with minutes

c. NDR Application Process
There was insufficient time at the meeting to review the NDR application process
Action:
1. JFG to send feedback to NB

d. NDR Appeals Process
There was insufficient time at the meeting to review this NDR Appeals process
Action:
1. JFG to send feedback to NB

e. CCG Funding request proforma
SBe had developed a proforma for submission to the CCGs financial committees in year (13/14) when additional funding is needed for a clinically appropriate drug to be added to the Formulary. From 2014, this proforma should not be necessary as the JFG will have undertaken horizon scanning for drugs which will be licensed in 2014/15 or for non-formulary drugs which are already licenced but which clinicians wish to be added to the formulary. The proforma covers the JFG decision for the inclusion of the drug into the Formulary, the patient cohort, prescribing responsibility, the financial implications and the summary of funding recommendation. SBe had road tested this proforma using the Alteplase and Dornase Alpha NDR. This completed form had not been circulated prior to this meeting as SBe was awaiting finance confirmation re the HRG coding. The circumstances in which this form is to used will depend on the level of delegated authority the CCGs board give the HoMMs in terms of the non-NICE, CCG commissioned, PbR excluded drugs budget e.g. would it be necessary to submit the proforma is the financial implications is less than 10K across BNSSG.
Action:
1. NB / SBe to circulated proforma for feedback by the JFG.

8. Items for discussion

a. Tolterodine approved as Formulary first line
Tolterodine now has the lowest acquisitions costs for the over active bladder drugs and is now first line on the Formulary.
Action:
1. None

b. UHB Cystic Fibrosis multivitamin drugs
UHB had raised the issue that they prescribed these vitamins but this had not been picked up in the gap analysis or when chapter 9.6 was reviewed. The treatment of cystic fibrosis is a prescribed service and paid for by Specialised Commissioning but it expected that GPs will prescribe non specialist drugs. A decision will be needed by the JFG as to whether a NDR is
required for this.

**Action:**
1. NB to added to the next meeting agenda

c. **UHB Eye Hospital**
   NB had been in contact with the Eye Hospital re the current treatments on the Formulary. There are five treatments that will need a NDR to be submitted for inclusion into the Formulary. However, they had also identified 17 treatments which are either historical drugs or new formulations of the current drugs that are stocked by pharmacy but which were not on the Formulary. A decision by the JFG will be needed on how this is taken forward.

**Action:**
1. NB to add to next meeting agenda

d. **Extend Formulary to allow UHB to prescribe Pivmecillinam**
   UHB microbiologists had requested that Pivmecillinam could be on the Formulary for UHB as well as NBT. As this request had NBT microbiology approval and been through the NDR application process within NBT, the JFG agreed to the change to the Formulary.

**Action:**
1. NB to update website to reflect usage at UHB

e. **NBT switch from cephradine (cefradine) to cephalexin**
   Cephalexin cost less than cephradine and this switch was part of the NBT CRES savings. This switch had been approved by microbiology. As this request had microbiology approval, the JFG agreed to the change to the Formulary.

**Action:**
1. NB to update website

9. **AOB**

   None
## 2013 Dates for Meetings

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<th>Date</th>
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<th>Cut off for SCPs</th>
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<td>14th May</td>
<td>10.00 – 13.00</td>
<td>NBT, Board Room Trust Headquarters Frenchay</td>
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<tr>
<td>Tuesday 23rd July</td>
<td>Change of date and time</td>
<td>18th June</td>
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<td>Tuesday 10th September</td>
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<td>Tuesday 15th October</td>
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<td>Wednesday 6th November</td>
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<td>Tuesday 10th December</td>
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<td>19th November</td>
<td>10.00 – 13.00</td>
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1. Welcome & Apologies & Declarations of Interest

Present
- Interface pharmacist, NHS Bristol CCG
- Interface pharmacist, NHS Bristol CCG
- HoMM, NHS Bristol CCG (Chair)
- Service Development Manager, NHS Bristol CCG
- HoMM, NHS North Somerset CCG
- Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust Bristol
- Consultant Neurologist and representative from NBT D&TC, North Bristol NHS Trust
- Formulary Pharmacist, North Bristol NHS Trust
- GP, North Somerset
- Rotational Pharmacist North Bristol NHS Trust

Apologies
- GP, Bristol
- GP, Bristol
- Joint D&TC Chair, North Bristol NHS Trust
- Joint D&TC Chair, North Bristol NHS Trust
- Chief Pharmacist, AWP
- Formulary Pharmacist, AWP
- Nurse Prescriber, Bristol
- Deputy Chief Pharmacist, Weston Area Health NHS Trust
- Clinical Effectiveness Research Lead, Bristol City Council
- Public Health Consultant, Bristol City Council
- HoMM, NHS South Gloucestershire CCG

Declarations of Interest

None

The meeting was quorate

2. Minutes from 14th May 2013 Meeting

The minutes from the Joint Formulary Group (JFG) meeting on the 14th May 2013 had been circulated by NB following the meeting. HF and TW were both present at the meeting and the attendance was amended to reflect this.

The minutes were approved and the decisions made at this meeting approved.
Matters arising from April 2013 Meeting

a. Retigabine and FDA warning

The FDA warning on Retigabine had been brought to the attention of the JFG at the last meeting. An ePACT search had shown no primary care prescribing within BNSSG in the last 12 months and within NBT the prescribing of this drug is restricted to 3 consultants. NB to add “for existing patients only” to formulary.

Action:
1. NB to update formulary website

Post meeting note and action: In light of this warning and that no patients are currently receiving prescriptions for retigabine from primary care, to consider changing the TLS status of Retigabine to Red. NB to liaise and consult with NBT Neurology.

b. Alteplase and Dornase Alpha NDR

Still awaiting financial sign off from NBT.

Action:
1. NBT to inform NB of funding agreement

c. Oxybutynin

At the last meeting it had been agreed to remove this drug from the formulary and replace it with tolterodine. Feedback had been received by NB from NBT that there was still a place on the formulary for this drug (neurology and paediatric enuresis clinic). The JFG agreed to add oxybutynin back onto the formulary second line TLS blue.

Action:
1. NB to update formulary website

d. Mycophenolate

Feedback from primary care was not supportive over the change from TLS red to amber. Primary care are not familiar with prescribing this drug and the indications for which the SCP relate to are all unlicensed, although all recognised uses. However, it was noted that how would primary care gain familiarity if the drug remains red?

The issue around blood testing (near patient testing) and the cost to primary care is not isolated just to mycophenolate. The Bristol audit of the Near Patient Testing LES shows variation across Bristol in terms of the blood monitoring undertaken and it was stated that this is probably reflected in secondary care as well. There may be cost savings if the monitoring is moved from secondary care to primary care and this could be used to fund GPs / use to establish a monitoring service.

The whole structure/process of blood monitoring related to these drugs needs to be reviewed. Currently it should be the responsibility of whoever is prescribing the drug to ensure that the bloods are taken and monitored, although it is known that individual variations exist. We are
aware that the current situation does not appear to be working and that there can be confusion as to whose responsibility it is to take and monitor bloods, which is why SCPs have been written, however there are issues around knowledge and safety of prescribing and the costs involved. It may well be advantageous for patients to attend for blood monitoring at the GP surgery as it is closer to home, but we need to ensure that whoever is monitoring the results are appropriate to do so.

Possible solutions include the possibility of establishing a primary care phlebotomy service or a secondary care long term conditions monitoring clinic.

**Action:**
1. SM / DC / MG to put together proposal re blood monitoring
2. NB to review formulary to check that all uses of this drug are included
3. MK to get BNSSG e PACT data on the prescribing of mycophenolate

### 3. NICE New Technology Appraisals published

There had been 4 positive TAs published in April 2013

2 affect the CCGs
- TA279 Vertebral fractures - vertebroplasty and kyphoplasty
- TA280 Rheumatoid arthritis - abatacept (2nd line) (rapid review of TA234)

2 affect Specialised Commissioning
- TA278 Asthma (severe, persistent, patients aged 6+, adults) - omalizumab (rev TA133, TA201)
- TA282 Idiopathic pulmonary fibrosis - pirfenidone

There was one terminated appraisal
- TA281 Gout - canakinumab (terminated appraisal)

**TAs adopted into the BNSSG Joint Formulary May 2013**
- TA274 Macular oedema (diabetic) – ranibizumab
- TA275 Stroke and systemic embolism (prevention, non-valvular atrial fibrillation) - apixaban

### 4. New Drug Requests (NDRs)

**Insulin Degludec (Tesiba®)**
- Clinically appropriate for inclusion into the formulary

**Lixisenatide (Lyxumia®)**
- Decision deferred awaiting public health appraisal of newly published trial data
Decision Criteria used by JFG for NDR

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

a. Insulin Degludec

This application was submitted by VR Specialist Pharmacist NBT and was presented by TW. This application was supported by Dr FC and PB.

Please see application form for full details

Insulin degludec would be used for the treatment of Type 1 diabetes mellitus in adults for a niche cohort of patients - those patients with poor control on current bolus insulin regimen, with problems with recurrent or severe hypoglycaemia especially nocturnal hypoglycaemia. The advantage of Degludec is reduced hypoglycaemia, lower doses of insulin required and reduced cost associated by not using continuous pump therapy. The reduction in hypoglycaemia will potentially lead to a reduction in admissions for hypoglycaemias, improved quality of life, and improved blood glucose control. It has a terminal half life of over 25 hours, which is twice that of insulin glargine. The disadvantage of the use of degludec is the cost of the drug compared with other basal analogues £72 compared with £42 for Levemir® and £41.50 for Lantus® for the same volume.

Insulin pump therapy is covered a NICE TA (TA 151\(^1\)) and is funded through the NICE College. The use of insulin pump therapy is evidence based. If Insulin degludec is added to the formulary, the number of patients on insulin pump therapy would decrease.

It has been estimate that by using Degludec in Type 1 patients, this could increase the annual costs by around £9000.00 across BNSSG.

The estimated number of patients in primary care is 20 – 25 and in secondary care is 10 – 15 across BNSSG and the application was for TLS status Amber 1 month.

The NICE evidence summary (ESMNS\(^2\)) had shown that evidence from an open-label randomised controlled trial in 629 adults with type 1 diabetes indicated that insulin degludec is non-inferior to insulin glargine in terms of glycaemic control: both basal insulins reduced glycated haemoglobin (HbA1c) levels to a similar degree.

The SMC rejected this drug because the manufacturer had not submitted a sufficiently robust economic analysis to gain acceptance by the SMC.

\(^1\) [http://guidance.nice.org.uk/ta151](http://guidance.nice.org.uk/ta151)

\(^2\) [http://www.nice.org.uk/mpc/evidencesummariesnewmedicines/ESNM5.jsp](http://www.nice.org.uk/mpc/evidencesummariesnewmedicines/ESNM5.jsp)
The Midlands Therapeutic Review and Advisory Committee\(^3\) has issued commissioning guidance on degludec. The evidence for the efficacy of insulin degludec was considered to be relatively weak but was suitable for restricted prescribing under defined conditions. In three short-term trials, insulin degludec was shown to be non-inferior to insulin glargine in adults with type 1 and type 2 diabetes. Insulin degludec has a lower place in therapy because there was no data comparing insulin degludec with NPH insulin, it has a greater cost and insufficient evidence of a substantial clinical advantage over insulin glargine. They also highlighted the recent MRHA safety warning over the availability of degludec at 200 units/mL giving rise to the potential of medication error.

The incidence of nocturnal hypoglycaemia, a secondary end point was significantly lower in patients given insulin degludec than insulin glargine in both the BEGIN T1 trials. In the BEGIN BBT1 trial, incidences were 72\% vs 74\% for degludec vs glargine (p = 0.021), resulting in about 1.5 fewer episodes per patient per year of exposure. This could be considered small and does this actually translate into any improvement in the quality of life.

Degludec comes in pre-filled pens and the dial up is in units so theoretically patients should not administer incorrect doses.

The JFG considered the application and the evidence in the critical appraisal. In terms of effectiveness, it has been shown that degludec is non-inferior to insulin glargine in terms of glycaemic control and that nocturnal hypoglycaemia was reduced (a small but statistically significant reduction). It is considerably more expensive than insulin glargine. The applicant has suggested restricted cohorts in order to restrict prescribing to those likely to benefit most. The drug is in tariff. The JFG agreed to add degludec to the formulary but due to the lack of strong evidence and its cost, only for patients who had failed on insulin glargine and were not suitable/had failed on insulin pump therapy, TLS Red.

**Action:**
1. TW to inform applicant of need to adjust numbers as the drug would only be used in secondary care
2. NB to add to formulary once funding sign off agreed

**b. Lixisenatide**

This application was submitted by Physician at Weston Hospital and was presented by NB and SB.

For full details please see application form.

The application was for the inclusion of lixisenatide for the treatment of type 2 diabetes to achieve glycaemic control in combination with oral glucose lowering medicinal products and/or basal insulin.

\(^3\) [http://www.keele.ac.uk/media/keeleuniversity/fachealth/fachealthsop/mtrac/documents/summary/Degludec%20sum%20final.pdf](http://www.keele.ac.uk/media/keeleuniversity/fachealth/fachealthsop/mtrac/documents/summary/Degludec%20sum%20final.pdf)
At the time of undertaking the critical appraisal for this NDR, the main studies relating to this drug had not been published in full and were only available as abstracts.

NICE had published an Evidence summary ESNM104 Type 2 diabetes: Lixisenatide in January 2013. Assessing the likely place in therapy of lixisenatide was difficult because limited clinical evidence has been published in full. NICE have stated that they will update the evidence summary once the trials have been published. Current NICE guidance on the two currently licensed GLP-1 does not include monotherapy or their use with insulin.

GetGoal-Mono does not provide evidence relevant to the proposed licensed indication for lixisenatide as this was a trial comparing lixisenatide as monotherapy. The GetGoal-L-Asia provides some evidence as it evaluated lixisenatide in combination with basal insulin with or without a sulfonylurea, but there are questions over its relevance to the UK population.

VR had sent in her comments regarding Lixisenatide. Currently she felt that Lixisenatide did not offer any advantage over the GLP-1 agonists already on the formulary. The UHB specialists’ opinions were also sought and they stated that the addition to the formulary of lixisenatide would not make an impact on prescribing practice, as it offers no additional benefit over and above existing drugs and therefore was a ‘me-too’ drug.

There may be a cost-benefit by using lixisenatide as it is priced cheaper than both liraglutide and exenatide.

The additional phase III trials have now been published and therefore the JFG agreed to defer the decision on this NDR until an appraisal by public health on the new evidence by public health had been undertaken.

**Action:**
1. NB to liaise with public health re appraisal of new evidence and to bring back to next meeting – July.

5. **Shared Care Protocols**

a. **Lithium AWP – update of out of date SCP**
This was an update of the current SCP which had been published in 2009. Alterations that are required:

- There needs to be clarity in the SCP around if the patients go back to AWP for their annual review or if they are discharged from AWP service.
- Also, clarity is needed on reducing the dose of lithium in an established patient.
- Section 11: Responsibilities for community pharmacist to be removed as this SCP is not seen by community pharmacies. AWP would need to highlight these responsibilities directly to community pharmacies.

Action:
1. NB to feedback to author and upload amended SCP to website

b. Blood monitoring and amber drugs
   See under Matters Arising Mycophenolate
   Action:
   1. None

6. Specialised Commissioning Statements
   a. Inhaled therapy for Adults and Children with Cystic Fibrosis - Aztreonam

      Aztreonam to be added to formulary third line in accordance with the National Commissioning Policy.
      Action:
      1. NB to add to formulary

7. MHRA Drug Safety Update

   The JFG agreed that this meeting was the correct forum for discussing these updates and therefore this will now be a standing agenda item.

   Insulin degludec – see under NDR
   Cilostazol – non formulary no action necessary

   Strontium ranelate - now restricted to patients with severe osteoporosis, in postmenopausal women at high risk of fracture and in men at increased risk of fracture. It should not be used in patients with ischaemic heart disease, peripheral arterial disease, cerebrovascular disease, a history of these conditions, or in patients with uncontrolled hypertension. Patients on this drug should be reviewed by their prescriber (at a routine appointment) to consider whether or not to continue treatment. It would be expected that the patient had tried two bisphosphonates before being prescribed strontium.

   Action:
   1. NB to obtain BNSSG ePACT data on prescribing of this drug.
   2. NB to amend the formulary and link to the MHRA drug safety update

8. Formulary Process
   a. BNSSG JFG Terms of Reference

      NB had received comments on the ToR and amended them to reflect these.

      The remit of the JFG was to make decisions on behalf of their respective organisations e.g. HoMMS for the CCGs or representation from the acute Trusts D&TCs/MAGs.

      DC had taken the JFG annual report to the North Somerset CCG board and they had agreed that the PbR excluded, non-NICE, CCG commissioned budget should be the responsibility of the JFG. The NS Director of Finance to speak to DoFs of Bristol and South Glos.
If there is a clinical need, in year, to fund a drug and there is no budget, it is the responsibility of the CCG board to make the decision re the financial risk.

Under section 1 Purpose it was agreed that 1d the management of PbR excluded, non-NICE, CCG commissioned budget was not the remit of the JFG.

NB to update ToR and to add horizon scanning including primary care NICE TA drugs. ToR to be sent to the appropriate CCG committees for information.

Action:
1. NB to update and circulate

b. NDR Decision Pathway (for finance approval)
Comments had been received and the pathway amended

Action:
1. NB to circulate pathway with minutes

c. NDR Application Process
The NDR form draws out the reasons why the drug will be used and also means that the applicant should not have to complete an additional form should there be no identified budget.

NB is also drafting a letter to be sent on behalf of the JFG Chair to the applicants once a decision has been made.

Further amendments to the formatting are necessary before this form is uploaded to the website.

Action:
1. NB to upload NDR when complete

d. NDR Appeals Process
The JFG agreed that the JFG Review Panel should include a CCG clinical lead /clinical governance lead who would act as chair and the other two members of the panel would consist of 2 out of the 3 other members listed below and include one representative of the submitting organisation:

- Medicines Management Pharmacist (Bristol South Gloucestershire or North Somerset)
- Director of Pharmacy (UHB, NBT, WAHT)
- GP/Secondary care consultant

The frequency of meeting to be amended to 28 days

Action:
1. SBe to amend draft document
2. KG to send amended process to UHB clinical effectiveness committee for information

9. Items for discussion

a. UHB Eye Hospital – review of chapter
This had been brought forward from the last JFG meeting. The Eye Hospital had identified 17 treatments not currently on the formulary which were either historical drugs or new formulations of current drugs. A review of chapter 11 will allow these drugs to be considered for inclusion in the formulary.

A review of Chapter 11 would also address the issue of the use of eye drops in the treatment of hay fever.

Action:
1. KG (UHB) to coordinate review of chapter 11

b. Natamycin Eye Drops

Natamycin is unlicensed in the UK (licensed in the USA) and can be used to treat fungal keratitis. Currently UHB use voriconazole and they make the eye preparation in house, as there is no eye preparation commercially available. UHB microbiology are recommending the use of natamyicin instead of voriconazole in a small cohort of 5 to 10 patients. There was discussion as to whether this would be the remit of Specialised Commissioning or not – this is very specialised eye conditions, but the drug itself does not appear on the PbR excluded list. If it is concluded that this is CCG commissioned, then a NDR will be needed before this can be routinely prescribed.

Action:
1. NB to forward email to TW to establish if this is Specialised Commissioning

c. CAF Policies and BNSSG Formulary

SBe had undertaken an analysis of CAF policies against the BNSSG formulary and anomalies had be noted. SBe had tried to contact Individual Funding Manager South West Commissioning Unit, to discuss. Criteria based access policies also need to be added to the formulary.

Action:
1. SBe to follow up with Niall Mitchell

d. Licence Extensions and Formulary Process

This had been added to the agenda following the BNSSG D&TC where the updated asthma guidelines had been tabled for approval and now included Fostair MART® which was recently licenced for reliever therapy as well as maintenance therapy.

Symbicort SMART® was already licenced for reliever as well as maintenance (for about 12 years) but the question raised was should Fostair MART® for reliever therapy automatically be added to guidelines because there was already historical use of another drug in this manner.

In relation to these specific guidelines, the JFG agreed that public health should undertake a review of Symbicort SMART® to see if there was good evidence for the use as a reliever as well as maintenance especially as this was exposing the patient to increase steroid use.

BNSSG guidelines should support formulary choices and not just be list of all licenced indications.

It was difficult to decide when a licence extension would require a NDR i.e. a new cohort of patients, new /additional spend. Therefore the JFG agreed that as part of horizon scanning,
license extensions would be reviewed and the JFG will be able to decide if a NDR is required.

**Action:**
1. NB to liaise with Public Health re a review of Symbicort SMART®
2. NB to ensure the process for license extensions is documented

10. **AOB**

**a. NDR for July 2013 meeting**

NB listed the current NDRs that are potentially on the agenda for the July meeting.

Mirabegron for over active bladder. NICE was due to publish the TA on this drug at the end of June 2013 and so a NDR was not necessary – the FAD recommended the use of this drug as an option for treating the symptoms of over activity for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects. NB has received an application for this.

Ozudex for uveitis – There is current confusion as to whether this is Specialised Commissioning, or CCG. At the current time, it is felt that Ozudex is CCG and therefore a NDR to the JFG is appropriate. There has been an application back at the end of 2012, to CAF, however a conclusion to the application was never reached. NB to liaise with Ophthalmology at UHB for an application.

Linaclotide for IBS-C – no application received at present, although an application form has been sent out.

**Action:**
1. NB to add to agenda as appropriate

**b. TW last meeting**

TW would be commencing her new job with NHS England Specialised Commissioning based in Bristol on the 22nd of July 2013. The JFG would like to express their thanks for the work she has undertaken on behalf of this group.

**Action:**
1. None

**c. Thalidomide in cough**

MHRA Drug safety Update 29th May 2013 - Thalidomide: risk of second primary malignancies
Patients treated with thalidomide have an increased risk of haematological second primary malignancies

**Action:**
1. NB to add to July agenda (MHRA Drug Safety Update May)

**d. MAG meeting**

SM had attended the UHB MAG meeting on the 29th May 2013. She expressed concern that
MAG still appeared to be unhappy about certain aspects of the JFG processes.

The JFG and its processes will require a culture change within UHB and divisional management will need to sign up to the processes especially around the funding of drugs.

The application for dexmedetomidine had been discussed at the JFG meeting on the 29th May 2012 but rejected as minuted below

- The JFG has to base any decision on the evidence available and in this case it did not support its inclusion for the drug on the formulary at this time. Whilst not wanting to hold back innovation, it was felt that this drug would be being used in more of an experimental way and it was felt that this use is outside of the Joint Formulary. The committee did discuss the potential for it to be added for a 6 month trial and for the data to be fed back, however it was not felt that significant data would be gained in this time period. The committee would be happy to reconsider the application when further information/evidence is available.

However UHB surgical division had supported this application and had agreed to fund this drug for 3 months. SM was concerned about the governance and processes used when this was agreed especially as there was no evidence to support its inclusion in the formulary. This drug had been used in 33 patients of whom about 70% benefited from its use and a report is to be drafted. Define data showed 3 other hospitals using this drug.

Engagement by UHB is essential for the Joint Formulary to work but they do not appear to be fully engaged.

A paediatric formulary from another acute Trust had been suggested as the solution for the need to a paediatric formulary within BNSSG. Whilst this could be used as a starting point for the paediatric formulary, a review of paediatric drugs used within the Children’s hospital and primary care, the needs of the local population identified, and engagement of the clinicians is necessary to ensure that it will be adopted.

**Action:**

1. NB /SM / SBe / KG to consider how to get UHB fully engaged in the Joint Formulary process.
## 2013 Dates for Meetings

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs</th>
<th>Cut off for SCPs</th>
<th>Time</th>
<th>Venue</th>
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<tbody>
<tr>
<td>Tuesday 23rd July</td>
<td>Change of date and time</td>
<td>18th June</td>
<td>2nd July</td>
<td>9.30 – 12.30</td>
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<tr>
<td>Tuesday 10th September</td>
<td>Additional Date</td>
<td>30th July</td>
<td>20th August</td>
<td>10.00 – 13.00</td>
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<tr>
<td>Tuesday 15th October</td>
<td>3rd September</td>
<td>25th September</td>
<td>10.00 – 13.00</td>
<td>NBT, Southmead Pharmacy Seminar Room</td>
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<tr>
<td>Wednesday 6th November</td>
<td>Additional Date</td>
<td>25th September</td>
<td>16th October</td>
<td>10.00 – 13.00</td>
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<tr>
<td>Tuesday 10th December</td>
<td>29th October</td>
<td>19th November</td>
<td>10.00 – 13.00</td>
<td>Board Room, South Plaza</td>
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</tbody>
</table>
1. Welcome & Apologies & Declarations of Interest

Present
HoMM, NHS Bristol CCG (Chair)
Public Health Consultant, Bristol City Council (Chair from 11am)
Interface pharmacist, NHS Bristol CCG
Service Development Manager, NHS Bristol CCG
HoMM, NHS North Somerset CCG
Consultant Neurologist, North Bristol NHS Trust
GP, North Somerset (until 11.30am)
Clinical Effectiveness Research Lead, Bristol City Council
HoMM, NHS South Gloucestershire CCG
Public Health Consultant, South Glos City Council (until 10am)
Specialist Registrar Public Health, Bristol City Council (until 11am)
Formulary Pharmacist, AWP
Pharmacy Clinical Team Manager NBT
Pharmacist University Hospitals NHS Foundation Trust Bristol, UHB
GP, Bristol and member of Bristol CCG Board

Apologies
Interface pharmacist, NHS Bristol CCG
GP, Bristol
GP, Bristol
Joint D&TC Chair, North Bristol NHS Trust
Joint D&TC Chair, North Bristol NHS Trust
Chief Pharmacist, AWP
Nurse Prescriber, Bristol
Deputy Chief Pharmacist, Weston Area Health NHS Trust
Director of Pharmacy Weston Area Health NHS Trust
Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust Bristol

Declarations of Interest
None

The meeting was quorate

2. Minutes from 4th June 2013 Meeting

The minutes from the Joint Formulary Group (JFG) meeting on the 4th June 2013 had been circulated by NB following the meeting.

The minutes of this meeting were approved.

Matters arising from April 2013 Meeting
a. **Alteplase and Dornase Alpha NDR**
   Still awaiting NBT financial sign off. Alteplase is part of the best practice tariff for stroke and should not be invoiced through the PbR excluded route.

   **Action:**
   1. SB to liaise with Andrew Davies Director of Pharmacy NBT.

b. **Natamycin**
   Still awaiting clarification from specialised commissioning to see if they fund this drug. If not a new drug request will need to be submitted to the JFG

   **Action:**
   1. SBe to email Tracey Williams (Specialised Commissioning Pharmacist)

c. **CAF policies vs Formulary**
   SBe updating Joint Formulary to incorporate relevant existing CAF policies for medicines. A number of the CAF policies on the CCGs websites were out of date / incorrect. SBe was liaising with Claire Beynon about getting this updated.

   **Action:**
   1. SBe to liaise with Claire Beynon re updating CAF policies list

3. **NICE New Technology Appraisals published**
   There were a total of 9 TAs published in May and June 2013

   **Positive TA affecting the CCGs**
   - TA 283 Macular oedema (retinal vein occlusion) – ranibizumab
   - TA 287 Pulmonary embolism and recurrent venous thromboembolism - rivaroxaban
   - TA 288 Type 2 diabetes - Dapagliflozin combination therapy
   - TA 290 Overactive bladder - mirabegron

   **Positive TA affecting Specialised Commissioning**
   - None

   **TAs not recommended**
   - TA 284 Bevacizumab in combination with paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer
   - TA 285 Ovarian, fallopian tube and primary peritoneal cancer (recurrent advanced, platinum-sensitive or partially platinum-sensitive) - bevacizumab
   - TA 289 Myelofibrosis (splenomegaly, symptoms) - ruxolitinib
   - TA291 Gout (tophaceous, severe debilitating, chronic) - pegloticase

   **Terminated appraisal**
   - TA286 Schizophrenia or bipolar disorder - loxapine inhalation (terminated appraisal) (TA286)
TLS Status for newly published TAs

- TA 283 Ranibizumab - TLS Red
- TA 287 Rivaroxaban - TLS Amber 1 month SCP required
- TA 288 Dapagliflozin combination therapy – TLS blue
- TA 290 Mirabegron – TLS blue (see NDR)

It is the responsibility of the NICE College to ensure the safe implementation of positive TAs within BNSSG and these will be added to the formulary in accordance with implementation of NICE TAs (90 days from publication) unless the TA meets the NICE College criteria for early implementation.

TAs adopted into the BNSSG Joint Formulary June 2013

- TA 276 Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis - TLS Red

4. New Drug Requests (NDRs)

Ozurdex® (dexamethasone intravitreal implant) UHB
Clinically appropriate to add to formulary for licenced indication (one implant only) but financial modelling not submitted to show a cost neutral or cost saving position. Therefore the JFG was unable to approve the application at this time.

Mirabegron NBT
NICE TA 290 – will be included on formulary in line with implementation of NICE TAs (90 days from publication) – TLS Blue after patient has tried bladder training and two anti-muscarinic drugs.

Lixisenatide WAHT
Clinical non-inferiority to exenatide was agreed however superiority data was lacking and therefore it is unclear whether lixisenatide should replace exenatide as requested. The JFG would like to further explore the cost-effectiveness of lixisenatide. The application was not approved at this time.

Denosumab for men UHB
Clinically appropriate (clinical effectiveness and equity of access) for inclusion in formulary in line with TA 204. SCP to be updated – TLS Amber. Awaiting directorate sign off.

Voractiv® (rifampicin, isoniazid, pyrazinamide and ethambutol) NBT
To be added to formulary due to the cost effectiveness of this drug - TLS Red. Awaiting directorate sign off.

Dermovate with 40% polypropylene UHB
To be added to formulary obtained due to its place in therapy relative to available treatments for use in severe hyperkeratotic psoriasis and eczema of the palms
and / or soles for 4 weeks - TLS Red specialist consultant only. Awaiting directorate sign off.

Decision Criteria used by JFG for NDR

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

a. Ozurdex® Dexamethasone 700 microgram implant UHB

This application was submitted by Dr CG Consultant Ophthalmic Physician who attended the meeting to present the application.

Please see application form for full details.

This application was for the inclusion of Ozurdex® for the treatment of uveitis. There are no licensed immunosuppressive agents for uveitis. The standard treatment for patients with non-infectious sight-threatening uveitis in the posterior segment is systemic corticosteroids +/- immunosuppressive agents, in Bristol the most commonly used agents are mycophenolate mofetil and tacrolimus for adults. Patients who have on going inflammation despite standard immunosuppression, have severe sight-threatening disease such as Behcet’s associated uveitis, or have side effects or contraindications to standard treatment may be considered for biological agents such as infliximab or adalimumab under a CAF criteria based access policy.

Ozurdex would be used in patients who are not suitable for immunosuppression, or have failed treatment with one or more immunosuppressants and would be used in place of Kenalog (triamcinolone) which is an off label use, and non formulary for ophthalmology. UHB would like to adopt the North East Retinal Treatment Group protocol which details the 3rd line or subsequent use of Ozurdex in the treatment of uveitis.

This application was first discussed at 9.45 when Dr CH, Public Health Consultant South Gloucestershire Council was present and then later with the applicant.

Discussion with Dr CH

An application had been submitted to the BNSSG Commissioning Advisory Forum (CAF) in July 2012. A public health review was undertaken by Dr CH for the November CAF meeting which did not occur. To summarise the public health review:

- This appraisal identified the evidence-base and policy support for commissioning Ozurdex® for adult patients with posterior non-infectious uveitis. Ozurdex® offers a new, licensed mode of delivery for steroid treatment of inflammation affecting the back of the eye (intravitreal use). Other steroid preparations for intravitreal use are available, but not licensed for use in posterior uveitis and are likely to have differing safety and efficacy profiles. There are no head to head trials, so there is no clinical trial evidence base for identifying the most clinically and cost effective option.
• The proposal to use Ozurdex® as a third line therapy has been accepted by the North-East of England Technology Appraisal Group (NETAG). One other English policy for restricted use has been identified and a ‘not commissioned’ policy for one PCT. Following the lack of manufacturer submission to Scottish Medicines Consortium and its Wales counterpart, their policies are currently to not support prescribing. Given the lack of licensed alternatives for intravitreal steroids, Ozurdex® has potential to provide new benefits, but there is little information available to understand costs and limitations compared with benefits.

Ozurdex® is a licenced treatment, whilst currently UHB are using off label alternatives.

The patient cohort would be a relatively uncommon subgroup of patients with uveitis, and would be used third line. The number given by Dr CG are 15 patients of which 50% would require bilateral implants (8 patients = 16 implants). Of these 23 implants 50% would require further implants totalling 45 implants per annum. The cost of one implant is £1,044 including VAT thus an annual drug cost would be £46,980 plus the outpatient attendance costs at £289 per visit.

The SCP states that the safety and efficacy of Ozurdex® administered to both eyes concurrently have not been studied. Therefore administration to both eyes concurrently is not recommended.

There is a lack of research concerning the long term safety of this drug and is only licensed for one off use. The SCP states there is currently no experience of repeat administrations in posterior segment non-infectious uveitis or beyond 2 implants in Retinal Vein Occlusion.

The North East Treatment Advisory Group noted the absence of any evidence for the cost effectiveness of Ozurdex® in uveitis although acknowledged that it delivers efficacy in terms of visual acuity on par with other high-cost ophthalmic treatments which have been determined as cost-effective for use within the NHS.

Ozurdex® (PbR excluded) falls into the list of CCG commissioned PbR excluded drugs. However, the condition of uveitis is commissioned by the Specialised Commissioning Group (SCG) and as of April 2014 they will also be commissioning the drugs associated with this condition. At the time of the application the JFG is unaware of any commissioning policy by NHS England for the commissioning of this drug.

The JFG discussed auditing of the patients if the application was approved and if there was a register of patients with uveitis at UHB. This would be able to provide prospective observational data on the use of this drug. The JFG accepted that clinical trial research into the use of this drug would be difficult due to the small number of patients. If approved assurance would be required over its use and also clarity on how clinical decisions was made about further implants.

Concern was expressed over indication creep – that approval of the drug would create a demand in excess of the number given in the application. It would not be possible to restrict the number of implants to 45 a year due to equity of access.

There is a lack of certainty around the cost implications of approving this application. As there is no additional funding available, unless this application could be shown to be cost neutral or cost saving then a paper would need to be submitted to the individual CCG boards to agree funding.

Discussion with Dr CG
Ozurdex® would be used in patients in whom conventional therapy had failed or who were contraindicated to systemic agents.

The use of Ozurdex® would be used alongside the anti TNF criteria based access policy and depending on the patient’s history they would either have an implant or use an anti TNF. It would not replace the use of anti TNFs – some patients may not wish to have an implant which involves an injection into the eye.

The implants last between 4 and 6 months and then another implant would be required. If the treatment was ineffective, the patient would not be considered for another implant.

Dexamethasone implants were approved by NICE in July 2011 for macular oedema (retinal vein occlusion). The manufacturer assumed that up to six treatments would be given when the evidence was submitted for this TA. However, the marketing authorisation is based on an evidence base trial with two re-treatments over 360 days.

When questioned Dr CG confirmed that it is standard practice to give more than one implant if the patient is suitable for uveitis.

There is no register at UHB for patients with uveitis. However this could easily be done to provide prospective audit data of the benefits and harm and would be a useful exercise for the unit and commissioners.

There would be a few additional patients who are not currently being treated but who are sub optimal and would benefit from Ozurdex.

The JFG considered the application and the evidence submitted. This is a novel licensed treatment for uveitis which provides clinicians and patients an alternative treatment in the pathway for uveitis supported by clinical trial data. Clinical evidence supports adoption.

However, the JFG’s concerns were around
- Unknown financial impact for the CCG
- No financial modelling / offset costs shown
- No evidence to support repeat implant

It would not be in the best interests of patients to decommission the criteria based access policy for the use of anti TNFs in the treatment of uveitis; this provides a treatment pathway for patients who fail on or are contraindicated to Ozurdex®. However the treatment pathway needs to be explored to determine the patient numbers at each stage (those on anti-TNFs and Ozurdex®) and to determine a financial model for this.

The JFG considered the use of Ozurdex® for uveitis as clinically appropriate (clinically effective) within its licenced indication (one implant only) and a good audit trail (local evaluation framework) would be necessary to ensure the appropriate use of this drug.

However, for the JFG to approve this application a cost neutral or a cost saving financial model needs to be submitted to the CCGs. Since this is absent the JFG were unable to approve the application at this time. The JFG requests a financial model of the uveitis pathway and how Ozurdex® could provide a cost neutral or cost saving option or how the department would take on this additional expenditure but still manage within the
existing budget. If additional funding is required the financial model will need to be submitted to the CCGs as a business case unless specialised commissioning release policy for the treatment of uveitis in the meantime.

Action:
1. MK to email TW re SCG commissioning policy for Ozurdex® for uveitis
2. KG to feedback to applicant

**Drug PbR excluded**

NBT – NA

UBT – Directorate sign off required

Weston – NA

Primary Care – NA

**Post meeting note**
Response from Tracey Williams Friday 26th July 2013

No policy in development yet. Asked for a view from the other AT Pharmacists. Most useful reply below:

- As CCGs are currently picking up the cost for Ozurdex® (because they pay for it in RVO) our local CCGs have developed an interim local commissioning policy for its use which was based on the old NETAG policy. This will be superseded by any NHSE policy if NHSE become the responsible commissioner for uveitis as a whole.

b. **Mirabegron NBT**

This application was submitted by Mr HH NBT Consultant Urologist. The applicant was not present at the meeting.

For full details please see application form.

The applicant was for the inclusion of mirabegron for overactive bladder and this had been received before the publication of the positive NICE TA.

The JFG did not consider the evidence for the inclusion of this drug to the formulary as this had already been considered by NICE. The JFG did consider where this drug would fit in the pathway for the treatment of patients with over active bladder. Mirabegron has a different mode of action from the other drugs currently on the formulary and is only slightly more expensive than 5mg Solifenacin (£29.00 compared with £27.62 for 30 days).

The JFG agreed that mirabegron should be prescribed third line – the patient should have under gone bladder training and tried two anti-muscarinic drugs before prescribing. There may be a cost pressure to the CCGs as patients who are not currently taking any drugs may wish to try this drug. The additional cost per 100,000 population is £40.8K and this will be a cost pressure to the primary care drugs budget.

Action:
1. NB/SBe to add to formulary (in accordance with implementation of NICE TAs 90 days from publication) after the patient has undergone bladder training and tried two antimuscarinic drugs – TLS Blue.

**Drug is in tariff**
- NBT – NICE TA
- UBT – NICE TA
- Weston – NICE TA
- Primary Care – NICE TA

c. Lixisenatide

This application was submitted by JK Consultant Physician Weston Hospital and had been deferred from the JFG meeting 4th June 2013 as minuted below.

The additional phase III trials have now been published and therefore the JFG agreed to defer the decision on this NDR until an appraisal by public health on the new evidence by public health had been undertaken.

For full details please see application form.

The application was for the inclusion of lixisenatide for the treatment of type 2 diabetes to achieve glycaemic control in combination with oral glucose lowering medicinal products and/or basal insulin.

The application requests that exenatide is replaced with lixisenatide.

Dr AL, Specialist Registrar Public Health, had undertaken a review to see if exenatide could be replaced by lixisenatide and presented her findings to the meeting. The use of lixisenatide with basal insulin was not considered in this review.

There is a single trial which compares efficacy and safety of lixisenatide once daily versus exenatide twice daily in type 2 diabetes inadequately controlled with metformin (this trial was drug company funded). The study does show non-inferiority (according to pre agreed criteria) of lixisenatide compared with exenatide in the primary outcome of reduction of HbA1c. The lixisenatide group reported significantly less symptomatic hypoglycaemia and reported less nausea however the exenatide lost significantly more weight and also appeared to have experienced less injection site reactions.

Her recommendation was that although lixisenatide has been shown to be non-inferior there was insufficient evidence to support superiority of efficacy and safety for lixisenatide and questioned whether this was enough to replace exenatide with lixisenatide on the JF.

The JFG noted that exenatide modified release (in triple therapy regimens) for the treatment of Type 2 diabetes is covered by NICE TA 248 (Feb 2012). Liraglutide (in triple therapy regimens) for the treatment of Type 2 diabetes is covered by NICE TA 203 (Oct 2010).

Clinical guideline 87 for the management of type 2 diabetes recommends the use of GLP1 mimetic in triple therapy with metformin and a sulphonylurea but not in combination with insulin.
The cost of lixisenatide for a year is £704 - £730 compared with £830 for exenatide and £954 for liraglutide so there may be cost savings associated with this application.

The JFG considered the application and the review undertaken by Dr AL and the scope in which this review had been undertaken.

The one study does show that lixisenatide is non inferior to exenatide in the reduction of HbA1c and reported significantly less symptomatic hypoglycaemia and reported less nausea. Evidence for its use with basal insulin had not been considered. The JFG agreed that on the basis of the clinical data available lixisenatide could be considered as a “me too” drug.

The JFG agreed that although it may be appropriate to add lixisenatide to manage the side effects associated with other drugs, they were unable to approve the application at this stage and would like to consider further the cost-effectiveness of lixisenatide versus exenatide. It was agreed that this would be considered at the next meeting. Trial data of lixisenatide in combination with basal insulin should also be considered as per application.

Action:
1. SBe to arrange for financial modelling and present cost-effectiveness data to JFG once obtained.

d. Denosumab for men

This application was submitted by Dr SC Lead Consultant Osteoporosis Service UHB who attended the meeting to present the application.

For full details please see application form. NBT & WHAT support this application.

The application was for the inclusion of denosumab for the treatment of osteoporosis in men with increased risk of fractures as assessed by a combination of clinical factors and bone mineral density and in whom alternative treatments are either contra indicated, not tolerated or impractical.

The advantages of denosumab over other treatments are that it can be used in patients with some renal impairment and it is administered by s/c injection 6 monthly thereby increasing concordance and allowing community based administration. The other alternative for male patients unable to tolerate oral bisphosphonates is IV Zolendronic acid which requires a day case admission. NICE TA 204 only recommends the use of denosumab for the prevention of osteoporotic fracture post-menopausal women.

Denosumab is not licensed in the UK for men and there is no indication that they are applying for a license. However, in September 2012 the US Food and Drug administration approved a new indication for denosumab as a treatment to increase bone density in men with osteoporosis at high risk for fracture.

On the NICE work programme (ID1558) is a MTA - to appraise the clinical and cost effectiveness of alendronate, denosumab, risedronate, strontium ranelate, teriparatide and zoledronic acid within their licensed indications for the prevention of osteoporotic fractures in men. Within the scope of the MTA it is recognised that the use of denosumab in this manner.
would be unlicensed. There is no publication date.

There a number of female patients within BNSSG whose GP has refused to accept to treat them with denosumab (under shared care as amber TLS) and these patients are having to attend an outpatient appointment to receive their 6 monthly injection – this equates to approximately 20 – 25% of patients started on denosumab (25 to 30 patients at UHB). Denosumab could possibly be administered through Homecare and reduce the need for patients to attend hospitals. There is an issue within North Somerset where GPs are expecting payment to undertake the administration of denosumab.

The long term data for the reduction in fractures for patients taking denosumab over 5 to 10 years is unknown.

Patients should now be reassessed after 3 to 5 years of treatment and this is being added to the letter sent to GPs.

The estimated number of male patients requiring denosumab is approximately 12 – 15 patients per annum across BNSSG. The annual additional cost to the primary care drugs budget is £3,111.

Zoledronic acid is now available as a generic preparation and so will be less expensive; however, there is also a day case tariff associated with the administration of Zoledronic acid.

The JFG considered the application and the evidence submitted and agreed the equivalence of clinical efficacy in both men and women. The JFG agreed that it was inequitable not to be able to offer this effective treatment in men as well as women. It was agreed to add to the formulary in accordance with the criteria from NICE TA204 (post-menopausal women). The SCP will need to be updated to include men.

Funding for the use of denosumab for men is not through the NICE College budget. Directorate approval for funding is required.

Action:
1. Directorate approval for funding to be confirmed.
2. SBe to add to formulary TLS Amber in accordance with NICE TA 204 (post-menopausal women) criteria.
3. SCP to be updated to reflect use in men
4. HoMMS to consider use of homecare for patients having to attend hospital for 6 monthly injections.

*Drug is in tariff*

NBT – await directorate sign off
UBT – await directorate sign off
Weston – await directorate sign off
Primary Care – NA

e. **Voractiv®** (rifampicin, isoniazid, pyrazinamide and ethambutol)

This application was submitted by Dr JC, Respiratory/ Dr B Bovill, Infectious Disease, Speciality
Consultants in TB Management NBT. This applicant was present by SB.

For full details please see application form. UHB supports this application.

The applicant was for the inclusion of Voractiv® for induction treatment of tuberculosis (first 2 months). This is a licenced indication for the use of this drug. The advantages of this drug over existing medication are

- The reduction in the pill burden on the patient 3 – 7 fewer tablets depending on weight.
- Reduced complexity of regimen
- Price is less expensive than current treatment (contract prices)

The estimated number of patients treated would be 50 to 100 in secondary care (NBT). The application stated that this drug would replace Rifater and ethambutol; however Rifater plus ethambutol is accepted standard treatment for suspected isoniazid resistant TB.

The JFG considered the application. Voractiv® simply reduces the pill burden and is cost neutral when looking at Mims prices and NBT contract prices. The JFG agreed to add this drug to the formulary due to its cost effectiveness – TLS Red. Rifater plus ethambutol to remain on the formulary until confirmed otherwise.

Action:
1. NB to add to formulary TLS Red once directorate sign off obtained.
2. DK to inform applicant.

Drug is in tariff
NBT – await directorate sign off
UBT – await directorate sign off
Weston – await directorate sign off
Primary Care - NA

f. Dermovate with 40% polypropylene

This application was submitted by Dr AD Consultant Dermatologist NBT. This applicant was present by Sasha Beresford.

For full details please see application form. UHB support this application.

The applicant was for the inclusion of Dermovate with 40% propylene for the treatment of severe hyperkeratotic psoriasis and eczema.

This is an unlicensed produce that is on British Association of Dermatologists national “preferred specials list” which supports the use of propylene glycol 40% in dermovate. Local expert opinion has seen success in using this product in a specific cohort of patients. It would be used for patients who are non responsive to plain dermovate preparations. Its use would be for 4 weeks only.

Although the application states that this drug is already in use at UHB it has not been prescribed since the JCA pharmacy system was installed in 2011.
There is an absence of clinical data, either clinical trials or case reports, supporting the use of this preparation.

The estimated number of patients would be 10 per annum (NBT) and the manufactured special cost for 100g was £29.75 (2011) compared with the cost of dermovate 100g £7.90 (2013). In primary care, the costs of unlicensed specials are not consistent, varying considerably, and so the prescribing and manufacture of this product should remain within secondary care.

The JFG considered this application. There is an absence of clinical data to support this application for a ‘special’ product which the JFG agreed would be limited. However, the JFG agreed to add this preparation to the formulary due to its place in therapy relative to available treatments. The JFG approved it for use only in patients with severe hyperkeratotic psoriasis and eczema of the palms and/or soles for 4 weeks – TLS Red specialist consultant only.

Action:
1. SBe to add to formulary once directorate sign off obtained - TLS Red for the treatment of severe hyperkeratotic psoriasis and eczema of the palms and/or soles for 4 weeks specialist consultant only.
2. DK to inform applicant

Drug is in tariff
NBT – await directorate sign off
UBT – await directorate sign off
Weston – NA
Primary Care - NA

5. Shared Care Protocols

a. Methotrexate in Dermatology UHB and NBT

SCP author Dr CK

Methotrexate currently on the formulary oral amber 3 months for the treatment of Eczema and Psoriasis (Chapter 13.5)

This SCP needs to be transferred to new template and to brought back to the next meeting

BaNES had recently produced a SCP for Methotrexate – BS to send

Action:
1. SBe / HC to transfer to new SCP template
2. BS to send BaNES methotrexate shared care protocols

b. Hydroxychloroquine in Dermatology (UHB)

SCP author RC (MI pharmacist)
Currently only on formulary for under section 10.1.3 Drugs which suppress the rheumatic disease process for which there is a SCP and is not on the formulary for dermatology.

**Action:**
1. **SBe to review formulary usage and if new drug request needed before SCP can be considered**

c. **Apriprazole**

SCP author BS Formulary Pharmacist AWP

On the formulary section 4.2.1 Antipsychotic drugs.

This is an update of an existing SCP written in 2009.

There was not sufficient time to discuss this SCP in detail but concern was expressed about the monitoring requirements for GPs including VTE and that the GPs were unlikely to accept this shared care. To be carried forward to next meeting.

**Action:**
1. **MK to add to next agenda**

d. **Typical Antipsychotic depots**

SCP author BS Formulary Pharmacist AWP

On the formulary section 4.2.2 Antipsychotic depot injections (amber 1 month)

- Flupentixol decanoate
- Fluphenazine decanoate
- Haloperidol decanoate
- Zuclopenthixol decanoate
- Pipotiazine palmitate

These drugs are on the formulary but there is no SCP for them.

Concern was expressed about what happens once patients are discharged from the mental health services and what do GPs do if there is a problem – this may be addressed by the mental health reprocurement which is being undertaken.

There was not sufficient time to discuss this SCP – to be carried forward to next meeting.

**Action:**
1. **MK to add to next agenda**

e. **Change in TLS Status Prucalopride – Amber to Green**

There was not sufficient time to discuss this – to be carried forward to next meeting

**Action:**
1. **MK to add to next agenda**

f. **Rotavirus live vaccine Change in TKS Red to Green**

This was for information as the change was in line with national guidance. Rotavirus live vaccine is now detailed in the DoH/PHE childhood immunisation vaccination schedule and will
be routinely offered to 2-3 month old infants. This has already been added to the formulary TLS green.

Action:
1. None

g. Tapentadol MR for chronic pain Change in TLS Red to Amber 3 months
There was not sufficient time to discuss this – to be carried forward to next meeting

Action:
1. MK to add to next agenda

6. Chapter Review

There was not sufficient time to discuss this – to be carried forward to next meeting.

Action:
1. MK to add to next agenda

7. Specialised Commissioning Statements

a. None

8. MHRA Drug Safety Update - May and June

There was not sufficient time to discuss this – to be carried forward to next meeting

Action:
1. MK to add to next agenda

9. Formulary Process

a. BNSSG JFG Terms of Reference
There was not sufficient time to discuss this – to be carried forward to next meeting

Action:
1. MK to add to next agenda

b. NDR Decision Pathway (for finance approval)
There was not sufficient time to discuss this – to be carried forward to next meeting

Action:
1. NK to add to next agenda
c. **NDR Application Form**  
   There was not sufficient time to discuss this – to be carried forward to next meeting  
   **Action:**  
   1. MK to add to next agenda

d. **NDR Appeals Process**  
   There was not sufficient time to discuss this – to be carried forward to next meeting  
   **Action:**  
   1. MK to add to next agenda

10. **Items for discussion**

   a. None

11. **AOB**

   a. **Lithium SCP**  
      BS had liaised NB re this SCP and it had been uploaded to the JF website but there may need to be slight adjustment to the information concerning dose adjustment.  
      **Action:**  
      1. BS to liaise with NB

   b. **Blood testing for Amber drugs**  
      DK raised the issue of blood monitoring for red / amber drugs. This will be discussed at the BNSSG D&TC meeting Thursday 25\textsuperscript{th} July 2013.  
      **Action:**  
      1. SM /DC to take to BNSSG D&TC
### 2013 Dates for Meetings

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs</th>
<th>Cut off for SCPs</th>
<th>Time</th>
<th>Venue</th>
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<tr>
<td>Tuesday 10(^{th}) September</td>
<td>Additional Date</td>
<td>30(^{th}) July</td>
<td>20th August</td>
<td>10.00 – 13.00 NBT Georgian Room, Trust Headquarters, Frenchay</td>
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<td>Tuesday 15(^{th}) October</td>
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<td>3(^{rd}) September</td>
<td>25(^{th}) September</td>
<td>10.00 – 13.00 NBT, Southmead Pharmacy Seminar Room</td>
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<td>Wednesday 6(^{th}) November</td>
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<td>25(^{th}) September</td>
<td>16th October</td>
<td>10.00 – 13.00 Board Room, South Plaza</td>
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<td>29(^{th}) October</td>
<td>19(^{th}) November</td>
<td>10.00 – 13.00 Board Room, South Plaza</td>
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### 2014 Dates for Meetings

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<tr>
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<th>Cut off for SCPs</th>
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<tr>
<td>Tuesday 25th November 2014</td>
<td>10 am to 1pm</td>
<td>Boardroom South Plaza</td>
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</table>
1. Welcome & Apologies & Declarations of Interest

Present
- Public Health Consultant, Bristol City Council (Chair)
- Interface Pharmacist, NHS Bristol CCG
- Interface Pharmacist, NHS Bristol CCG
- HoMM, NHS Bristol CCG
- Service Development Manager, NHS Bristol CCG
- HoMM, NHS North Somerset CCG
- Clinical Effectiveness Research Lead, Bristol City Council
- HoMM, NHS South Gloucestershire CCG
- Formulary Pharmacist, AWP
- Pharmacy Clinical Team Manager NBT
- MI Pharmacist University Hospitals NHS Foundation Trust Bristol, UHB
- Education and Training Pharmacist University Hospitals NHS Foundation Trust Bristol, UHB

Apologies
- Consultant Neurologist, North Bristol NHS Trust
- GP, North Somerset
- GP, Bristol and member of Bristol CCG Board
- GP, Bristol
- GP, Bristol
- Joint D&T Chair, North Bristol NHS Trust
- Chief Pharmacist, AWP
- Nurse Prescriber, Bristol
- Deputy Chief Pharmacist, Weston Area Health NHS Trust
- Director of Pharmacy Weston Area Health NHS Trust
- Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust Bristol
- Consultant Emergency Medicine University Hospitals Bristol NHS Foundation Trust Bristol

Declarations of Interest
- None

The meeting was not quorate and therefore all decisions will need to be ratified and actioned once approved.

2. Minutes from 23rd July 2013 Meeting

The minutes from the Joint Formulary Group (JFG) meeting on the 23rd July 2013 had been circulated by NB following the meeting.
The minutes of this meeting were approved.

Matters arising from April 2013 Meeting

a. Natamycin

Natamycin eye drops for fungal keratitis – NB had received an email from the Chair of the Clinical Reference Group for Ophthalmology (AD) who confirmed that that Fungal Keratitis is not commissioned via SCG, and therefore neither is the drug.

NB has informed UHB that they will need to submit a NDR for the JFG to consider if this drug should be go onto the JFG.

Action:
1. UHB to submit a NDR application

b. Amber / red blood testing

LM (Specialist Respiratory Pharmacist NBT) had hoped to attend the meeting to discuss the blood monitoring requirements for mycophenolate and the request to change from red to amber three months (discussed at 14th May 2013 meeting). However issue of blood monitoring of red and amber drugs is not just associated with this particular drug.

The BNSSG QIPP group are coordinating an audit of red drugs within the acute trust to scope out the size of the problem and to identify any safety issues if these drugs are not being monitored as they should be. It is thought that 100 patients each at UHB and NBT will be audited and 50 at Weston.

It was suggested that amber drugs were included in the audit as this would test the robustness of shared care and also that the secondary care pharmacists were involved in the development of the audit criteria.

The issue of red and amber drug blood monitoring sits with the BNSSG D&TC committee as this is a quality / governance issue and may require system changes to address any issues identified. Therefore discussions will continue within BNSSG D&TC but with updates being brought to the JFG.

Some of the blood monitoring requirements are covered by a Local Enhanced Service (LES) and could be addressed through performance management.

Action:
1. DC to send copy of draft audit.

c. CAF policies vs Formulary

SBe was liaising NM (South West CSU Exceptional Funding Manager) to align the interventions not normally funded (INNF) with the joint formulary and to include a link to the joint formulary.

Action:
1. None

d. Alteplase and Dornase Alpha NDR

Director of Pharmacy UHB, was taking the issue of alteplase and PbR exclusion to the DoH
PbR panel for review. If the DoH confirm that it is PbR excluded for all indications and not just claimed for through the stroke best practice tariff then a business case will need to be submitted to each CCG board for approval of funding.

**Action:**

1. **SB to update JFG once information is received**

3. **NICE New Technology Appraisals published**

There were a total of 4 TAs published in July and August 2013

Positive TA affecting the CCGs

- TA 292 Bipolar disorder (children) – aripiprazole
- TA 293 Thrombocytopenic purpura – eltrombopag
- TA 294 Macular degeneration (wet aged related) – aflibercept (1st line)

Positive TA affecting Specialised Commissioning

- None

TAs not recommended

- TA 295 Breast cancer (HER2 negative, oestrogen receptor positive, locally advanced or metastatic) - everolimus (with an aromatase inhibitor)

Terminated appraisal

- None

**TLS Status for newly published TAs**

- TA 292 Aripiprazole - TLS to be confirmed *
- TA 283 Eltrombopag - TLS Red
- TA 294 Aflibercept - TLS Red

It is the responsibility of the NICE College to ensure the safe implementation of positive TAs within BNSSG and these will be added to the formulary in accordance with implementation of NICE TAs (90 days from publication) unless the TA meets the NICE College criteria for early implementation.

* Post meeting note

TA 292 Aripiprazole was discussed at the NICE College meeting 12th September 2013 and the TLS status will be red until there is an application to change to amber is received by the JFG.

**TAs adopted into the BNSSG Joint Formulary July and August 2013**

- Asthma (severe, persistent, patients aged 6+, adults) - omalizumab (rev TA133, TA201) (TA278) TLS Red
- Rheumatoid arthritis - abatacept (2nd line) (rapid review of TA234) (TA280) TLS Red
4. New Drug Requests (NDRs)

**Linaclotide UHB and Primary Care**
Rejected as the clinical evidence did not support the inclusion into the formulary although the JFG acknowledged that this was a novel drug and there would be an emerging evidence base.

**Ozurdex UHB**
Awaiting patient pathway and cost impact information.

**Lixisenatide WAHT**
Approved for inclusion due to non-inferiority in comparison with other GLP-1 agonists and overall most cost effective. TLS Green, first line.

**Renavit**
Approved for inclusion in the JF for the dietary management of water soluble vitamin deficiency in patients with chronic kidney disease in place of Dialyvit as a direct substitution that is more cost-effective. TLS blue for patients on renal dialysis.

**Artiss**
The JFG was unable to consider the application fully due to insufficient clinical evidence provided at this time.

**Teriparatide**
The decision for the inclusion of this drug to the JF was deferred as the applicant was unable to attend the meeting and insufficient clinical evidence was provided.

**Insulin Degludec**
JFG to reconsider the decision of the position of insulin degludec in the patient pathway as at the time of the discussion around the inclusion into the JF the applicant was not present.

**Decision Criteria used by JFG for NDR**
- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

**a. Linaclotide UHB and Primary Care**
This application was submitted by Dr AB Consultant gastroenterology UHB and Dr MC GP NHS
Bristol. Dr MC (GP with Special Interests in Gastroenterology, based at the community based Prime endoscopy Bristol unit at the GP practice at Westbury on Trym) attended the meeting to present the application. This is a joint application between primary and secondary care.

Please see application form for full details.

This application was for the inclusion of linaclotide (Constella®). Linaclotide is indicated and licensed for the symptomatic treatment of moderate to severe irritable bowel syndrome with constipation (IBS-C).

The anticipated number of patients to be treated per year in the application is 454 in primary care and 50 in secondary care which is approximately 1/10 of the possible patients who could be treated on this drug as indicated in the costing model. This lower end prediction could be explained by a slower uptake of prescribing Linaclotide whilst experience is gained.

There have been two placebo controlled RCTs evaluating the Linaclotide. It is difficult to choose meaningful endpoints in IBS as symptoms vary between patients and can be very subjective. The endpoints chosen were co-endpoints including responses to individual as well as combined symptoms and some global measures. The trials also allowed rescue therapy but there was no additional analysis on the extent of the use of these. These were industry sponsored trials. The trials showed that Linaclotide improved abdominal discomfort, abdominal pain and the degree of relief of IBS symptoms in at least 6 of 12 weeks compared to placebo. There was discussion around the limitations of the trials, and how it would fit in the pathway.

There is a clinical guideline on irritable bowel syndrome in adults: diagnosis and management of irritable bowel syndrome in primary care (NICE clinical guideline 61) published in 2008.

There have been a number of regional and national reviews of Linaclotide and these have been reviewed in the critical appraisal for BNSSG. A NICE evidence study was published April 2013 on linaclotide and concludes that local decision makers will need to consider the place of linaclotide alongside existing treatments that may be used to manage symptoms of IBS-C such as concomitant use of antispasmodics and laxatives. The publication of head to head studies against existing treatments would facilitate a better understanding of its place in the management of IBC-S.

NB had undertaken the critical appraisal and estimated the financial impact to the BNSSG primary care budget to be between £67,643 and £1,352,867 depending on how many eligible patients are initiated on it. The use of linaclotide for IBS-C does not appear to offer any net savings to the CCGs. There is no evidence to support the predicted cost savings outlined in the costing model associated with reduced secondary care outpatient appointments.

Discussion with Dr MC

Prime endoscopy Bristol provides two levels of service – endoscopy and clinical opinion.

IBS is very common but poorly managed and there is not a lot available to treat intractable IBS-C. This drug would be used for patients with moderate to severe symptoms who had failed to respond to first line treatment antispasmodic and laxatives. The endoscopy service is currently working at maximum capacity and there will be further pressures when screening patients over 55 for bowel cancer is introduced.

This drug may be useful in young patients who do not have Inflammatory Bowel Disease (IBD) or any of the “alarm signs” of cancer and reduce the need for endoscopy.
Dr MC identified a significant need for education / guidelines for GPs in the management of IBS-C.

Dr MC also spoke about faecal calprotectin measurement which is a biochemical test for intestinal inflammation and is a useful screening tool for identifying patients who are most likely to need endoscopy for suspected inflammatory bowel disease but is only available in secondary care at the moment. Dr MC is working with TC and PM to get this test available in primary care. There are draft NICE Diagnostics guidance (Faecal Calprotectin diagnostic tests for inflammatory disorders of the bowel) which show the cost of the test as £22.79 per patient, while a colonoscopy was estimated to cost £741.68 per person. These guidelines are due to be published in October 2013.

Linaclotide has a known effect on the gut wall where as other recognised treatments, e.g. amitriptyline (Unlicensed), the effect is unknown.

The manufacture of linaclotide is investing in GP education and is developing an education unit called “Unlocking GI”.

IBS is more of a primary care issue and less so a secondary care problem.

Dr MC indicated that he had trialled Linaclotide in two patients. The first patient stopped due to lack of benefit and the second stopped due to side effects (diarrhoea).

The JFG considered the application and the evidence submitted. Guidelines from other areas of the country recommend its use after laxative, antispasmodics and amitriptyline. The SMC accepted the use of linaclotide (May 2013) but it is restricted for use in patients with moderate to severe IBS-C who have not responded adequately to or cannot tolerate all other suitable treatment. The studies failed to report on the rescue medication used. Also the mean age of patient in the trials were 43 and 44 and therefore not representative of the young population that it is suggested that it is used in.

On review of the criteria used by the JFG for NDR
- **Clinical effectiveness** – there is evidence to show that Linaclotide is more effective than placebo in the treatment of IBS-C.
- **Cost effectiveness or resource impact** – there would be a large impact on the primary care budget - the direct acquisition cost is higher than any of the indicated treatments.
- **Strength of evidence** – The evidence is weak, there are no head to head trials against active comparators. The two trials showed that Linaclotide was more effective than placebo in composite outcomes relating to abdominal discomfort and bowel movements. There was no further analysis of the rescue trial medication used during the trial.
- **Place in therapy relative to available treatments** – there are other licenced and unlicensed alternatives (accepted medical practice) and due to the lack of active comparator trials it makes it difficult to place Linaclotide in the treatment pathway.
- **National guidance and priorities** – NICE evidence summary
- **Local health priorities** – IBS is not a current local health priority

The JFG felt that the criteria for inclusion into the JFG has not been meet. It is a novel agent, but this not sufficient to accept it on to the formulary. The JFG would reconsider the use of this drug within BNSSG if the evidence base changes.

The JFG also acknowledged that education of GPs is key in the management of this
condition, and felt that Medicines Management would be able to assist in this. This should be taken forward by the BNSSG D&TC.

Action:
1. NB to feedback to applicant decision of JFG

   Drug is in tariff
   NBT – NA
   UBT – NA
   Weston – NA
   Primary Care – NA

b. Ozurdex UHB Update

This application was submitted by Dr CG Consultant Ophthalmic Physician and was discussed at the JFG on the 23rd July 2013.

For full details please see application form.

From this meeting on the 23rd July, it is minuted that

- The JFG considered the application and the evidence submitted. This is a novel licensed treatment for uveitis which provides clinicians and patients an alternative treatment in the pathway for uveitis supported by clinical trial data. Clinical evidence supports adoption.

- However, the committee concerns were around
  - Unknown financial impact for the CCG
  - No financial modelling / offset costs
  - No evidence to support repeat implants

SBe had met with Dr CG was looking at the costing the patient pathway for uveitis to show that using Ozurdex would at least be cost neutral.

Action:
1. To be added to agenda once cost impact model and pathway have been defined.

   Drug is PbR excluded
   NBT – NA
   UBT – directorate approval needed if approved
   Weston – NA
   Primary Care – NA

c. Lixisenatide

This application was submitted by Dr JK, Consultant Physician, Weston Hospital and had been deferred from the JFG meeting 4th June 2013 and discussed 23rd July 2013 as minuted below.

- The JFG considered the application and the review undertaken by Dr AL and the scope in which this review had been undertaken.
The one study does show that lixisenatide is non inferior to exenatide in the reduction of HbA1c and reported significantly less symptomatic hypoglycaemia and reported less nausea. No evidence had been provided for its use with basal insulin. The committee considered that lixisenatide was a “me too” drug.

The committee considered that although it may be appropriate to add the drug to manage the side effects associated with other drugs, they were unable to approve the application at this stage as there was no financial modelling.

The committee was unable to approve the use lixisenatide with insulin as no evidence was submitted to support its use.

**Action:**

1. SBe to arrange for financial modelling and to bring back to JFG once obtained

SBe presented a Sanofi budget impact analysis based on primary care IMS data. SBe highlighted that for a pharma model this was straightforward. Figures were based on annual growth in GLP-1 agonist prescribing divided by the cost of existing products gives a number of new patients being started on GLP-1 agonists. The estimated savings shown for Bristol in year 1 (2014) are £49,381 progressing in 2018 to £243,917 – however it was highlighted the real significance of the latter given the rate of advancements in medical technologies was probably not significant. The cost savings for North Somerset and South Glos were not included in the papers for the meeting, however tabled for the HoMM. If lixisenatide is used first line for new initiations, the estimated savings is £100,000.00 for BNSSG in year 1.

The expected outcomes from using lixisenatide should be the same as those given in NICE Clinical guidelines 87 although these may be seen as aspirational and the ABCD criteria (Association of British Clinical Diabetologists) may be more considered more appropriate.

The wider use of lixisenatide in combination with insulin was discussed, although not critically appraised, considered appropriate.

The JFG considered the application for the inclusion of lixisenatide in the formulary and as previously minuted it was considered non-inferior to other GLP1-agonists or a “me too” drug. The manufacturers list price for lixisenatide places it as the most cost-effective GLP-1 agonist on the market and although in general pharma costing models should be used with caution the simplicity of the model does provide evidence that lixisenatide has the potential to be the most cost-effective option in new patients.

The JFG agreed to add this drug first line as per criteria in NICE clinical guidance 87 TLS Green. Exenatide and liraglutide would remain on the formulary but would be an alternative agents, and therefore TLS blue. All new patients to be recommended to initiated on Lixisenatide.

**Action:**

1. NB to add to formulary first line for use in line with the NICE criteria given in clinical guidelines 87 TLS Green

2. NB to inform applicant

*Drug is in tariff*

*NB – await directorate sign off*

*UBT – await directorate sign off*
Weston – await directorate sign off
Primary Care – approved for use

d. Renavit

This application was submitted by Dr CT Consultant Renal Physician who was not present at the meeting to present the application. The application was presented by NB.

For full details please see application form.

The application was for the inclusion of Renavit for the dietary management of water soluble vitamin deficiency in patients with chronic kidney disease. It is approved as ACBS – food for special medical purposes and thus is listed in the drug tariff. If approved, this application would replace Dialyvit® which is an unlicensed drug and therefore can attract large acquisition costs within the community.

There is more vitamin C in Renavit which the applicant considered, but concluded that this should not be an issue, as the change in plasma oxalate concentration associated with this change in ascorbic acid intake is likely to be minimal.

The number of patients this would affect was not included in the application but the number of patients that would be treated with Renavit would not differ compared to those currently taking Dialyvit.

Renavit is in tariff and is approximately half the price of Dialyvit. There will be additional cost savings compared to Dialyvit as this is not an unlicensed special.

NB to confirm with the applicant if it is safe to switch patients from Dialyvit® to renavit and to establish numbers.

The JFG considered the application and the cost savings to the primary care drugs budget due to this product being approximately half the cost of Dialyvit. The committee agreed to add this drug TLS blue for patients receiving renal dialysis in place of Dialyvit as a direct substitution that is more cost-effective.

If it is possible to switch patients from Dialyvit® to renavit, then Dialyvit® to be removed from formulary. The prescribing guidance will need to be updated to reflect use of renavit.

Action:
1. NB to confirm if it is possible to switch patients to renavit and to update the website and establish numbers.
2. DK to inform applicant.

Drug is in tariff
NBT – awaiting directorate approval
UBT – NA
Weston – NA
Primary Care – NA
e. Artiss®

This application was submitted by Mr PW Consultant Plastic Surgeon NBT. The applicant had been invited to attend the meeting.

For full details please see application form.

The application was for the inclusion of Artiss®, which is a tissue glue/seal subcutaneous tissue in plastic, reconstructive and burn surgery as a replacement or an adjunct to sutures or staples.

Treatment with Artiss® would be considered on a case by case basis where the use of standard surgical techniques may be insufficient to produce the required fixation or subcutaneous haemostasis and where the desire to eliminate the existing or potential intra operative or post-operative complications is considered essential.

Artiss® is a modified version of Tisseel® (currently used at NBT and on the formulary, chapter 2.11) produced by Baxter. The annual spend at NBT for Tiseel is around 50K. Artiss is more appropriate for plastic surgery (and reconstructive and burns) procedures as it does not set as quickly, allowing more time for manipulation of tissue. Artiss will all enable a wider usage in a different spectrum of surgery and therefore a different cohort of patients compared to Tiseel.

The cost of Artiss® is £88.75 more expensive than Tisseel® for 10mls although the 4ml vial would be most likely used which costs £195.00.

The formulary pharmacist who undertook the critical appraisal recommended the inclusion of Artiss® to the formulary. In order for a product to be included in the formulary, the group have to assess the product on against a number of criteria (see above). It was felt in this case, that there was insufficient appraisal of the evidence to enable to the JFG to accurately assess efficacy and thus its place in therapy.

The JFG was unable to consider the application fully as:
- the applicant was unable to attend the meeting to present the application
- the application lacked the financial impact of using this drug i.e. the number of patients it would be used on
- the application lacked sufficient clinical evidence.
- the application lacked an appraisal of the evidence to supports it’s use

NB to write to applicant and invite to a future meeting.

Action:
1. NB to inform applicant and invite to future meeting

Drug is PbR excluded
NBT – await directorate sign off
UBT – NA
Weston – NA
Primary Care - NA

f. Teriparartide
This application was submitted by Dr KH Consultant Orthogeriatrician NBT. The applicant had hoped to attend the meeting to present the application but was unable to attend.

For full details please see application form.

The applicant was for the inclusion of teriparatide (Forsteo®) onto the formulary to improve the healing of atypical femoral fractures (AFF). The product is not licenced for this indication. The incidence of atypical femoral fractures is rare but actual numbers are unknown. It is suggested that it would be used in 4 patients per annum at NBT.

CM had undertaken an evidence summary on teriparatide for atypical femoral fractures. The conclusions to this…

‘Unfortunately, at present, is impossible to set out exactly the positive effect of teriparatide on AFF healing in humans. The low quality observational literature reporting use of teriparatide in promoting bone healing is only able to suggest efficacy with a very low degree of certainty. Reports of successfully treated non-unions are increasing, but publication bias is likely to play a part. Moreover, there are a few reported cases of patients sustaining an AFF whilst taking teriparatide and a bisphosphonate. The available randomised studies have been undertaken in different fracture populations and do suggest a role for teriparatide as a healing promoter. However the study on wrist fractures failed to demonstrate a dose dependent effect and the study on pubic fracture was not double-blinded.

Although use of teriparatide could be an alternative option during conservative treatment of AFF, evidence of its usefulness is still lacking, and well-designed studies are necessary to verify the efficacy of teriparatide for this indication. However, given the rarity of the condition, adequately powered robust RCTs are unlikely. The current guidelines Atypical subtrochanteric and diaphyseal femoral fractures: Second report of a task force of the American Society for Bone and Mineral Research reflect the uncertainty around the evidence base, stating that there is inconsistent evidence that teriparatide may advance healing of AFFs.

The Individual funding route (IFR) would not be appropriate because there is an identified cohort of patients.

The cost for 30 days treatment is £291.30 and the patient could be treated for 12 months.

The JFG was unable to fully consider this application as Dr KH had been unable to attend the meeting to present the application and the clinical evidence did not support the inclusion of the drug into the formulary. The JFG decided to defer the decision to a future meeting when the questions raised could be answered.

NB to write to applicant to request further information and invite to a future meeting.

Action:
1. NB to write to applicant and invite to future meeting to discuss inclusion

Drug is PbR excluded
NBT – directorate approval would be required in approved
UBT – NA
Weston – NA
g. Insulin Degludec

This application was submitted by VR Specialist Pharmacist NBT and was supported by Dr FC and Prof B. It had been discussed at the 4th June 2013 JFG meeting but the applicant had been unable to attend. From this meeting, it is minuted that

- The JFG considered the application and the evidence in the critical appraisal. In terms of effectiveness, it has been shown that degludec is non-inferior to insulin glargine in terms of glycaemic control and that nocturnal hypoglycaemia was reduced (a small but statistically significant reduction). It is considerably more expensive than insulin glargine. The applicant has suggested restricted cohorts in order to restrict prescribing to those likely to benefit most. The drug is in tariff. The JFG agreed to add degludec to the formulary but due to the lack of strong evidence and its cost, only for patients who had failed on insulin glargine and were not suitable/had failed on insulin pump therapy, TLS Red.

However, in discussion around the request for change from TLS Red to amber (minuted in section 5), it was highlighted that the decision to place insulin degludec after insulin pump therapy in the patient pathway would not be appropriate, as a patient would be unlikely to be taken off a pump if it is initiated. Its use should be before insulin pump.

The JFG considered the information supplied and agreed that as the applicant had been unable to attend to present, NB would write to the applicant (and those supporting the application) requesting further information on the cohort of patients in which this would be used and to bring back to the next meeting for further discussion.

Action:
1. NB to write to applicant and add to agenda once information received.

5. Shared Care Protocols

SCP had been raised at the BNSSG D&TC meeting held on the 25th July 2013 as a quality issue because there had been insufficient time to discuss these at the last few JFG meetings. It was agreed that extra support would be provided by North Somerset CCG and that there would be greater involvement of the GP members of the JFG before the SCPs are brought to the JFG meeting for ratification.

Comments has been received from CR and KA about the SCPs

a. Methotrexate in Dermatology UHB and NBT

SCP author Dr CK

Methotrexate currently on the formulary oral amber 3 months for the treatment of Eczema and Psoriasis (Chapter 13.5)

The methotrexate SCP had been transferred to the new template but NB to check as some of the information appears to be repeated (subsequent tests page 2) and also subsequent tests to
be reviewed against the rheumatology SCP. Page 5 - other specific to drug point 2 to be removed. CR had raised a workload issue and not a clinical issue in relation to this SCP. Monitoring of methotrexate is covered by the near patient testing LES and thus the GPs will be paid through this for the monitoring of this drug. The SCP was signed off subject to the amendments.

Action:
1. NB to check SCP and make amendments and add to formulary

b. Aripiprazole
SCP author BS Formulary Pharmacist AWP
On the formulary section 4.2.1 Antipsychotic drugs.
This is an update of an existing SCP written in 2009.
There was concern expressed as to whether AWP was undertaking the baseline and 3 month monitoring.
NB to amend SCP to reflect actual required monitoring that is realistic and safe for the patient. The current SCP is quite detailed and includes some monitoring that would be best practice but not actually required. The SCP monitoring should be appropriate for the drug only and not the disease. GP systems have a template for the annual review of mental health patients. Side effects could have a link to the SPC (summary of product characteristics).
The amended SCP to be sent to JFG GP members and then to be brought back to the meeting

Action:
1. NB to amend SCP and circulate to JFG GP members for comment

c. Atypical Antipsychotic depots
SCP author BS Formulary Pharmacist AWP
On the formulary section 4.2.2 Antipsychotic depot injections (amber 1 month)
- Flupentixol decanoate
- Fluphenazine decanoate
- Haloperidol decanoate
- Zuclopenthixol decanoate
- Pipotiazine palmitate
These drugs are on the formulary but there is no SCP for them.
There are metabolic problems associated with these drugs and therefore monitoring is required. NB to amended SCP in light of comments made above and the amended SCP to be sent to JFG GP members and then to be brought back to the meeting

Action:
1. NB to amend SCP and circulate to JFG GP members for comment

d. Change in TLS Status Prucalopride – Amber to Green
Currently on formulary chapter 1.6 amber in accordance with TA 211. This drug had been added to the formulary with a TLS status of amber to ensure that the patient was seen by a consultant / specialist and that the constipation was not masking anything more serious.

The NICE TA 211 specifies a clinician with experience of chronic constipation which the applicant feels GPs have. Most patients have functional problems and restricting of prescribing to amber will not mean that those few patients with other issues e.g. sub-acute bowel obstruction will not be missed. There needs to be guidance and education for GP.

The JFG agreed the change in TLS status from amber to blue on the advice of a specialist service.

Action:
1. NB to change TLS status to blue on the advice on a specialist service
e. Tapentadol MR for chronic pain Change in TLS Red to Amber 3 months
SCP author Dr PB Feb 2013, amended DK September 2013.
‘Tapentadol (Immediate release IR and modified release MR) (TLS Red) Chapter 4.7.2
• should be reserved for the management of severe chronic pain in adults who cannot tolerate other strong opioids e.g. morphine sulphate or oxycodone, on recommendation of the pain team or palliative care.’

The initial SCP was for modified release only but DK requested that immediate release was also considered (the SCP would need to be amended to reflect this if this was approved).

An issue with Tapentadol being red is that this is a controlled drug a prescription can only be written for 4 weeks and therefore there is more of an administrative burden in the prescribing of this drug compared with other red drugs.

There was concern that this drug especially IR would be prescribed by GPs without referring to the specialist clinics.

DK to supply the number of patients currently on this drug in order for medicines management teams to be able to monitor growth in the primary care budget.

The safety and monitoring of this drug is no different from other opioid drugs and the risk of abuse / diversion is the same. Tapentadol MR has been on the formulary for over 1 year now, and so local experience has been gained.

SM requested slight amendments to the SCP.

The JFG agreed to the application for the change in modified release from red to amber but for immediate release to remain red.

DK to link with RB N Somerset CCG author of the chronic pain guidelines

Action:
1. DK to amend SCP and supply number of patients currently on this drug
2. NB to update website to reflect change in status for modified release from red to amber once SCP completed.
f. Rufinamide

No SCP had been received

Action:
1. None

g. Azathioprine for IBD (NBT)
SCP author AP

Chapter 1.5.3 TLS Amber with SCP.

See below for joint discussion

Action:
1. See below

h. Mercaptopurine for IBD (NBT)

SCP author AP

Chapter 1.5.3 TLS Amber with SCP.

These are updates of the current SCPs which require review. Prior to the JFG group becoming a stand-alone committee and no longer reporting to the BNSSG D&TC, it had been agreed at BNSSG D&TC meeting on 22nd November 2012 as minuted below

- The committee agreed that although ideally SCPs should be BNSSG wide, it is better to have an up to date SCP for one / two trusts than to have an out of date SCP or no SCP at all.

However, at this meeting the Chair of the JFG felt that there should be a joint SCP across UHB and NBT and that since these updates were provided because the current NBT SCPs were due to be reviewed (last approved September 2010) and not a result of a significant change in the monitoring requirements of these drugs and that as the UHB SCPs were also due to be reviewed, then a joint SCP should be written.

Action:
1. HC to liaise with AP over joint UHB / NBT SCPs for IBD

i. Insulin Degludec (NBT)

SCP author VR

Insulin degludec had been approved for the inclusion to the formulary in June 2013 TLS red. There was discussion over the place of insulin degludec in the patient pathway and this is minuted in Section 4 NDRs.

The request for change was because if the TLS remains red then there will be a need for the patient to attend an outpatient appointment in order for the drug to be prescribed but this is the case with all red drugs. GPs will not be familiar with Degludec. There is a need to gain experience / safety data in using this drug. The consultants at NBT had been involved with the
trials and therefore are in a position to know how to manage patients on Degludec.

The JFG did not approve the request to change from red to amber 3 months as this drug is currently unknown in primary care.

**Action:**
1. NB to inform author

j. **Hydroxychloroquine in Dermatology (UHB)**

SCP author RC (MI pharmacist)

Currently only on formulary for under section 10.1.3 Drugs which suppress the rheumatic disease process with a note that it is also licensed for active rheumatoid arthritis, systemic and discoid lupus erythematosus and dermatological conditions caused or aggravated by sunlight

No comments had been received from the GPs and therefore the SCP was approved amber 3 months

**Action:**
1. NB to add SCP to amend SCP to show amber 3 months section 8 and 9 and add to website

6. **Individual Funding Requests**

No discussion occurred at this meeting

**Action:**
1. None

7. **Chapter Review**

NB and HC to take this forward

**Action:**
1. None

8. **Specialised Commissioning Statements**

No new statements for discussion.

TW (NHSE SW Area Team Specialised Commissioning Pharmacist) notes for the JFG (not discussed at the meeting):

- The specialised commissioning manual is being republished in October and the drugs list will be an appendix. The plan is to have a mini update of the drug list monthly and a full review once a quarter.
• IFRs are now being directed by the indication and not the drug list.
• The drug list will be reviewed to include information on whether each drug should stay with secondary care or is suitable for shared care with the GP.
• Approved NHS England policies and service specs have been published on the website (www.england.nhs.uk)
• There are some new policies this month (circulars attached with link to the policy at the bottom of each circular):
  
  Plerixafor for stem cell mobilisation
  Eculizumab for atypical Haemolytic Uraemic Syndrome (aHUS)
  Stribild® for the treatment of HIV-1 infection in adults
  Stereotactic Radiosurgery (SRS) / radiotherapy (SRT) for Glomus Tumour (skull base para
  Stereotactic Radiosurgery (SRS) / Radiotherapy (SRT) for Meningioma
  Stereotactic Radiosurgery (SRS) / Radiotherapy (SRT) for Pituitary Adenoma and Ocular
  Stereotactic Radiosurgery (SRS) / Radiotherapy (SRT) for Cavernous Venous Malformation
  Rituximab for Systematic Lupus Erythematosus

• There are a number of other policies in development. It is expected that the first tranche will be published on or just after 1st April 2014.
• The Medicines Optimisation CRG has been recruited to and will meet for the first time in October. Andrew Davies and Steve Brown are local members. The 2 initial priorities for the CRG will be a national gain share agreement and national guidance on repatriation of transplant drugs from GPs to secondary care (not necessarily the specialised centre at this stage)
• QIPP discussions are on-going and open to new ideas.
• Derogation will be starting on 1st October 2013 based on the self-assessment service spec compliance from each provider. Happy to discuss further if anyone wants more info and I will be talking to the SPMs on Friday.

  Action:
  1. None

9. MHRA Drug Safety Update – May to August

  NB to send out summary after meeting

  Action:
  1. NB to send out summary

10. Formulary Process

  a. Update

  NB to send out summary after meeting

  Action:
  1. NB to send out summary
11. Items for discussion

a. **Strontium advice for referral**
   This advice had been written by Dr SC Consultant Osteoporosis Service UHB in light of the MHRA drug safety update April 2013. Weston AHT was in agreement with the advice but NB awaiting response from NBT (KH). Guidance to be amended to reflect CCG rather than PCT.

b. **Sodium Chloride 7% (Nebusal®)**
   For information only
   There had been discussion between NBT and UHB concerning the use of sodium chloride 7% (Nebusal®) instead of sodium chloride 6% (Mucoclear®) which was currently on the formulary as TLS red for sputum induction. Mucoclear® and Nebusal® are the same price per unit. Chapter 3.7 was updated to include sodium chloride 7% TLS red without a NDR being submitted.

12. AOB

a. **NDRs**
   It was agreed that due to time constraints that the number of NDRs would be reduced to 6 per meeting.

b. **Consultant Representation from UHB**
   ER Consultant Emergency Medicine University Hospitals Bristol NHS Foundation Trust Bristol would be adding these meetings.
### 2013 Dates for Meetings

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<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs</th>
<th>Cut off for SCPs</th>
<th>Time</th>
<th>Venue</th>
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<tr>
<td>Tuesday 15&lt;sup&gt;th&lt;/sup&gt; October</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; September</td>
<td>25&lt;sup&gt;th&lt;/sup&gt; September</td>
<td>10.00 – 13.00</td>
<td>NBT, Southmead Pharmacy Seminar Room</td>
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<tr>
<td>Wednesday 6&lt;sup&gt;th&lt;/sup&gt; November</td>
<td>Additional Date</td>
<td>25&lt;sup&gt;th&lt;/sup&gt; September</td>
<td>16&lt;sup&gt;th&lt;/sup&gt; October</td>
<td>10.00 – 13.00</td>
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<td>29&lt;sup&gt;th&lt;/sup&gt; October</td>
<td>19&lt;sup&gt;th&lt;/sup&gt; November</td>
<td>10.00 – 13.00</td>
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### 2014 Dates for Meetings

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<tr>
<th>Date</th>
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<th>Cut off for SCPs</th>
<th>Time</th>
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<td>Tuesday 21&lt;sup&gt;st&lt;/sup&gt; January 2014</td>
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<td>Tuesday 4&lt;sup&gt;th&lt;/sup&gt; March 2014</td>
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<td>Tuesday 22&lt;sup&gt;nd&lt;/sup&gt; April 2014</td>
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<td>Tuesday 2nd September 2014</td>
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<td>Tuesday 14th October 2014</td>
<td>10 am to 1pm</td>
<td>Pharmacy Seminar Room Brunel Building Southmead Hospital</td>
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<tr>
<td>Tuesday 25th November 2014</td>
<td>10 am to 1pm</td>
<td>Boardroom South Plaza</td>
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1. Welcome & Apologies & Declarations of Interest

**Present**
- Public Health Consultant, Bristol City Council (Chair)
- Interface pharmacist, NHS Bristol CCG
- Interface pharmacist, NHS Bristol CCG
- HoMM, NHS Bristol CCG
- Service Development Manager, NHS Bristol CCG
- HoMM, NHS North Somerset CCG
- Clinical Effectiveness Research Lead, Bristol City Council
- HoMM, NHS South Gloucestershire CCG
- Pharmacy Clinical Team Manager North Bristol NHS Trust
- Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust Bristol
- Consultant in Emergency Medicine, University Hospitals Bristol NHS Foundation Trust and Associate Director of Patient Safety, and Chair of UHB Medicines Advisory Group
- GP, Bristol and member of Bristol CCG Board
- Acting Formulary Pharmacist, North Bristol NHS Trust

**Apologies**
- Consultant Neurologist, North Bristol NHS Trust
- GP, North Somerset
- GP, Bristol
- Joint D&TC Chair, North Bristol NHS Trust
- Joint D&TC Chair, North Bristol NHS Trust
- Chief Pharmacist, AWP
- Nurse Prescriber, Bristol
- Director of Pharmacy Weston Area Health NHS Trust
- Formulary Pharmacist, AWP
- Pharmacist, University Hospitals NHS Foundation Trust Bristol, UHB

**Declarations of Interest**

None

The meeting was quorate until 11.30am

In accordance with the ToR of this group, the formulary pharmacist determined that the meeting should continue and will secure endorsement of any decisions ex-committee via email. Therefore decisions taken after this time will need to be ratified and actioned once approved.

2. Minutes from 10th September 2013 Meeting
The minutes from the Joint Formulary Group (JFG) meeting on the 10th September 2013 had been circulated by NB following the meeting.

The minutes of this meeting were approved.

Matters arising from September 2013 Meeting

a. CAF policies versus formulary
   SBe was continuing to work with the SWCSU to ensure they reflect formulary decisions and vice versa.
   
   Action:
   1. None

b. Alteplase and Dornase Alpha NDR
   No further progress on this – to be brought back to meeting once funding source confirmed.
   
   Action:
   1. None

c. Teriparatide
   The applicant Dr KH was unable to attend the 10th September to discuss the application but will be attending the JFG meeting on the 6th November 2013
   
   Action:
   1. None

3. NICE New Technology Appraisals published
   There were a total of 4 TAs published in September 2013
   
   Positive TA affecting the CCGs - none
   • None

   Positive TA affecting Specialised Commissioning
   • None

   TAs not recommended
   • TA 296 Lung cancer (non-small-cell, anaplastic lymphoma kinase fusion gene, previously treated) - crizotinib

   Terminated appraisal
   • None

   TLS Status for newly published TAs
   • NA
TAs adopted into the BNSSG Joint Formulary September 2013

- Pulmonary embolism and recurrent venous thromboembolism – Rivaroxaban TA 287 TLS Red until SCP agreed
- Type 2 diabetes - Dapagliflozin combination therapy TA 288
- Overactive bladder – Mirabegron TA 290 TLS Blue
- Macular degeneration (wet age-related) - Aflibercept (1st line) TA 294 TLS Red (early implemented)

4. New Drug Requests

Lisdexamfetamine
Approved for inclusion onto the formulary for a second line option for those patients with an inadequate response to methylamphetamine, TLS Red.

Levobupivacaine
Approved for inclusion onto the formulary on the grounds of improved patient safety compared to bupivacaine. TLS Red.

Dexmedetomidine
Approved for inclusion to the formulary for patients who are failing to wean from invasive ventilation with traditional management due to agitation. TLS Red.

Linaclotide
The decision to reject the application made at the meeting on the 10th September was upheld. More evidence is needed, and if submitted the group would reconsider. In order to identify a niche patient group that would derive the most benefit, the applicant could undertake a local research project.

Ingenol
Approved for inclusion to the Joint Formulary on the grounds of efficacy, cost, and ease of administration. TLS Green. Solaraze to remain on formulary.

Ferinject
Approved for inclusion to the Joint Formulary on the grounds of efficacy, cost, and reduction in administration time. TLS Red. There would potentially be a need for ongoing discussion relating to the tariff for the pre-op assessment clinic.

Ozurdex UHB
Approved for inclusion to the Joint Formulary – clinically appropriate and the financial modelling has shown that there are no cost implications by using Ozurdex. It is a licensed treatment for Uveitis, compared to the current pathway which involves using the biologics which are not licensed.

Decision Criteria used by JFG for NDR
- Patient safety
• Clinical effectiveness
• Cost effectiveness or resource impact
• Strength of evidence
• Place in therapy relative to available treatments
• National guidance and priorities
• Local health priorities
• Equity of access

a. Lisdexamfetamine NBT

This application was submitted by Dr RW Consultant Community Paediatrician NBT and attended the meeting to present the application.

Please see application form for full details.

This application was for the inclusion Lisdexamfetamine dimesylate (Elvanse) for the management of ADHD in children and adolescents. Lisdexamfetamine is indicated as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged 6 years of age and over when response to previous methylphenidate treatment is considered clinically inadequate. Lisdexamfetamine is a pharmacological inactive prodrug and on absorption from the GI tract is hydrolysed to dexamfetamine which is responsible for the drug’s activity.

It was initially presented by NB who undertook the critical appraisal work. In terms of evidence, there have been a number of trials published, of which 6 were included in the application. These were generally of short duration and some were open label and so it is difficult to make any definitive conclusions from these. There have been a number of national and regional reviews on Lisdexamfetamine. NICE have produced an evidence summary which was included in the papers, and its conclusions were based on one trial, which involved 300 children – both lisdexamfetamine and methylphenidate provided clinically meaningful and statistically benefits compared with placebo in controlling symptoms of ADHD. Also the SMC have reviewed the use of this drug in April and approved its use in line with its licensed indication. The All Wales Medicines Strategy Group has also recommended the use of lisdexamfetamine as an option. A recently published RCT, active comparator trial, comparing lisdexamfetamine with atomoxetine showed that there was a shorter time for first response for those treated with lisdexamfetamine compared with atomoxetine, and also a greater proportion of lisdexamfetamine patients achieved improvements in symptom scores and functioning than those treated with atomoxetine.

Concern was expressed over a lack of long term data, although it was suggested that as there is long term data for dexamfetamine, and lisdexamfetamine is broken down to dexamfetamine, there is unlikely to be any significant unknown long term problems.

Discussion with Dr RW

D RW suggested that the financial impact of using lisdexamfetamine may be less than stated in the application due to the use of drug holidays, which some patients chose to take whilst on stimulants, which is not possible when taking atomoxetine. Dr RW felt that there was still a place for atomoxetine and dexamfetamine on the formulary, and needs to be able to gain experience with the use of lisdexamfetamine before he can have an opinion on whether
lisdexamfetamine may replace dexamfetamine. It is not possible to extract this information from clinical trials. The choice of drugs is based on a threshold in terms of behaviour and agreed self-management. It is felt that by having lisdexamfetamine available, this is an option in a very small number of patients. Dr William’s case load is 40 to 50 patients with only 2 or 3 not taking methylphenidate.

Discussion by JFG following presentation

As there is a risk of diversion then only 28 days should be prescribed on a prescription at any one time. If its status as a controlled drug under Schedule 2 of the Misuse of Drugs Regulations (2001) is confirmed, then only 28 days prescribing is legally allowed.

NB raised the TLS status of dexamfetamine in children as this drug was included in TA 98 (published 2006) but there were only SCPs for methylphenidate and atomoxetine. NB to arrange for SCP for dexamfetamine to be written.

The drug is in tariff and is less expensive than atomoxetine.

- **Patient safety** – Lisdexamfetamine has a similar side effect profile compared to other stimulant agents. Very common adverse effects include decreased appetite, insomnia, dry mouth, headache, weight decrease and upper abdominal pain.
- **Clinical effectiveness** – Lisdexamfetamine has been evaluated in a number of clinical trials. In a 7 week RCT, both Lisdexamfetamine and methylamphetamine showed clinically and statistically significant benefits compared with placebo in controlling the symptoms of ADHD. When compared to atomoxetine in a RCT, treatment with lisdexamfetamine was associated with a shorter time to first response compared with atomoxetine. A greater proportion of lisdexamfetamine treated patients, achieved improvements in symptom scores and functioning than those treated with atomoxetine.
- **Cost effectiveness or resource impact** – Lisdexamfetamine can cost up to £1084.05 per year at maximum licensed dose, which is greater than dexamfetamine and methylamphetamine, but slightly less than atomoxetine. In the case submitted to the SMC (comparing lisdexamfetamine and atomoxetine), the result of the base case analysis was a cost per QALY of £6,969.
- **Strength of evidence** – Whilst there are limitations to the studies included in the original application, the 7 week European trial was appropriately designed and the analysis of results was appropriate to demonstrate the short term effectiveness of lisdexamfetamine compared with placebo. Longer term trial data have not been published fully as yet, but do show maintenance of response at 26 weeks. Lisdexamfetamine has been compared to an active comparator – atomoxetine, which is appropriate as it is considered as an alternative to atomoxetine.
- **Place in therapy relative to available treatments** – Lisdexamfetamine is licensed in ADHD refractory to methylamphetamine. It is appropriate as a second line agent, it has not been shown to be more efficacious than methylamphetamine.
- **National guidance and priorities** – There is a NICE summary reporting on lisdexamfetamine, using the European 7 week trial as a basis of analysis. The SMC have accepted its use, as the All Wales Group has.
- **Local health priorities** – It is suggested that locally the prevalence rate of 5% in school age children. Mental Health is a local health priority.
- **Equity of access** – The SMC and All Wales group have accepted it for use within Scotland and Wales.
The JFG considered the application and the evidence and information submitted. There is evidence to suggest that it is an appropriate second line agent alongside dexamfetamine and atomoxetine. It was approved as a second line option when there has been an inadequate response to methylphenidate, TLS Red. The JFG has requested that the applicant brings a report back to the group in 18 month’s time documenting the number of patients that it has been initiated in, duration of treatment and outcomes.

Action:
1. NB to add to formulary website once directorate approval received
2. SCP for dexamfetamine in accordance with TA 98 to be written.

b. Levobupivacaine NBT and UHB

This application was submitted by Mr JW, Consultant Anaesthetist, NBT and supported by Mr MM, Consultant Anaesthetist, UHB. Mr JW attended the meeting to present the application with TK anaesthetist Registrar UHB.

For full details please see application form.

This application was for the inclusion levobupivacaine for regional anaesthesia and epidural top up allowing surgery to be carried out in a pain free manner with the possibility of avoidance general anaesthesia. Bupivacaine would continue to be used for local infiltration and other indications where large doses are not used. Levobupivacaine is currently used at UHB – it was agreed by MAG a few years ago for use in Ophthalmology only.

Discussion with Mr JW and Mr TL

Levobupivacaine is a stereoisomer of bupivacaine, which has been in use since the 70’s. Toxicity is an issue with bupivacaine which is why levobupivacaine was developed, and has been available since 1999. It has been shown to have a better safety profile, with a reduced number of arrhythmias seen. It has a 1.5 times greater toxic threshold compared to bupivacaine. Bupivacaine binds to the sodium channels in the heart, and levobupivacaine has less of an affinity for these, and is therefore less cardiototoxic.

The manner in which Levobupivacaine would be used would be identical to the current use of bupivacaine. It has less potent motor blockade (spinal) than bupivacaine but this may be considered advantageous as there is quicker motor recovery. They considered that the use would be in patients undergoing regional anaesthesia for orthopaedic and vascular surgery and mothers in labour who require a local anaesthetic top up of their epidurals.

Levobupivacaine and Bupivacaine are considered equipotent in terms of dose. The safety of having two similar drugs available and the potential of a medication error in using the wrong drug was raised but this was not considered to be a problem. If there was a decision that there would be a larger switch from bupivacaine to levobupivacaine then there would be need for some education.

- **Patient safety** – Levobupivacaine is a safer agent than bupivacaine with a lower risk of CNS and cardiac toxicity.
- **Clinical effectiveness** – There are trials and reviews that have shown that
levobupivacaine has a clinical profile similar to bupivacaine.

- **Cost effectiveness or resource impact** – These are in tariff agents. The resource impact is related to the use of non-sterile versus sterile wrapped products. Both the levobupivacaine products are costed equally; however the sterile wrapped bupivacaine product is £1.17 per vial more. Therefore if a switch was to be made for all products, there would be a cost pressure by using the non-sterile wrapped, but a cost saving when using sterile wrapped levobupivacaine.

- **Strength of evidence** – A series of reviews and RCTs have evaluated the use of these agents.

- **Place in therapy relative to available treatments** – Choice of agent is down to anaesthetist. Levobupivacaine has been shown to have a better safety profile and therefore should be used first line.

- **National guidance and priorities** - None

- **Local health priorities** – NA

- **Equity of access** – NA

The JFG considered the application and the evidence and information submitted. It has been approved for inclusion to the Joint Formulary on the grounds of patient safety. The individual acute trusts to determine appropriate roll out strategy

**Action:**

1. NB to add to formulary TLS Red

c. **Dexmedetomidine**

The original application was submitted by Dr KR and was discussed on the 29th May 2013. The application was for the use of the drug in:

- a) the sedation of adults on ICU who require a sedation level not deeper that arousal in response to verbal stimulation
- b) for the weaning of patients in previous / anticipated difficult to wean
- c) the prevention of delirium in at risk patients

Dexmedetomidine is an alpha-2 agonist which represents an alternative sedative agent to standard agents, such as propofol and midazolam, with anxiolytic and analgesic properties. It facilitates the concept of “awake sedation” and whilst it has only been licensed as sedative agent in Europe since September 2011 the USA and Australia have over 10 years of experience.

At this meeting, the decision made was minuted:

- Whilst not wanting to hold back innovation, the committee decided not to approve this application as it considered the drug was being used in an experimental way which was out of the remit of this committee and the evidence and cost did not support its use. It was also thought that a 6 month trial would not add to the evidence base as the numbers of patients would be so small. The committee would be happy to reconsider the application once further evidence is available.

UHB medical division had approved the financial spend associated with this drug whilst the original NDR had been submitted to the JFG. Subsequent to the JFG decision, Dexmedetomidine has been used in UHB and Dr KR had undertaken an audit of those patients
Discussion with Dr KR and JW (ITU pharmacist)

The audit was undertaken to identify patients groups in which Dexmedetomidine would have the most benefit and impact. Over the 6 month audit period, Dexmedetomidine was given in 32 patients, with 21 of these (66%) showing benefit from using the agent. Dexmedetomidine was used on 32 patients in the first 6 months and a further 39 patients in the following 6 months (the second 6 month audit has not been evaluated as yet). This is a total of 71 patients which is approximately 5% of the patients through ITU (1200 patients).

Extubation was facilitated after failing on conventional therapy in 18 patients and intubation was avoided due to clinical improvement on Dexmedetomidine in 3 cases. The group of patients identified as having most benefit was in ventilated patients where there is no physical reason not to extubate, though it is not safe due to agitation, and thus the patient would remain in ITU with the possibility of needing a tracheostomy. The use of Dexmedetomidine can facilitate extubation thus freeing up resources (ITU beds). This will reduce the penalty applied to the hospital (£680.00) for the cancellation of operations in patients who require ITU following surgery.

It is known that:

- Dexmedetomidine is safe for sedation on adult ICU (PRODEX Study)
- Dexmedetomidine not inferior to propofol in terms of time at target sedation level
- A shorter time to extubation with respect to propofol
- Significant increase in nurse’s visual analogue scale (assessment of arousability, co-operation and communication of pain)
- Multiple (small) studies showing trend to reduced agitation/delirium with Dexmedetomidine, but nothing scientifically rigorous
- Increasingly included in sedation guidelines for hyperactive patients internationally
- Audits from other trusts have suggested benefits in patients suffering from delirium

Over 80 trusts are now using this drug on their formulary with 39 of these having trialled the drug first to show the benefits of using it. Many trusts had similar concerns as expressed by the JFG back in 2012 when the original application was discussed. Since the original application, both the SMC and the All Wales Medicines Strategy Group have evaluated Dexmedetomidine. Both the groups accepted its use for sedation in intensive care.

There were very little adverse effects but it does not work in every patient. If the drug has not worked within 48 hours it is stopped and the patient will then be given a tracheostomy, thus the use of this drug will increase length of stay in ITU in a few patients. 37% of patients in the first 6 months failed on dexmedetomidine (11 out of 32).

The audit also worked through the potential financial benefit by using Dexmedetomidine. It was identified that over the 6 months period, savings greater than the cost of the drug have been realised.

Discussion

The process followed in May 2012 and the decision to reject the application due to a lack of evidence made by the group was assessed as correct at the time. This review and presentation of the audit had provided the JFG with more evidence in terms of patient benefit.
• **Patient safety** – Dexmedetomidine has been shown to be well tolerated, with little adverse effects.

• **Clinical effectiveness** – Two similar, phase III studies are pivotal in supporting the use of dexmedetomidine in ICU patients requiring light to moderate sedation: one versus propofol (PRODEX) and one versus midazolam (MIDEX). They were of multi-centre, randomised and double-blind design. They were designed first to determine non-inferiority (using a margin of 15%) of dexmedetomidine versus either propofol or midazolam in terms of maintaining a target depth of sedation, and then superiority in terms of reduced duration of mechanical ventilation. These studies provide data versus relevant comparators (propofol and midazolam) using co-primary endpoints of direct health outcomes. In both studies, dexmedetomidine was found to be as effective as (non-inferior to) the active comparator (propofol or midazolam) in terms of time in the target sedation range.

• **Cost effectiveness or resource impact** – This is in tariff. The audit identified that there were savings made by using Dexmedetomidine, by reducing ITU stay, and the number of operations being cancelled due to lack of ITU beds. These savings offset the additional acquisition cost of Dexmedetomidine.

• **Strength of evidence** – Whilst there are some limitations of the trials, they are generally well designed RCTs.

• **Place in therapy relative to available treatments** – Only to be used in those patients who are appropriate to extubate but can’t due to agitation.

• **National guidance and priorities** – The SMC and AWMSG have approved its use, in a larger patient group than the group identified here.

• **Local health priorities** – NA

• **Equity of access** – It is widely used throughout England.

The JFG considered the audit results for use of Dexmedetomidine in ITU. It was considered that an appropriate niche group of patients had been identified, that would provide it as a cost-effective option, bringing also a number of additional benefits to the patient and the ITU department. Approved for inclusion to the formulary for patients who are failing to wean from invasive ventilation with traditional management due to agitation. UHB to submit ongoing audit on the use of dexmedetomidine.

**Action:**
1. NB to added to formulary TLS Red for use at UHB only
2. UHB to undertake on going audit of this drug.

d. **Linaclotide UHB and primary care**

This application had been discussed at the last meeting which was not quorate. The decision made by the group at the meeting was to reject the application as the clinical evidence did not support the inclusion into the formulary, although the JFG acknowledged that this was a novel drug and there would be an emerging evidence base. After the September meeting, NB had sent out the minutes for e-approval in accordance with the Terms of Reference of the group. The applicant had also been informed of the decision who subsequently expressed a number of
concerns.

- **Evidence** – the applicant feels that although the numbers in the studies are small, the results are still highly significant
- **IBS and its management** – the applicant feels that the group did not have a handle on IBS and the impact on primary care. The decision made was felt to be more based on drug cost rather than the wider impact on the health economy.
- **The meeting was not quorate**, and therefore why did it go ahead.

In order to address the concerns, NB had sent these comments for further consideration by HF, KA and JB – the clinician members of the group. Both HF and KA felt that whilst this was a novel agent, a niche cohort of patients needs to be identified. Whilst the two RCTs are not without merit, there is a lack of cost-benefit analysis. If Linaclotide were to be prescribed widely, this would be inappropriate based on current evidence, but if a selected population with severe IBS who have failed all other therapy could be clearly established then the use of Linaclotide may be appropriate. DC had also spoken with JB who approved the decision made by the group to reject the application. KA stated that the evidence does not support its use and there is no evidence that it will reduce the number of patients sent for a colonoscopy.

The JFG decision was supported by other area prescribing teams e.g. East Kent Prescribing group who had also rejected it.

In response to the applicants concerns, the group felt:

- **Evidence** – The absence of active comparator studies makes it difficult to assess linaclotide’s place in therapy or relative effectiveness compared to existing treatments. The precise size of the target population for linaclotide is difficult to estimate, and there is a high probability that it may be larger than anticipated.
- **IBS and its management** – The criticism of the group not looking at the whole patient pathway was felt to be invalid. The decision made was based on looking at all of the criteria: Patient safety, Clinical effectiveness, Cost effectiveness or resource impact, Strength of evidence, Place in therapy relative to available treatments, National guidance and priorities, Local health priorities, Equity of access. Overall the JFG felt that the higher cost of linaclotide compared to existing treatments was not offset by a sufficiently large clinical benefit.
- **The meeting was not quorate.** The group followed the process as outlined in the JFG if the meeting is not quorate, and sent around the decisions for e-approval.

Chair – more evidence is needed, and if submitted the group would reconsider. The group upheld the decision made at the previous meeting, which is supported by the clinician members. The group felt that in order to identify a niche patient group that would derive the most benefit, the applicant could undertake a local research project.

**Action**

1. NB to inform applicant

KA and ER left the meeting, therefore the group was no longer quorate, and any decision will need e approval.

e. Ingenol (Picato)
This application was submitted by Dr MK, Consultant Dermatologist, WAHT who attended the meeting the present the application.

For full details please see application form.

The applicant was for the inclusion of ingenol for non hyperkeratotic, non hypertrophic actinic keratosis of the face, scalp, trunk and extremities.

NB conducted the critical appraisal and presented to the group. The main advantage to this agent is that it has a shorter duration than products currently on the formulary and is suitable for larger areas than existing products. It is reported that compliance is around 97-98%.

Currently on the formulary are

- Fluorouracil cream (Efudix) for the management of superficial malignant and pre-malignant skin lesions.
- Diclofenac 3% gel (Solaraze) - actinic keratosis
- Fluorouracil 0.5% and salicylic acid 10% (Actikerall) - hyperkeratotic actinic keratosis

The SMC and the All Wales group have approved the use of Ingenol and there is a NICE evidence summary. There have also been a number of regional reviews that were used to appraise this drug for BNSSG. Against placebo, the trials conducted have shown that Ingenol is more efficacious than placebo. There have been no active comparator studies. However, a Cochrane conducted a review on interventions for actinic keratosis, and Ingenol was included. The conclusions to this were that for field directed treatments there was no one option that was significantly better than another. All had similar efficacy, but their associated adverse events and cosmetic outcomes were different. A Medicines and Embase search identified a Network analysis of interventions for AK – this was a follow up on the Cochrane review. A Medline and Embase search identified a Network analysis of interventions for AK. This was a follow up on the Cochrane review. The conclusions to this were that 5 FU was ranked top, with 5 amino-laevulinic acid, photodynamic therapy, Imiquimod, Ingenol and methyl aminolaevulinate photodynamic therapy equally ranked second, and cryotherapy as sixth, Diclofenac seventh, and placebo Eight. It appears that 5 FU on the basis of this should be the treatment of choice, however this is not as well tolerated by patients. No further studies were identified.

Costs – It is currently less expensive than Solaraze but Solaraze is likely to go generic in the next few years and therefore it is likely to become cheaper.

Somerset have included Ingenol on their formulary and removed Solaraze.

Analysis of Bristol CCG E-pact data showed that there have already been 11 prescriptions of Ingenol since May this year. Within Bristol CCG during Aug 12 - July 13, the total amount spent on the AK field directed treatments was £78,086.19. Diclofenac holds approximately 50% of the market share currently within BNSSG.

ePACT data shows ingenol has already been prescribed in Bristol.

Discussion with Dr MK

Treatment options - if the AK is well defined, these can be excised. With the other local treatments, patients need to be counselled due to the inflammatory reaction that will occur.
Ingenol is used for 2 to 3 days and the reaction occurs after this and therefore compliance is increased. Other available drugs are not licensed for use on large areas except for Solaraze. When using Ingenol, a positive change will be evident within two weeks, compared to Solaraze can take up to 3 months to see effect.

The applicant sees ingenol to be essentially a primary care drug and for GPs to refer into secondary care if necessary e.g. unsure of diagnosis. If it is mild moisturiser can be used and some will disappear spontaneously.

- **Patient safety** – In trials, the majority of the reported adverse reactions and local skin responses were mild to moderate in intensity and all resolved without sequelae. Application site reactions were the most commonly reported treatment-related AE (apart from LSRs, which were reported separately).

- **Clinical effectiveness** – Ingenol has been shown to be more efficacious than placebo, but there are no active comparator studies. Cochrane’s review on AK treatments found that within the field directed options, no one option was significantly better than another.

- **Cost effectiveness or resource impact** – The acquisition cost of Ingenol is less than Solaraze currently (100g tube). It is felt that if Ingenol were to be added to the formulary, it would reduce the amount of Solaraze prescribing and therefore a cost reduction should be seen.

- **Strength of evidence** - the four pivotal trials involving Ingenol were all phase III studies, multicentre, randomised, double blind, vehicle controlled trials. A significant issue is that we have not got access to active comparator trials which limit our assessment in terms of place in therapy. The studies were however well designed and used a suitable primary outcome measure of ‘complete clearance.’ There is no data on repeated use, although a study id due to be reported in 2014. Blinding may have been an issue due to the presence of local skin reactions. Long term data is limited to observational 12 month follow up.

- **Place in therapy relative to available treatments** – there are no active comparator studies, therefore it makes it difficult to place Ingenol in the pathway. However, the network meta-analysis found that 5FU was the most efficacious, with the other agents equally as efficacious. With the advantages that Ingenol has in terms of administration, it, and also cost, it would seem sensible to place this as an option, behind 5FU.

- **National guidance and priorities** – NICE summary discussed.

- **Local health priorities** – Dermatology not a local health priority currently.

- **Equity of access** - NA

The JFG considered the application and the evidence and information submitted. It has been approved for inclusion to the Joint Formulary on the grounds of efficacy, cost, and ease of administration. TLS Green. Solaraze to remain on formulary. The Formulary to recommend use of moisturiser as first line for very mild cases. Education of GPs necessary on the use of ingenol and the reaction.

**Action:**

1. NB to add to the formulary, TLS Green

f. Ferric Carboxymaltose (Ferinject)
This application was submitted by Dr JB, Consultant Haematologist at NBT and supported by Dr Tom Latham, Consultant Haematologist at UHB. Dr JB was unable to attend and the application was presented by Dr SL, Consultant Anaesthetist – lead for pre-operative assessment and Chair of the pre-operative meeting.

For full details please see application form.

The application was for the inclusion of Ferinject for the treatment of iron deficiency anaemia when oral iron is ineffective or not appropriate. It will be primarily used for outpatients e.g. pre-operative assessment and most day case settings because this reduces staff time and length of stay. Cosmofer and Venofer may continue to be used for inpatients and for day case dialysis.

Ferinject is an iron product that can be given over 30 minutes although the procurement cost of the drug is greater. The total time for Ferinject infusion is one hour compared with 5 – 6 hours for the other iron infusions.

There is a higher acquisition cost for Ferinject compared to the other IV Iron preparations. The drug is in tariff and thus the cost for the CCG will remain the same for those already receiving iron infusion as a day case.

A meta-analysis identified 14 studies with 2,348 randomised patients exposed to ferric carboxymaltose. Serious adverse events and deaths were similar in incidence in ferric carboxymaltose and comparators; rates of constipation, diarrhoea, and nausea or vomiting were lower than with oral iron. Ferinject is the only i.v. iron preparation which is not contraindicated in patients with asthma, allergic eczema or other atopic allergy making it accessible to this patient group.

It has been approved by both the SMC and the All Wales Medicines Strategy Group, but excluding use in patients receiving haemodialysis.

Currently on the formulary
- Iron dextran (CosmoFer®)
- Iron sucrose (Venofer®)
- Iron Isomaltoside 1000 (Monofer®) - UHB only

Discussion with Dr SL

The discussion centred around the pre-operative use of Ferinject® and not it’s wider use within the Trusts.

25% of patients seen in pre-operative assessment are anaemia. In Orthopaedics, if a patient is identified as anaemic at pre-op clinic, patients would be treated with oral iron, but only 45% of patients are compliant and this does not increase the haemoglobin quickly enough for surgery. Patients may need a blood transfusion post operatively which results in an increased risk of wound infection and if the patient has cancer then there is an increased risk of reoccurrence, increased risk of distance metastases.

An audit has shown that if a patient is anaemic before a total knee replacement then the patient is 4 times as likely to end up in CCU following surgery.

When patient are seen in pre-operative assessment 2 weeks before surgery then there is not
time for oral iron to increase the haemoglobin level. Ferinject is a one off dose that increases haemoglobin by 1 – 2 g.

It has been agreed with haematology that the blood results for patients in pre op assessment to be available within 45 minutes and if necessary to receive Ferinject injection then without having to come back for another appointment.

Ferinject is currently being used at NBT as part of the national “prevent trial” – IV iron for colorectal patients.

Dr Lewis has previously raised with the Bristol South Locality the need for GPs to undertake blood test and blood pressure before they referred for major surgery but the response was that the GPs would be expected to be paid for this but these tests could save 25K a week.

GPs currently refer to orthopaedic surgery via MATs and CATs and therefore the blood results may be “old” by the time they are seen by the surgeon and placed on the waiting list.

The cost of a blood transfusion is £400 (which is PbR excluded) and the cost given in the application for Ferinject injection is £292 giving a saving of £108.00 , however the day case tariff is unknown.

**Discussion**

Due to the shorter length of stay there would be an increase throughput which could be an increase cost to the CCGs. This is outside the remit of the CCGs.

It is unclear what will be charged for e.g. if the cost of Ferinject will be included in the cost of a pre op assessment or if a separate charge / day case tariff will be raised. Ferinject is not PbR excluded and therefore should be included in the tariff costs.

Use of Ferinject will improve successful outcomes for surgery and is advantageous as patients do not need to have a transfusion post operatively.

- **Patient safety** – Clinical trials report similar or favourable safety and tolerability when compared to comparators.
- **Clinical effectiveness** – There have been trials of Ferinject versus placebo, oral iron and other IV iron preparations. It has been shown to results in a quicker response compared to oral iron, and to increase haemoglobin levels compared to iron dextran.
- **Cost effectiveness or resource impact** – Ferinject is more expensive than the other IV iron preparations, however there has a locally agreed discount.
- **Strength of evidence** – There have been many studies on large numbers of patients taking Ferinject, comparing it with placebo, oral iron and other IV iron preparations. These involved different patient cohorts, and therefore difficulty to extrapolate across to all patients.
- **Place in therapy relative to available treatments** – It would appear that were timing of administration is an issue, that this would be a suitable choice. Equally it would be a suitable choice over oral iron when used pre-operatively in order to reduce the number of blood transfusions.
- **National guidance and priorities** – None
- **Local health priorities** – NA
- **Equity of access** – Ensure that all patients are fit for surgery, and reduce the need for


In terms of the place of cosmoFer and venofer on formulary, these would be used in inpatients as there are no time constraints and Ferinject would be used in outpatients.

DK to establish views at NBT of removing Monofer from formulary and KG to obtain view from gastro.

The JFG considered the application and the evidence and information submitted. It has been approved for inclusion to the Joint Formulary on the grounds of efficacy, cost, and reduction in administration time. TLS Red. There would potentially be a need for ongoing discussion (with planned care teams) relating to the tariff for the pre-op assessment clinic, as the CCGs would want to be assured that the trust could absorb the additional cost of Ferinject within this tariff, as it is an in tariff drug.

Action:

1. NB to add to the formulary TLS Red.
2. NB/SBe to investigate further the Tariff costs.

g. Ozurdex

This application for use in Uveitis, was submitted for discussion at the meeting on the 23rd July. The decision made by the group at this time was minuted as:

Clinically appropriate to add to formulary for licenced indication (one implant only) but financial modelling not submitted to show a cost neutral or cost saving position. Therefore the JFG was unable to approve the application at this time.

SBe has worked with DrCG to look at the treatment pathway costs comparing the current treatment pathway with a proposed pathway in order to show that it was either cost neutral, or that there are cost savings to be made.

Dr CG had reviewed notes from the last 20 months and there were 7 patients that had been treated with Ozurdex instead of a biologic. A total of 17 implants had been used, with 4 eyes having a repeat Implant.

SBe looked into the financial costings of using Ozurdex in this patient cohort compared to the biologics, and estimates use of Ozurdex instead of biologics would save approximately 170K a year.

The issue of multiple implants was discussed as Ozurdex is not licensed specifically for more than one implant. It is accepted practice that Ozurdex is used outside its marketing authorisation in this manner, although there is no evidence to support this. The SPC stated that clinicians can use more than one implant but the clinician takes responsibility for this. If Ozurdex is not available for multiple use, then this only leaves the biologics available, which are again not licensed.

There is currently a criteria based access policy for the use of biologics in Uveitis, and this will need to be looked at in light of Ozurdex being agreed to be added to the formulary. A treatment
A pathway should be developed, and added to the formulary website.

The JFG considered the Proposed versus the current treatment pathway costs for using Uveitis, and agreed that Ozurdex should be included onto the formulary as it is clinically appropriate and that the financial modelling has shown that there are no cost implications by using Ozurdex. It is a licensed treatment for Uveitis, compared to the current pathway which involves using the biologics which are not licensed. UHB should review the numbers in a year’s time (to include repeat implants, costs and outcomes).

Action:
1. NB to add to formulary TLS Red.
2. SBe to produce a Treatment pathway for Uveitis, which should be uploaded to the website.

5. Shared Care Protocols

a. Rifaximin for Hepatic Encephalopathy (NBT)

SCP author AP specialist pharmacist gastroenterology.

Rifaximin currently on the formulary section 5.1.7

Comments from GPs had been sought. A number of queries had arisen, some in support of the SCP and some not. The main concern was around the care of the patient, and not the actual prescribing of the drug. It was confirmed that patients would not be not discharged from clinic whilst on Rifaximin. NICE due to produce a TA in January 14, and the ACD has stated that ‘Rifaximin-a is not recommended within its marketing authorisation, that is, for reducing the recurrence of episodes of overt hepatic encephalopathy in people aged 18 years or older.’ The JFG has therefore decided to wait until this is fully published in January, as if this remains as it is we would have to decommission the use of the drug locally and the SCP would not be appropriate.

Action:
1. NB to inform applicant.

b. Rivaroxaban for Pulmonary Embolism

SCP author SBe Interface pharmacist.

On the formulary section 2.8.

The SCP is largely based on a SCP approved for DVT. There has been no feedback from the GPs that it has been sent to.

Action:
1. NB to upload SCP and change TLS status to amber 1 month
c. Methotrexate for IBD (NBT / Weston)
   SCP author AP
   On the formulary section 1.5.3, and is an unlicensed use, although accepted practice use of the drug
   The SCP needs to be sent out to the GPs for comments.
   Action:
   1. NB to send out for comments

6. Individual Funding Requests
   No discussion occurred at this meeting
   Action:
   1. None

7. Chapter Review
   Post meeting note – Chapter 11 is currently being reviewed with the Eye hospital (NB and HC leading), and will be sent around for general comment shortly.
   Action:
   1. Continue to work on chapter 11

8. Specialised Commissioning Statements
   No new statements for discussion
   Action:
   1. None

9. MHRA Drug Safety Update – May to August
   No action for this group
   Action:
   1. None

10. Formulary Process
   a. Update
      There is a meeting on the 21st October to discuss further
      Action:
1. none

11. Items for discussion

   a. **Management of Biosimilars**
      There needs to be a discussion on how these are dealt with locally, and do we expect NDRs for each? Within the application, there should be submitted clinical evidence of similarity. It is hoped that there will be some national guidance, and the majority will affect specialised commissioning.

   b. **Fesoterodine**
      Not discussed.

12. AOB

   a. None
### 2013 Dates for Meetings

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<tr>
<th>Date</th>
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<th>Cut off for SCPs</th>
<th>Time</th>
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<td><strong>Wednesday 6(^{th}) November</strong></td>
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<td>25(^{th}) September</td>
<td>16th October</td>
<td>10.00 – 13.00 Board Room, South Plaza</td>
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<td>Tuesday 10(^{th}) December</td>
<td>29(^{th}) October</td>
<td>19(^{th}) November</td>
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### 2014 Dates for Meetings

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BNSSG Joint Formulary Group
Meeting held on Tuesday 10th December 2013
10.00am – 13.00pm Board Room, South Plaza, Bristol CCG

1. Welcome & Apologies & Declarations of Interest

Present
- Public Health Consultant, Bristol City Council (Chair)
- Interface pharmacist, NHS Bristol CCG
- Interface pharmacist, NHS Bristol CCG
- HoMM, NHS Bristol CCG
- Medicines Management Pharmacist, North Somerset CCG
- Clinical Effectiveness Research Lead, Bristol City Council
- HoMM, NHS South Gloucestershire CCG
- Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust Bristol
- Consultant in Emergency Medicine, University Hospitals Bristol NHS Foundation Trust and Associate Director of Patient Safety, and Chair of UHB Medicines Advisory Group
- GP, Bristol and member of Bristol CCG Board
- Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust
- Rotational Pharmacist, Pharmacoeconomics, North Bristol NHS Trust
- Formulary Pharmacist, AWP

Apologies
- HoMM, NHS North Somerset CCG
- Consultant Neurologist, North Bristol NHS Trust
- GP, North Somerset
- Joint D&TC Chair, North Bristol NHS Trust
- Joint D&TC Chair, North Bristol NHS Trust
- Chief Pharmacist, AWP
- Nurse Prescriber, Bristol
- Nurse Prescriber, Bristol
- Director of Pharmacy Weston Area Health NHS Trust
- Pharmacist, University Hospitals NHS Foundation Trust Bristol, UHB

Declarations of Interest
- None

The meeting was quorate until 11.00am

In accordance with the ToR of this group, the formulary pharmacist determined that the meeting should continue and will secure endorsement of any decisions ex-committee via email. Therefore decisions taken after this time will need to be ratified and actioned once approved.

2. Minutes from 15th October 2013 Meeting
The minutes from the Joint Formulary Group (JFG) meeting on the 15th October 2013 had been circulated by NB following the meeting.

KG requested clarification regarding the Dexmedetomidine application which was approved at the October meeting. The original application was submitted by General ICU anaesthetists within UHBristol, and the JFG approved Dexmedetomidine for inclusion in the formulary ‘For those patients failing to wean from invasive ventilation with traditional management due to agitation.’ Cardiac intensive care within UHBristol have expressed an interest in using dexmedetomidine as well in the same group of patients, though being treated on CICU. It was clarified by the group that this was acceptable.

The minutes of this meeting were approved.

Matters arising from October 2013 Meeting

a. Ferinject NDR

The JFG approved the use of Ferinject at the October meeting. The financial sign off of the NDR has not occurred as yet. This is an in tariff medication and as such, the directorates/divisions of the acute trusts need to approve the application and the potential cost pressure that is incurred by using the drug. The Ferinject application suggested it would be used in several different settings, e.g. pre-op assessment clinic, and day case. It is has become evident that the pre-op assessment tariff would not cover the cost of using Ferinject, and therefore the trust would like to negotiate a higher local tariff for this. Discussions of this nature are outside the remit of the JFG. It was noted that there will be internal processes within the acute trusts to raise a situation such as this via the commissioners to negotiate via the annual Operational Planning Process (OPP). Ferinject will not be placed on the formulary until we have assurance that either the directorate/division accept the cost pressure, or that we are made aware that an amendment to the local tariff has been accepted.

Action:
1. MP and KG to progress financial sign off for Ferinject at respective trusts and to report back to the group at the next meeting.

b. Ozurdex and Idiopathic Thrombocytopenic purpura (ITP) pathways

SB had updated the BNSSG Treatment pathway for Uveitis after the JFG agreed at the October meeting that Ozurdex could be used. The treatment pathway now reflects this decision. The pathway was therefore accepted.

As part of the work being undertaken reviewing the BNSSG CAF policies in relation to the formulary, SB had also identified that the ITP pathway needed updating to incorporate the NICE TA 293 involving Etilrombopag. SB presented the updated pathway and this pathway was also accepted.

Action:
1. NB/SB to upload onto the Formulary website.
3. NICE New Technology Appraisals published
There were a total of 6 TAs published in October and November 2013

Positive TA affecting the CCGs - 3

- TA 297 Vitreomacular traction - ocriplasmin
- TA 298 Choroidal neovascularisation (pathological myopia) – ranibizumab
- TA 301 Diabetic macular oedema - fluocinolone acetonide intravitreal implant (rapid review of TA271)

Positive TA affecting Specialised Commissioning - 1

- TA 300 Hepatitis C (children and young people) - peginterferon alfa and ribavirin

TAs not recommended - 1

- TA 297 Leukaemia (chronic myeloid) - bosutinib

Terminated appraisal - 1

- TA 302 Juvenile idiopathic arthritis (systemic) - canakinumab

**TLS Status for newly published TAs**

- All Red

**TAs adopted into the BNSSG Joint Formulary October and November 2013**

- TA 292 Bipolar disorder (children) – aripiprazole
- TA293 Thrombocytopenic purpura – eltrombopag

**4. New Drug Requests**

**Midazolam and Lignocaine**

Approved for inclusion onto the formulary for intranasal administration for conscious sedation to enable dental treatment in adults when a titratable technique is not possible. TLS Red, UHB only

**Lactulose**

Approved for inclusion onto the formulary for use as part of the Enhanced recovery Programme following colorectal resection, following insertion of colonic stent and post-surgery following minor anorectal surgery. TLS Blue, UHB only

**Tamoxifen**

Approved for inclusion onto the formulary for the reduction in breast cancer incidence in people with a family history of breast, ovarian or related (prostate/pancreatic) cancer as recommended in NICE CG164, only after the patient has been identified, been appropriately counselled by and treatment recommended by the Bristol Breast Cancer Family History Service. TLS Blue

**Ultibro**

Approved for inclusion onto the formulary as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease. TLS Blue

**Dundee sunscreen**
Approved for inclusion onto the formulary as a sunscreen when visible light range causes photodamage in paediatric patients. TLS Red, UHB only

Temocillin
Approved for inclusion onto the formulary for the treatment of sepsis/UTIs/Respiratory tract infections that are caused by susceptible gram negative bacilli. TLS Red, UHB only, Restricted to Microbiology advice only.

Decision Criteria used by JFG for NDR
- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

a. Midazolam and Lignocaine intranasal administration, UHB submitted.

This application was submitted by AD, Specialist Dentist in Oral and Maxillofacial Surgery and supported by NR, Reader/Honorary Consultant in Restorative Dentistry and CB, Specialty Lead for oral surgery. AD and NR attended the meeting to present the application.

Please see application form for full details.

This application was for the inclusion of a Midazolam and Lignocaine product for intranasal administration produced by Guys and St Thomas Trust, Pharmacy Manufacturing Unit. It would be used in adult patients for conscious sedation to enable dental treatment in those patients who are needle phobic or have learning difficulties or other disabilities.

The application was initially presented by CM who had completed further work searching for evidence. There are known to be health inequalities within this cohort of patients. There are reported case series that looked at whether this technique was better than oral - The carer reported back that they favoured the IN route. These patients had previously been treated with alternative techniques and therefore in a position to be able to compare. A concern was raised about the numbers quoted in the application and whether this was realistic or could there be a risk of spread.

Discussion with AD and NR

The application has been put forward to enable more opportunity to treat the more challenging patients, and to make dental treatment more accessible to these groups of patients – needle phobic and learning difficulties. The unit does see a small but steady number of patients that are really needle phobic. Intranasal midazolam has the advantage that it has a faster onset of action and a more predictable absorption. This has advantages for the patients, the dentists and the unit as a whole. With a faster onset of action, the patient is not required to sit and wait for it to work and this can lead to the patient becoming more agitated. Using oral midazolam, the patient is required to sit and wait for anything between 20 to 40mins whilst it works,
compared to 10mins for the intranasal route. Recovery from using midazolam does not differ from the route that it was administered, and the patient is able to be discharged generally 1.5hours after the last administration of midazolam. Therefore the benefits are that it is more acceptable for the patient, and that the patient can be discharged potentially quicker. Nigel Robb has experience of using both routes and states that the sedation is more unpredictable with the oral routes. Having the IN route available will provide a wider range of options for the specialist dentists. The disadvantages of using the IN route is that it may sting a little, which is why the lignocaine is present and also that it is not a titratable technique. It has been available since 2005, and the unit at Guys and St Thomas’ which manufacture it supply it to over 100 hospitals, and certainly many of the main dental units use it e.g. Cardiff, The Royal London, Kings, Liverpool, Portsmouth. The papers show that it is a safe and effective technique. It would be stored in a lockable medicine cupboard and all use would be logged.

When questioned about whether the numbers were realistic, and could there be a potential for the use to spread, the applicants were clear that the IN route would only be used in these patients where a titratable technique cannot be used, and this is standard practice. It is considered a standard technique within the Standards for Conscious Sedation in Dentistry: alternative techniques. Within this it states that oral or intranasal sedation should only be used where it is not possible to use one of the titratable techniques e.g. where intravenous cannulation cannot be achieved due to patient phobia, learning difficulties or other disabilities or where inhalation sedation with nitrous oxide does not provide sufficient relaxation or the patient has been assessed as being too anxious for this to be successful.

From a safety point of view, a question was asked about the potential for mix up between the oral/IV/IN products. The applicants felt that this would be very unlikely due to the packaging of the different products looking very different, and also, the size of the products vary considerably – the IV product being 5mls, and the IN being 1mls. As far as they know, there has never been a problem with a mix up between products.

Used as a stand-alone technique versus a prelude to IV midazolam was discussed. It was felt, that generally, the needle phobic patients are generally treated with just IN midazolam, whereas the learning disability patients may need IV midazolam in addition. Regardless of this, cannulation of all patients is required. The papers investigating IN midazolam generally involved patients with learning disabilities and therefore the majority did need IV sedation in addition in the papers.

Discussion by JFG following presentation

It was felt that including in the formulary was appropriate.

- **Patient safety** – Non-comparative evidence has shown that the rates of adverse events are low from using IN midazolam.
- **Clinical effectiveness** – The majority of evidence for use of intranasal midazolam in conscious sedation comes from studies (some prospective, comparative) involving healthy, paediatric populations. However, although it is unlicensed, it is considered to be a standard technique within the Standards for Conscious Sedation in Dentistry: alternative techniques.
  There is evidence to suggest that intranasal midazolam can successfully be used prior to IV midazolam in conscious sedation in a majority of adult patients with LD or other disabilities, avoiding general anaesthesia and enabling dental treatment. It is reported
that patient and carer acceptability of the procedure is generally favourable. There is no evidence to show:

- how any of these outcomes compare with oral or buccal administration of midazolam in this group of patients (also unlicensed)
- use of intranasal midazolam as a stand-alone sedative – all participants across both relevant studies received subsequent sedation via IV midazolam apart from 6 for whom intranasal administration alone was provided sufficient sedation to allow for completion of treatment without additional intravenous titration.
- effectiveness in a needle-phobic population

- **Cost effectiveness or resource impact** – The acquisition cost of this product is more than the alternatives i.e. buccal use, or using the injection via the oral route. This product would be considered in tariff, and therefore there would potentially be a cost pressure to the acute trust using this. It has been confirmed that the acute trust accepts this. The number of patients is expected to be low, and therefore the cost pressure is not expected to be significant.

- **Strength of evidence** – Evidence presented included prospective, comparative and non-comparative evidence from case series with high risk of bias.

- **Place in therapy relative to available treatments** – When considering the evidence and the Standards for Conscious Sedation in Dentistry, it seems appropriate to use IN midazolam when cannulation cannot be achieved due to patient phobia, learning difficulties (LD), or another disability and/or when inhalation sedation with nitrous oxide does not provide sufficient relaxation or the patient has been assessed as being too anxious for this to be successful.

- **National guidance and priorities** – It is included in the Standards for Conscious Sedation in Dentistry: alternative techniques.

- **Local health priorities** – Having IN midazolam available helps to support the Learning difficulties and Medicines management delivery theme of the Bristol 3 year plan. It is noted that there are health inequalities in the LD group, and using IN midazolam may help to reduce this.

- **Equity of access** – It is also known that dental care in people with learning difficulties is challenging, possibly contributing to health inequalities in this group.

The JFG considered the application and the evidence and information submitted. Whilst there is not strong evidence for the use of IN midazolam in this patient group, it is included in the Standards for Conscious Sedation in Dentistry: alternative techniques. It has obvious advantages and there are no safety concerns. It was therefore approved for addition to the formulary in those ‘adult patients in when cannulation cannot be achieved due to patient phobia, learning difficulties (LD), or another disability and/or when inhalation sedation with nitrous oxide does not provide sufficient relaxation or the patient has been assessed as being too anxious for this to be successful,’ TLS Red.

**Action:**

1. NB to add to formulary website, divisional approval has already been received.

b. Lactulose for Enhanced Recovery Programme, following colorectal resection, following insertion of colonic stent and post-surgery following minor anorectal surgery, UHB submitted.
This application was submitted by Mr RL, Consultant Colorectal Surgeon, UHBristol. Currently, NBT are not looking to use Lactulose in their Enhanced recovery programme.

For full details please see application form.

This application was for the inclusion lactulose only in selected cohorts of patients – Enhanced Recovery Programme (ERP), following colorectal resection, following insertion of colonic stent and post-surgery following minor anorectal surgery. The ERP is a special evidence based programme of care given to patients following different types of surgery, which has been designed to enable patients to recover more quickly and therefore be discharged more quickly. Bowel management and laxative use is part of this. Many ERPS do not specify which laxative could be used, but some specify lactulose, others specify a macrogol such as movicol. NBT currently use movicol in their ERP, and are not looking to change this practice currently. Lactulose is not currently on the BNSSG formulary as a first line option as it is not the most effective laxative available and needs to be taken regularly for effect.

Discussion with Mr RL

RL stated that Lactulose is an osmotic laxative that he has been prescribing for many years, but now he can’t as it is not included in the BNSSG formulary. He is aware that Movicol/Laxido is an alternative, and that is acceptable for some patients, though the advantages of this is a reduction in the fluid that the patient would have to drink - 125 – 250mls of fluid with Movicol, compared to 20mls of lactulose. Post-surgery, patients generally don’t want to have to drink that amount of fluid. There are no research or trials, and it is extremely unlikely that there ever will be, however it is being requested on the grounds of better patient acceptability.

Discussion by JFG following presentation

The group discussed the potential for including lactulose on the formulary for all patients. This was decided to be looked at during the chapter review.

- **Patient safety** – Many years of experience of using lactulose, with no major adverse effects.
- **Clinical effectiveness** – No trials or research in this patient cohort.
- **Cost effectiveness or resource impact** – Potentially cheaper than movicol/laxido, depending on the dose used. In tariff. The acute trust have approved this application financially.
- **Strength of evidence** – NA
- **Place in therapy relative to available treatments** – Use in the patient cohorts listed above.
- **National guidance and priorities** – Listed in some ERPs around the country.
- **Local health priorities** – NA
- **Equity of access** – NA

The JFG considered the application and the evidence and information submitted. It has been approved for inclusion to the Joint Formulary for use in the ERP following colorectal resection, following insertion of colonic stent and post-surgery following minor anorectal surgery, UHB only, TLS Blue, on the grounds of patient acceptability.

Action:
1. **NB to add to formulary TLS Blue as above, UHB only, divisional approval has already been received.**

2. **MP to discuss with NBT to confirm whether they would like to include it in their ERP or not.**

c. **Tamoxifen for the reduction in breast cancer in people with a family history of breast, ovarian or related cancer as recommended in NICE CG164, BNSSG Primary Care submitted.**

This application was submitted by SB, Interface Pharmacist, Bristol CCG on behalf of BNSSG.

Please see application form for full details.

This application was for the inclusion of Tamoxifen for the reduction in breast cancer in people with a family history of breast, ovarian or related cancer as recommended in NICE CG164. The Bristol Breast Cancer Family History Service currently has 1000 patients that they are aware of that would be eligible for treatment with tamoxifen in accordance with this NICE guidance. It is unlicensed for this use, and it's unlikely that it will ever get a license for this use. The Bristol service has produced an information leaflet on this subject, which has been approved at BNSSG D&TC.

The discussions centred around the holistic management of patients in terms of who would initiate, who would counsel patients, and who would follow these patients up. Various routes within BNSSG are currently discussing this, and the reason for the application to the JFG was to ensure that the medication had been considered by the JFG in this cohort. The prescribing of tamoxifen in this manner, along with it being unlicensed was felt to be specialist prescribing. The evidence and national guidance does support tamoxifen. The counselling and necessary guidance involved in this was not felt to be as straightforward that GPs would/should manage this. The adverse effects of tamoxifen are such that only those patients that felt strongly about this would initiate and continue taking it.

Once the service and infrastructure is in place to deliver it, the use of tamoxifen in this manner is supported by the JFG.

- **Patient safety** – not discussed – NICE CG164
- **Clinical effectiveness** – not discussed NICE CG164
- **Cost effectiveness or resource impact** – Not significant in terms of tamoxifen acquisition. The cost of 1 year's treatment for 1000 patients is estimated to be £2,410. The cost of the service required as a whole is currently being considered within BNSSG.
- **Strength of evidence** – NICE CG 164.
- **Place in therapy relative to available treatments** – No other treatment is licensed. There are no trials comparing the clinical and cost effectiveness of aromatase inhibitors and tamoxifen for reducing the incidence of breast cancer in women with a family history of breast or ovarian cancer.
- **National guidance and priorities** – NICE CG 164.
- **Local health priorities** – Using tamoxifen in this cohort of patients helps to support the Cancer delivery theme of the Bristol CCG 3 year plan – improving the prevention of
• **Equity of access** – It is included in the NICE CG.

The JFG considered the application and the NICE CG. It was considered that tamoxifen use in this patient cohort was acceptable. However the group would like assurance that the service and infrastructure is in place to deliver this and surveillance of patients is part of this. The JFG did not want to hold up any discussions within BNSSG relating to the commissioning of a service and therefore were happy to approve the application and include tamoxifen on the BNSSG formulary for those patients that have been identified, counselled and treatment recommended by the Bristol Breast Cancer Family History Service, TLS Blue. Patients therefore will only be eligible once the structure is in place and the service starts to see patients. GPs would not be expected to initiate patients unless there is support from this service.

**Action:**

1. NB to add to the formulary TLS Blue as above, financial approval of drug use has been obtained.

d. **Ultibro (Indacaterol and glycopyrronium) BNSSG wide application**

This application was submitted by Dr JC Respiratory Consultant, NBT and also supported by the Respiratory Consultants at UHBristol. No one was available to attend the meeting however the application continued to be discussed.

For full details please see application form.

This application was for the inclusion of the combination inhaler, Ultibro as a maintenance bronchodilator treatment to relieve symptoms in adult patients with Chronic obstructive pulmonary disease (COPD). This is the first inhaler that combines a Long acting muscarinic antagonist (LAMA) and a long acting beta agonist (LABA), and would be used in the final stage of the COPD pathway. Both indacaterol and glycopyrronium are already on the formulary as individual inhalers, and therefore the combination is more than likely being prescribed in this manner already. SM explained that the consultants currently have a view of using the different LAMAs in different cohorts, and time is required to enable the specialists to form an experienced view of the hierarchy of LAMAs. Their current view is that tiotropium is used in those patients who experience frequent exacerbations, aclidinium for those patients who experience night symptoms, have CVS or have problems with dexterity, and glycopyrronium is useful for those patients who need dual bronchodilators with indacaterol.

There are more fixed dose combination inhalers comprising of a LABA and a LAMA that are forecasted to be launched over the next few years.

There is no evidence supporting where it is likely to be placed, and the evidence available shows that it is either comparable or slightly better than its comparators.

The advantages of Ultibro are that it will help to improve compliance being a combination inhaler and once a day dosing, the device is relatively easy to use, and the acquisition cost is less than any other combination that you would use for COPD. Wastage associated with non-
adherence will potentially be reduced.

- **Patient safety** – The safety profile is characterised by typical anticholinergic and beta-adrenergic effects related to the individual components of the combinations, which are both already included on the formulary. Compared to other available therapies, Ultibro has demonstrated an acceptable safety profile. The incidence of adverse and serious adverse effects did no differ between Ultibro and its comparators in the studies. The study ENLIGHTEN showed that there adverse event rates were similar in both the ultibro group and the placebo group.

- **Clinical effectiveness** – Various well designed, comparator trials have taken place involving Ultibro. Ultibro has been shown to produce statistically significant symptomatic improvements in FEV1, breathlessness, rescue medication use and health related quality of life compared to glycopyrronium, indacaterol, tiotropium in patients with GOLD stage II – III COPD. In patients with GOLD Stage II - III COPD, and without a COPD exacerbation in the preceding year, Ultibro was superior to combination LABA/ICS (salmeterol / fluticasone) in terms of FEV1 changes and associated with a lower composite rate of adverse outcomes (although short duration and patients relatively low risk for COPD exacerbation). In patients with GOLD Stage III - IV COPD with a history of COPD exacerbation in the preceding year, the rate of COPD exacerbations (moderate and severe) was significantly reduced with Ultibro compared to glycopyrronium 50mcg and tiotropium 18mcg.

- **Cost effectiveness or resource impact** – Ultibro has a lower acquisition cost compared to any combination of LAMA/LABA as separate inhalers. It is in tariff.

- **Strength of evidence** – Good quality trials, though not entirely conducted with the exact cohort of patients that it is intended to be used in.

- **Place in therapy relative to available treatments** – The submission aims to place Ultibro when a LABA and a LAMA would normally be employed in combination with or without and inhaled corticosteroid.

- **National guidance and priorities** – No other area appears to have assessed it as yet. NICE are due to publish an evidence summary in early 2014.

- **Local health priorities** – Including Ultibro in the formulary would support the Long Term conditions themes i.e. reducing admissions associated with LTCs.

- **Equity of access** – NA

The JFG considered the application and the evidence and information submitted. It has been approved for inclusion to the Joint Formulary for use when a LABA and a LAMA would be indicated in combination with or without and inhaled corticosteroid. There will be a future need to discuss further novel inhalers, and also COPD pathway once more experience is gained. TLS Blue.

**Action**

1. NB to add to the formulary TLS Blue as above, financial approval of drug has been obtained from primary care and UHBristol. Awaiting NBT directorate approval.

e. **Dundee Sunscreen, UHB only application**

This application was submitted by Dr LS, Consultant Paediatric Dermatologist, UHBristol. No one was available to attend the meeting to present the application; however the application was
still discussed and considered.

For full details please see application form.

The applicant was for the inclusion of a specially manufactured product of a sunscreen, manufactured by Tayside Pharmaceuticals in Dundee, specifically for paediatric patients that need sunscreen when visible light range causes photodamage. This is an unlicensed special, and this is not prescribable on the NHS as it is not in the Drug Tariff in the ACBS (Advisory Committee on Borderline Substances) section.

There are no trials or papers that have been found to investigate Dundee sunscreen in particular. The reason that this product was manufactured was to incorporate zinc oxide and pigmentary grade titanium dioxide to provide effective topical photoprotection. Other commercial preparations only include a reflecting agent and not a camouflaging agent and this is an additional benefit of Dundee sunscreen over other commercially available sunscreens. It contains a 'tinted' reflectant available in three colours: coral pink, beige, and coffee which can be mixed to obtain a good colour match with the skin and improve cosmetic appearance. This avoids the whitish appearance given to the skin which occurs because of the reflective component of the cream with normal sunscreens.

It is more expensive than other reflected sunscreens but it is cosmetically more acceptable for the patient and currently when it has been prescribed it has been when other reflectant sunscreens have failed.

- **Patient safety** – There is no data sheet and no trials.
- **Clinical effectiveness** – A study has shown that in some patients with photosensitivity disorders, who are sensitive to visible radiation, sunscreens that incorporate zinc oxide and pigmentary grade titanium dioxide as active ingredients do provide protection.
- **Cost effectiveness or resource impact** – Dundee SS would not be able to be prescribed on the NHS, and therefore any prescribing would have to remain in secondary care. It is more expensive that other reflected sunscreens but it is cosmetically more acceptable for the patient. The acute trust has accepted the financial consequences of this application.
- **Strength of evidence** – No good quality RCTs, though this is not unexpected.
- **Place in therapy relative to available treatments** –
- **National guidance and priorities** – It is recommended by the British Porphyria Association and the British Association of Dermatologists.
- **Local health priorities** – NA
- **Equity of access** – The product is cosmetically more acceptable to patients, and therefore more likely to achieve compliance.

The JFG considered the application. It has been approved for inclusion on the Joint Formulary on the grounds that it can be used in patients when visible light causes sun damage and better patient acceptability. TLS Red.

**Action:**

1. NB to add to the formulary, TLS Red. Financial approval has been confirmed from the acute trust.
f. **Temocillin, UHB only application**

This application was submitted by Dr RB, Consultant Microbiologist. Dr Brindle also attended the meeting to present the application.

For full details please see application form.

The application was for the inclusion of Temocillin for the treatment of sepsis, urinary tract and respiratory infections caused by susceptible gram negative bacilli. It will be used as a meropenem sparing agent.

**Discussion with Dr RB**

Temocillin would be used as a carbapenem sparing agent, which has been increasing over the last 5 years. It would help to reduce the occurrence of carbapenemase-producing organisms. At the moment, patients with sepsis/UTIs/respiratory infections that are caused by susceptible gram negative bacilli are treated with piperacillin/tazobactam, and then meropenem. If temocillin was to be included in the formulary, it would be used instead of meropenem. This would not be a significant number of patients. Temocillin has been available for over 8 years, but it has a limited market and there are unlikely to be RCTs. It would be restricted to prescribing only on the advice of a microbiologist at UHB. This would also apply to Weston. NBT to investigate whether the microbiologists are interested in including in their microbiology restricted antibiotic list.

- **Patient safety** – It is a penicillin therefore adverse effects are as with other penicillins.
- **Clinical effectiveness** – Consensus gained from multiple retrospective studies, using data from patients' medical notes who received treatment with Temocillin is that the use of this agent is justified as it is an effective alternative to carbapenem antibiotics in the treatment of confirmed-non-pseudomonal urinary, respiratory and septic infections from susceptible gram-negative bacilli.
- **Cost effectiveness or resource impact** – Temocillin is more expensive than meropenem – a 1 week course of temocillin is £712.60 compared to £336 for meropenem. This would be in tariff, and the acute has confirmed acceptance of the financial consequences.
- **Strength of evidence** – No RCTs exist, but this is not to be unexpected due to the length of time on the market.
- **Place in therapy relative to available treatments** – Only use in the treatment of sepsis, urinary tract and respiratory infections caused by susceptible gram negative bacilli when meropenem would have been used.
- **National guidance and priorities** – nil
- **Local health priorities** – NA
- **Equity of access** - NA

The JFG considered the application and the evidence and information submitted. It has been approved for inclusion to the Joint Formulary on the grounds of the potential to reduce the carbapenem use. TLS Red, UHB only, and restricted to microbiology advice only. Financial approval has been confirmed from UHBristol.
Action:
1. NB to add to the formulary TLS Red, UHB only, restricted to microbiology advice.
2. MP to investigate NBT interest.

5. Shared Care Protocols

a. Methotrexate for IBD (NBT and Weston)

SCP author AP specialist pharmacist gastroenterology.

Methotrexate is on the formulary for IBD, section 1.5.3. It is currently classified as an amber drug, although it does not have a SPC associated with it for this indication. The SCPs for methotrexate along with a number of other Rheumatology DMARDs have been discussed at length, over a long period of time. The vision was to agree one BNSSG wide SCP for each drug, covering all specialities. In reality this has proven on a number of occasions not to be possible, with each speciality and each directorate/division having particular nuances. It was felt that there was a greater risk by not having any SCP associated with IBD management and therefore an individual SCP for this indication was developed.

Comments from GPs had been sought. No concerns had been raised over the SCP and therefore the SCP was accepted.

Action:
1. NB to upload the SCP to the website.

b. Aripiprazole (AWP)

SCP BS AWP Formulary Pharmacist.

On the formulary section 4.2.1. The SCP has been discussed at length over a long period of time, and many BNSSG healthcare professionals have commented on the content. BS and NB met recently to review the SCP and to ensure that the content was as concise as possible.

The group did not have any further comments to discuss, therefore the SCP was agreed.

Action:
1. NB to upload SCP to the formulary website.

c. Typical Antipsychotic depots (AWP)
SCP BS AWP Formulary Pharmacist.

On the formulary section 4.2.2. Like the Aripiprazole SCP, this SCP has been discussed at length. Comments have also been sought from a GPwSI in mental health and these comments were taken on board when NB and BS met to discuss the SCP. No further comments were discussed. The SCP was therefore agreed.

**Action:**
1. NB to upload SCP to the formulary website.

d. **Denosumab (BNSSG)**

SCP author Dr SC, UHBristol Consultant

On the formulary, section 6.6.2. At the July 2013 meeting, a NDR was discussed for Denosumab to be included on the formulary for the treatment of osteoporosis of men. This was agreed and therefore a revision of the current Denosumab SCP was required. Dr Shane Clarke has lead on this and liaised with SB. The group had no further comments on the SCP and therefore this was approved.

During the SCP discussion, it was raised that we have other treatments available on the formulary for the treatment of osteoporosis in women such as strontium. It was felt that the JFG should look at reviewing this in light of the decision made to include men to be treated with denosumab for the treatment of osteoporosis to ensure equity of access.

**Action:**
1. NB to upload SCP to the formulary website.
2. NB to contact Dr Shane Clarke to discuss other treatments that may be initiated in men.

e. **Ticagrelor (BNSSG)**

This was an error in the agenda. This item related to Ranolazine, which is included in the BNSG formulary, section 2.6.3 for the treatment of angina. It has been on the formulary since December 2011 after being agreed by UHB MAG. The cardiologists would like the JFG to review the TLS status of ranolazine from red to amber. The number of patients that they have initiated it in is not high but the drug is not complex to dose or monitor, therefore it is their opinion that it is suitable for GP continuation. This was discussed, and it was felt that this was appropriate and therefore the group would invite a SCP to be presented to the group at the next
meeting.

**Action:**
1. NB to contact UHB and NBT cardiologists to write a SCP for ranolazine.

**f. Dithranol cream (BNSSG)**

It has been brought to the attention of the interface pharmacists that there may be an error in the TLS classification of Dithranol cream, and it has been suggested that this should not be a red drug. The group needs a formal request for re-classification, or it will be discussed within the chapter review.

**Action:**
1. NB to contact UHB and NBT dermatologists.

6. **Individual Funding Requests**

No discussion occurred at this meeting

**Action:**
1. None

7. **Chapter Review**

Chapter 11 is currently being reviewed with the Eye hospital (NB and HC leading), and will be sent around for general comment in the new year.

Work is required to plan for the chapter reviews in the new year, and the logistics involved with this.

**Action:**
1. Continue to work on chapter 11
2. NB to present a work plan for the chapter reviews at the January meeting.

8. **Specialised Commissioning Statements**

No new statements for discussion
Action:
1. None

9. MHRA Drug Safety Update – October and November 13

The MHRA have provided advice on switching between different manufacturers' products for a particular drug. Anti-epileptics have been divided into three risk-based categories to help healthcare professionals decide whether it is necessary to maintain continuity of supply of a specific manufacturer's product. The link to this guidance will be uploaded to the website.

Action:
1. NB to upload the guidance to the website.

10. Items for Discussion

a. Metolazone

This licence for metolazone was withdrawn from the market in October 2012. NBT cardiology have requested the JFG to consider what steps are required in relation to the formulary status. The group were unaware of the finer details of the reason for the withdrawal of the product. The group have requested NBT, in conjunction with UH Bristol and Weston produce a summary document that includes the reason why it is has been withdrawn, the unlicensed product details, including costs to secondary and primary care (also considering that it will be an unlicensed special), and the view of the specialists in terms of whether it is still required on the formulary, and advice to GPs for those patients maintained in the community. It will then be brought back to the JFG to decide whether it is to remain on the formulary, and TLS classification, and to include an advice document for GPs.

Action:
1. MP to lead on producing a summary document for the JFG to consider.

b. Fesoterodine

Dr HH from NBT Urology had submitted a NDR for Fesoterodine in the summer. Various discussions had taken place regarding the appropriateness of considering a NDR. The over active drugs were considered in detail during compilation of the chapter. It was felt that a review of this section could be brought back to the JFG.

c. Omega-3 fatty acids

Recently NICE have published clinical guideline 172 MI secondary prevention. Within this guideline, it states that

‘Do not offer or advise people to use the following to prevent another MI:

• omega-3 fatty acid capsules
• omega-3 fatty acid supplemented foods.
If people choose to take omega-3 fatty acid capsules or eat omega-3 fatty acid supplemented foods, be aware that there is no evidence of harm.'

Omega 3 fatty acids are only on the formulary:

**Omega-3 fatty acid compounds**

Specific indication: (TLS Blue)
**Omega-3-acid ethyl esters**
- Brands include Omacor® and Prestylon®
- for use in primary care only in accordance with NICE clinical guidance CG48

Clinical guideline 48 has been replaced by this new guideline 172 and therefore the second bullet point is no longer valid. The group would like to take guidance from secondary care, and primary care will support this view.

**Action:**

1. MP to liaise with cardiology at NBT for advice on omega 3 fatty acids, in conjunction with UHB.

11. AOB

   a. None
## 2014 Dates for Meetings

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SPCs</th>
<th>Time</th>
<th>Venue</th>
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</thead>
<tbody>
<tr>
<td>Tuesday 21st January 2014</td>
<td>3rd December 2013</td>
<td>10 am to 1pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 4th March 2014</td>
<td>21st January 2014</td>
<td><strong>1.30 – 4.30pm</strong></td>
<td>Bevan Room South Plaza</td>
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<tr>
<td>Tuesday 22nd April 2014</td>
<td>11th March 2014</td>
<td>10 am to 1pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<tr>
<td>Tuesday 3rd June 2014</td>
<td>22nd April 2014</td>
<td><strong>1.30 – 4.30pm</strong></td>
<td>Bevan Room South Plaza</td>
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<tr>
<td>Tuesday 15th July 2014</td>
<td>3rd June 2014</td>
<td>10 am to 1pm</td>
<td>Pharmacy Seminar Room Brunel Building Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 2nd September 2014</td>
<td>22nd July 2014</td>
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<td>Bevan Room South Plaza</td>
</tr>
<tr>
<td>Tuesday 14th October 2014</td>
<td>2nd September 2014</td>
<td>10 am to 1pm</td>
<td>Pharmacy Seminar Room Brunel Building Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 25th November 2014</td>
<td>14th October 2014</td>
<td>10 am to 1pm</td>
<td>Boardroom South Plaza</td>
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</table>
BNSSG Joint Formulary Group
Meeting held on Tuesday 21st January 2014 10am - 1pm
Venue: Seminar Room, Pharmacy Department, Southmead Hospital

Minutes

Present:

Public Health Consultant, Bristol City Council (Chair)
Interface Pharmacist, Bristol CCG
Interface Pharmacist, Bristol CCG
Clinical Effectiveness Research Lead, Bristol City Council
HoMM, NHS South Gloucestershire CCG
HoMM, NHS North Somerset CCG
Medicines Management Pharmacist, NHS North Somerset CCG
Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust
Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust
Chief Pharmacist, Bristol Children’s Hospital, University Hospitals Bristol NHS Foundation Trust

Apologies:

HoMM, NHS Bristol CCG
Consultant in Emergency Medicine, University Hospitals Bristol NHS Foundation Trust and Associate Director of Patient Safety, and Chair of UHB Medicines Advisory Group
GP, Bristol and member of Bristol CCG Board
Formulary Pharmacist, AWP
GP, North Somerset
Joint D&TC Chair, North Bristol NHS Trust
Joint D&TC Chair, North Bristol NHS Trust
Chief Pharmacist, AWP
Nurse Prescriber, Bristol
Nurse Prescriber, Bristol
Director of Pharmacy Weston Area Health NHS Trust
Pharmacist, University Hospitals NHS Foundation Trust
Bristol, UHB

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest
The meeting was not quorate. In accordance with the ToR of this group, the Chair of the group determined that the meeting should continue and the Formulary Pharmacist will secure endorsement of any decisions ex-committee via email. Therefore decisions taken during this meeting will need to be ratified and actioned once approved.

NB informed the group that HF had informed her of his intention to leave the group with immediate effect as he was no longer able to commit the time required. The JFG would like to thank HF for all of his time and invaluable contributions to the group. MP will be discussing the lack of consultant representation from NBT within the trust and will be taking appropriate action to ensure that this is rectified in a timely manner. The timings of the meetings were also discussed. This year, they alternate between mornings and afternoons in order that the same clinic session is not compromised each time. The JFG have also decided to bring the morning meetings forward so that they start at 9am.

2 Minutes of the meeting of 10th December 2013 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 10th December 2013 had been circulated by NB following the meeting. No further comments had been submitted regarding the decisions made. The minutes of this meeting were approved.

Matters arising from December 2013 meeting

a. Dornase alfa and Alteplase NDR

The interface pharmacists had been contacted by the NBT respiratory specialist pharmacist requesting further information about the formulary status of the above for the treatment of empyema. Long discussions have taken place over the course of 2013 regarding this NDR, mainly regarding the funding. The group accepted the application and approved its use for those patients who were not fit for surgery or where a delay to surgery would be detrimental to the patient, however the funding of the two medicines was unclear. It has been since clarified that:

- Dornase alfa – based on the 80:20 split, specialised commissioning will pick up the funding as 80% of its use is for cystic fibrosis.
- Alteplase – dealt with as an adjustment for stroke only. This has been confirmed with the DoH. Therefore any other use would be in-tariff use, and therefore secondary care would be expected to fund this.

The specialist pharmacist is aware that if the directorate is not prepared to fund the alteplase then a business case would have to be prepared and submitted to the individual CCG boards during the annual commissioning intentions round. AD has also written to the Department of Health through the Medicines Management Optimisation Group requesting the alteplase is reviewed. This is not likely to alter in year. This is therefore to remain non-formulary.

Action:

1. **MP to report back to the group if there is any further progress on the financial sign off. Until such time, this well remain non-formulary**

b. Ferinject

The NDR was accepted in September 2013, but the trusts were as yet to confirm the financial acceptance. Ferinject is an in-tariff medication and as such the financial risk
from using the more expensive Ferinject product compared to the existing formulary parenteral iron products i.e. Monofer and Cosmofer lies with secondary care. There is interest in using Ferinject in the out-patient setting and specifically the pre-op assessment clinic due to its faster administration time, and the obvious benefits associated with this. However, the tariff for the pre-op assessment does not cover the cost of Ferinject, and therefore the directorates have not agreed its use. MP is therefore putting together a business case to be presented at the main commissioning intentions round. If it can be demonstrated that there are advantages to all by using Ferinject then a favourable response is anticipated.

**Action:**

1. **MP to report back to the group if there is any further progress on the financial sign off. Until such time, this will remain non-formulary**

3 **NICE New Technology Appraisals Published**

   - There were no TAs published in December 2013.

   TAs adopted into the BNSSG Joint Formulary December 2013

   - None

4 **New Drug Requests (NDRs)**

   **Infloran (Bifidobacterium infantis, Lactobacillus acidophilus)**

   Approved for inclusion onto the formulary for prevention of necrotising enterocolitis in preterm infants. TLS Red.

   **Lisdexamfetamine (adults)**

   Approved to be added to the BNSSG formulary, as TLS Red, for prescription within AWP only.

   **Decision Criteria used by JFG for NDR**

   - Patient safety
   - Clinical effectiveness
   - Cost effectiveness or resource impact
   - Strength of evidence
   - Place in therapy relative to available treatments
   - National guidance and priorities
   - Local health priorities
   - Equity of access

   **a. Infloran (Bifidobacterium infantis, Lactobacillus acidophilus), UHB submitted**

   This application was submitted by Dr PC, Neonatal Consultant, UH Bristol. AM, Chief Pharmacist at Bristol Children’s Hospital attended the meeting to present the application.

   Please see application form for full details.

   **Discussion with AM**
This application was for the inclusion of Infloran, a combination of two different probiotics in order to prevent necrotising enterocolitis (NEC) in preterm infants. NEC appears to be strongly associated with patterns of gut microbial colonisation. It can lead to bowel necrosis and perforation. If it is not possible to get the condition under control with the use of antibiotics, surgery will be required, which can lead to short bowel syndrome. Some babies will require long term total parenteral nutrition (TPN), and in some severe cases, it results in death. It is estimated that 5-10% of preterms will develop NEC, though UHBristol does not have exact figures. 20-40% of these will require surgery, and 30% will die. There has been long term interest in methods to decrease the risk of developing NEC, and it has been shown that formula fed infants are at a higher risk of developing NEC. No specific treatment is available to treat NEC – generally enteral feeds are stopped and IV nutrition is commenced along with broad spectrum antibiotics.

The use of probiotics to reduce the risk of NEC has been evaluated in clinical trials. It appears that the most beneficial products contain one bifidobacterium strain and one lactobacillus strain. By supplementing newborns with probiotics trials have shown to reduce the incidence of NEC and all-cause mortality. The studies have been conducted abroad, but the subjects are relevant to our patient population. There has been shown to be good morbidity and mortality reduction by using probiotics. A NNT can be equated to be around 25. The duration of treatment required would depend on the age of the infant but AM estimates that an average would be a 7.5 week course. This would not impact on primary care as the baby would not be discharged until after they reach 34 weeks.

Infloran has been approved for use in other areas, including Bath, Cardiff, Newcastle, and others.

Discussion with Dr PC

Several areas of discussion were explored with Dr PC.

Given the evidence supporting the use of probiotics to reduce NEC, why is there still controversy over the use of them? In papers published 4 years ago investigating the role of probiotics and NEC concluded that it was now unethical to conduct placebo controlled studies as the evidence showed significant benefits that outweighed the adverse effects. The Cochrane review stated that ‘Enteral supplementation of probiotics prevents severe NEC and all-cause mortality in preterm infants. Our updated review of available evidence supports a change in practice.’ CM stated that the meta analysis had been heavily criticised, and that many of the trials included in this lacked quality. Two of the higher quality trials were conducted in Taiwan and therefore it may be difficult to apply the results to the local population. The issue of the appropriateness of using meta analysis to pool data from heterogenic trials was raised. Specifically the use of different probiotic products and strains. The meta analysis makes it difficult to consider probiotic supplementation as a homogeneous intervention. Further large clinical trials using specific microbial cultures are required, but it is unlikely that this will be a reality.

Why Infloran? The meta analysis listed in the application included studies that involved different combinations of probiotics. It was shown that lactobacillus was not as important and bifidobacterium more so. However the combination together appeared the most beneficial. Infloran has been studied the most, and has the most safety data. It is used in other centres and in Ireland. UHBristol have discussed the manufacturing process with the manufacturers and they are reassured about this. It is also relatively easy to administer. Given the concerns of the appropriateness of a meta-analysis
involving different products, it has been suggested that the best approach would be to perform a meta-analysis that evaluates the effect of administering a clearly defined single organism probiotic preparation. However, a lack of data makes this not feasible.

Essentially, there are three categories of babies that develop NEC. The first, with mild NEC will be treated with antibiotics and TPN. The second is the severe form of NEC, in which the babies will not survive. The third group is the middle group in which the babies will lose part of their gut and be in hospital for many months and suffer a reduction in neurological function. It is this group that therapy should be focussed on.

Discussion by JFG following presentation

The group concluded that there were lots of studies involving probiotics and NEC. There are concerns over the types of product used, and in the quality of some of the studies. But there is evidence that probiotics as a whole do show a decrease in morbidity and mortality. Even if one case of NEC is saved this will be of significant benefit. There is no other treatment available.

NBT (Dr AP, neonatal consultant) have expressed a potential interest in using Infloran in these babies. MP to follow this up.

- **Patient safety** – No significant adverse effects have been reported. The only safety concerns raised are an increase in wheezing and asthma between the ages of 2 and 7, but it is difficult to associate the cause of this to probiotics, and these safety concerns are much less than the effects of NEC.
- **Clinical effectiveness** – Even without the meta-analysis and Cochrane reviews, the individual RCTs have shown a positive effective on the reduction of NEC by using probiotics. As discussed, the difficulty is knowing which strain and product.
- **Cost effectiveness or resource impact** – This would be a highly cost effective intervention, with the cost of the capsules being negligible.
- **Strength of evidence** –
- **Place in therapy relative to available treatments** – Use
- **National guidance and priorities** – There are no national guidelines.
- **Local health priorities** – NA
- **Equity of access** – Other centres currently have evaluated and approved the use of infloran in their centres.

The JFG considered the application and the evidence and information submitted. Infloran has been approved for inclusion to the Joint Formulary for use in pre-term infants, TLS Red. It was requested that the unit bring back to the JFG audit results after 1 year.

**Action:**

1. **NB to add to formulary TLS Red as above, divisional approval has already been received.**
2. **MP to discuss with NBT to confirm whether they would like to use it or not, and to confirm directorate approval.**

b. **Lisdexamfetamine (in adults)**

A formal NDR has not been completed for this. Dr OB at AWP currently uses lisdexamfetamine in some adult ADHD patients, and it is on the AWP formulary (approved for inclusion on the 22.3.13). There was discussion as to whether it was needed to be on the BNSSG formulary because it is on the AWP formulary red i.e. BNSSG patients are treated in
AWP and if lisdexamfetamine is chosen then it is prescribed and monitored within AWP. If AWP wishes for BNSSG GPs to take on the prescribing of these patients, then a change in status request should be completed. It should be noted, that the BNSSG JFG approved the inclusion of lisdexamfetamine in the BNSSG Joint Formulary for the treatment of children and adolescents in September 2013, TLS Red. Shire pharmaceuticals have a license for continuation in adults, however initiation in adults would be considered off-label. It would seem to make sense to allow lisdexamfetamine on the formulary for continuation in adults.

E-pact data should be analysed to ascertain what the prescribing costs are within BNSSG at the moment, and to see if there is an upward trend. It may also be of value to contact AO’K, Mental Health Commissioner at the CSU.

Post meeting note:

From the AWP new drug application, the particular patient cohorts that Lisdexamfetamine would be prescribed for are:

a) In those where methylphenidate is not effective or inadequate duration of action.
b) Lisdexamfetamine would have primary use in replacing dexamphetamine tablets in most people who currently take dexamphetamine 3 times a day.
c) A small group would use a small dose of dexamphetamine alongside Lisdexamfetamine as a ‘top up’ dose when Lisdexamfetamine runs out
d) Second-line medication ahead of atomoxetine (so after methylphenidate) if the patient has had a history of overdose or self-harm. (Atomoxetine has a slightly higher reported rate of these events, so as a consideration of clinical risk, lisdexamfetamine could potentially have a major role)
e) Lisdexamfetamine can be considered as a harm-minimisation drug in people who have used street amphetamine to treat their ADHD. It is hard to get these patients to currently respond to medication- methylphenidate seems to lack efficacy in them, and dexamphetamine is too short acting to be of actual use. (this would be not more than 2 or 3 patients out of the caseload of about 400, so the material costs would be low, and the potential benefits to the people concerned are good).
f) As supplementary prescribing for first line drugs which may be insufficiently effective at maximum dose.

Action:

1. NB to add to formulary TLS Red, to be prescribed within AWP only.
2. NB to contact Dr Badat to discuss change in status request and potential SCP.

5 Shared Care Protocols/TLS status

a. Hypertonic Saline SCP
This SCP has been written by LM, Respiratory Specialist Pharmacist at NBT. Prior to being presented here at the JFG it has been extensively reviewed across NBT and UHBristol by consultants, specialist nurses, and pharmacists. It has also been reviewed by GPs within BNSSG and comments acted upon. The JFG approved this SCP.

Action:

1. NB to upload SCP to the formulary website.

b. Zoledronic acid – Change in status request from Red to amber
No paperwork included. To be deferred until the next meeting.

c. **GnRH analogues – Change in status request from amber to blue**
   See general discussion below.

d. **General discussion on TLS definitions**
   NB requested a discussion regarding how drugs are classified within the BNSSG TLS system. The definitions have not been reviewed for some time. There seems to be increasingly a need to use the blue category to indicate that a medication needs to be recommended for initiation by a specialist; however this may not be an appropriate use of the category blue. There is a need to define a group of medicines that the decision to initiate would never be made in primary care, though the actual drug itself is not specialist in that it needs intense monitoring or the dosage schedule is difficult/subject to specialist interpretation.

   It was felt that if a GP was not likely to see more than one patient per year, then it would not be appropriate for the drug to be considered for primary care prescribing.

   It was decided that a new category would be implemented – ‘amber (Specialist recommendation, no SCP). There will be a need for some drugs that are classified as this to have Prescribing Guidance attached, but there will be no need for secondary care to initiate. The decision to initiate must be made by a specialist but primary care would be able to initiate the prescribing. The GnRH analogues would fit this category – to be discussed during chapter review.

   **Action:**
   1. *NB to make changes to the TLS guidance document on the website.*
   2. *Drugs will be able to be considered to change to this category from now.*

6  **Individual Funding Requests**

None to discuss

7  **Chapter review and formulary process**

a. **Chapter 11 chapter review progress**

   A review of the BNSSG JF chapter 11 had been undertaken by the Consultants at the Eye Hospital, and the comments collated and presented at the group. The comments were separated in terms of drugs that were currently in use but not currently on the formulary (historic use), new drugs to consider including, drugs to remove, TLS changes and other suggestions.

   The group were not happy to include the historic use drugs without proper consideration of whether they had been through UHB MAG previously, and also to consider were whether NHS England would be involved in some of the preparations used.

   **Action:**
   1. *NB to review the comments received regarding chapter 11 and include information on current usage, whether the drug has been through MAG, if is*
specialised commissioning or not, and if it is PbR excluded or not.
2. NB to discuss with TW.
3. NB to bring back to future JFG.

b. Work plan for Chapter review

NB presented a gantt chart for the process of reviewing all of the chapters of the BNSSG Joint Formulary. Chapter 1 officially needed reviewing and updating by December 2012, with the rest of the chapters needing review throughout 2013 and 2014. This piece of work needs to be addressed to ensure that the formulary is kept up to date.

The process of chapter review would be similar to the first edition chapters. Each chapter will be sent out for specialist review for 4 weeks. NB will email out the chapters to the trusts and the CCGs for further dissemination within each organisation (i.e. to appropriate specialists). Comments should be sent back to NB to collate. NB will organise a meeting of a subgroup of the JFG to discuss these comments, and a summary made for presentation at the next JFG. NB will make approved changes to the chapter, and then send out for general comment (4 week) – again to the trusts and CCGs for further dissemination. Comments sent back to NB and meeting arranged for discussion of these comments. The final chapter will then be presented to the JFG.

NB to revise the work plan so that those chapters that we are already aware that there are issues that need reviewing are considered first e.g. chapters 7, 8 and 13. Chapter 3 was suggested to review later due to the number of new inhalers becoming available.

Action:
1. NB to revise the work plan.
2. NB to initiate the work on chapter review, with the help from CCGs and acute trusts.

c. New Drug application Form

NB presented the new application form that had been finalised during the summer of 2013. A couple of changes are required to this e.g. including a section showing that directorate/divisional approval had been sought. The form needs to be trialled in order that we find out if it works or not.

Action:
1. NB to alter the new application form.
2. NB to add to the website. Once available, this form should be used for all new applications.

8 Specialised Commissioning Statements

None

9 MHRA Drug Safety Update

There was insufficient time to discuss this.
10 Items for Discussion

a. Metolazone – MP to lead on producing a summary document for the JFG to consider regarding the withdrawal of metolazone and proposed actions.

   Action:
   1. **MP to bring back paper to future JFG**

b. Omega 3 fatty acids – MP to liaise with cardiology at NBT for advice on the use of omega 3 fatty acids after NICE guidance 172 stated that:
   *‘Do not offer or advise people to use the following to prevent another MI:*
   *• omega-3 fatty acid capsules…’*

   Currently, omega-3 fatty acid capsules are on the BNSSG formulary, and therefore there appears to be a need to remove these.

   Action:
   1. **MP to bring back paper to future JFG**

c. NDRs for March Meeting – NB presented the NDRs to be discussed at the March meeting.

   Post meeting, the NDRs have been finalised:

   1. Timolol eye gel for paediatric haemangioma (unlicensed)
   2. Anticoagulant solution for use with the cell saver
   3. Memantine for the treatment of nystagmus
   4. Relvar (fluticasone and vilanterol) for asthma and COPD
   5. Ibopamine eye drops for low intraocular pressure following retinal detachment or severe uveitis.

11 AOB

None

NB
Interface Pharmacist
3rd February 2014
MEETING DATES 2014

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SPCs</th>
<th>Time</th>
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<tbody>
<tr>
<td>Tuesday 21st January 2014</td>
<td>3rd December 2013</td>
<td>10 am to 1 pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<tr>
<td>Tuesday 4th March 2014</td>
<td>21st January 2014</td>
<td>1.30 – 4.30 pm</td>
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<tr>
<td>Tuesday 22nd April 2014</td>
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<tr>
<td>Tuesday 3rd June 2014</td>
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<tr>
<td>Tuesday 15th July 2014</td>
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<td>9am to 12 pm</td>
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<td>Tuesday 14th October 2014</td>
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<tr>
<td>Tuesday 25th November 2014</td>
<td>14th October 2014</td>
<td>9am to 12 pm</td>
<td>Boardroom South Plaza</td>
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NB. The times of the morning meetings have changed so that the meetings now start at 9am and finish at 12 midday.
BNSSG Joint Formulary Group
Meeting held on Tuesday 4th March 2014 1.30pm - 4.30pm
Venue: Bevan Room, South Plaza, Bristol CCG

Minutes

Present:

Public Health Consultant, Bristol City Council (Chair)
Interface Pharmacist, NHS Bristol CCG
Interface Pharmacist, NHS Bristol CCG
Clinical Effectiveness Research Lead, Bristol City Council
HoMM, NHS South Gloucestershire CCG
HoMM, NHS North Somerset CCG
HoMM, NHS Bristol CCG
Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust
Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust

Apologies:

Consultant in Emergency Medicine, UHBristol NHS Foundation Trust and Associate Director of Patient Safety, and Chair of UHB Medicines Advisory Group
GP, Bristol and member of Bristol CCG Board
Formulary Pharmacist, AWP
GP, North Somerset
Joint D&T Chair, North Bristol NHS Trust
Joint D&T Chair, North Bristol NHS Trust
Chief Pharmacist, AWP
Nurse Prescriber, Bristol
Nurse Prescriber, Bristol
Director of Pharmacy Weston Area Health NHS Trust
Medicines Information Pharmacist, UHBristol

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest
None

The meeting was not quorate. In accordance with the ToR of this group, the Chair of the group determined that the meeting should continue and the Formulary Pharmacist will secure endorsement of any decisions ex-committee via email. Therefore decisions taken during this meeting will need to be ratified and actioned once approved.
2 Minutes of the meeting of 21st January 2014 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 21st January 2014 had been circulated by NB following the meeting. No further comments had been submitted regarding the decisions made. The minutes of this meeting were approved.

It was agreed to include an action log at the end of the minutes to ensure that all actions are taken forward.

Matters arising from January 2014 meeting

No matters arising

3 NICE New Technology Appraisals Published

3.1 Relapsing-remitting multiple sclerosis - Teriflunomide TA302
   - BNSSG TLS status to be Red.

TAs adopted into the BNSSG Joint Formulary January and February 2014
   - TA297 Vitreomacular traction - Ocriplasmin
   - TA298 Choroidal neovascularisation (pathological myopia) – Ranibizumab (TLS Red)
   - TA300 Hepatitis C (children and young people) – peg interferon alfa and ribavirin
   - TA301 Diabetic macular oedema – fluocinolone acetonide intravitreal implant

4 New Drug Requests (NDRs)

SUMMARY

4.1 Timolol 0.5% eye gel – Paediatric Haemangioma
Rejected for inclusion onto the formulary for paediatric haemangioma on the grounds of a lack of sufficiently robust available evidence in this patient cohort, and by accepting its use as routine in this cohort this would be conflicting with the BNSSG Policy on Cosmetic Surgery/Treatment.

4.2 Anticoagulant solution – For use with Cell Saver
Approved for inclusion onto the formulary as an anticoagulant solution for use with the cell saver. By using this solution over the current procedure of using heparin this would reduce a number of risks involved by doing this. TLS Red.

4.3 Memantine – Nystagmus
Rejected for inclusion onto the formulary on the grounds of insufficiently robust
evidence available in this patient cohort and the predicted numbers are so low, that inclusion into the formulary for routine prescribing was not considered appropriate.

4.4 Relvar (Fluticasone and vilanterol) – Asthma and COPD

Approved for inclusion onto the formulary for Asthma and COPD. Evidence has shown that Relvar is comparable to Seretide in both COPD and asthma, and there are advantages of this new device; it is a once a day dosage and is relatively easy to use, which is of significance in this patient cohort. TLS Green.

4.5 Ibopamine eye drops – Abnormally low intraocular

Rejected for inclusion on the formulary on the grounds of insufficiently robust evidence available in this patient cohort to make this available for routine prescribing.

Decision Criteria used by JFG for NDR

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

Full Discussion

4.1 Timolol 0.5% eye gel – Paediatric Haemangioma

This application was submitted by Dr LS, Paediatric Dermatologist, UHBristol. No one was available to attend the meeting to present the application.

Please see application form for full details.

CM and NB presented a summary of the application and the evidence available. The application was for the inclusion of timolol 0.5% eye gel for the treatment of infantile haemangiomas (IHs) specifically when oral propranolol is not justified but the cosmetic effects of a growing haemangioma is still likely to have significant long term effects. There are no licensed treatments available to treat IHs and a lack of high quality clinical research data; consequently evidence based recommendations are not possible and no national guidelines exist. Therefore treatment is based on expert opinion and observational studies. The use of propranolol has increased in recent time mainly due to it being readily available in a paediatric formulation. There is difficulty in identifying when treatment is necessary, but generally it is considered appropriate when ulceration is present, there is impairment of vital function or there is a risk of permanent disfigurement.

The only robust comparative data that the evidence review uncovered was from one RCT. Whilst this RCT does provide evidence of efficacy against placebo, it does have to be considered that this was a single centre study, involving only 41 infants, and treating only small, focal superficial IHs, not requiring systemic therapy. The application states that this would be used in patients when systemic treatment is not necessary, however the group were not able to ascertain exactly which patients this would involve. It was felt that the use of timolol in this patient cohort may be more relating to cosmetic issues and as such agreeing for the inclusion of timolol on the formulary would be in contrast to the BNSSG Cosmetic Surgery/Treatment policy (http://www.swcsu.nhs.uk/media/12288/Cosmetic-Surgery-Policy.pdf) which states that
‘Surgery and Treatments to alter physical appearance alone is not routinely funded by
the Commissioner unless the patient is suffering from a post-trauma injury and is also
suffering from significant functional impairment.’

In terms of safety, the RCT did not provide evidence of any significant issue. It has
been suggested that there is some systemic absorption of timolol that may cause side
effects, but there is nothing to provide evidence of this.

Whilst the cost of the medication is negligible, there is a tariff for the patient attendance
which does have to be considered as this feels like a new cohort of patients being
treated, and it is those that require treatment for cosmetic reasons. It was also noted
that a significant number of IHs are seen in primary care, and there was a concern that
if timolol was included on the formulary specifically for IH treatment, that there could be
inappropriate creep of prescribing in primary care.

During the discussions it was noted that IHs are very common, occurring in about 3-5%
of babies and that 80-90% regress spontaneously (though this can take up to 10
years).

Two areas have been identified that have included timolol onto their formularies for the
treatment of IHs. Great Ormond Street Hospital have a policy for the use of timolol in
small IHs. It states that patients could be considered for treatment if the IH is less than
2cm, and in certain areas. Patients would be reviewed monthly. Leeds have also
accepted it onto their formulary stating that the proposed place in therapy would be
reserved for use in patients with IHs where systemic therapy is contraindicated or
clinically inappropriate, therefore this would be after a trial of oral propranolol if
appropriate.

KG to ascertain if this is already being prescribed within UHBristol.

- **Patient safety** – No evidence has been identified that there are any issues
  around patient safety with the use of topical timolol.
- **Clinical effectiveness** – One small RCT has shown that topical timolol is more
effective than placebo. However alongside this, it should be noted that this is
in the treatment of small superficial IHs, and it is known that 80-90% of these
will resolve spontaneously over time. However, there is no robust evidence for
any treatment for IHs
- **Cost effectiveness or resource impact** – Topical timolol has a very low drug
acquisition cost, however it should be considered that there will be a tariff
incurred for the clinic appointments, especially significant if patients are seen
monthly as it is suggested in the Great Ormond Street protocol.
- **Strength of evidence** – The RCT is a well designed trial, however it is small
and a single centre study, and it is difficult to translate the results to all patients,
with only small superficial IHs being treated. There is no robust evidence
available for any treatment for IH.
- **Place in therapy relative to available treatments** – it is suggested that this
would be used when treatment with systemic propranolol is not considered
appropriate.
- **National guidance and priorities** – No National guidance exists, and
treatment is based on expert opinion.
- **Local health priorities** - NA
- **Equity of access** – GOSH and Leeds have included it on their formularies.
BNSSG have Cosmetic Surgery/Treatment policy as described above, and if
this is treatment is for the cosmetic issues that exist with IHs, then allowing this
on the formulary would be inconsistent with this policy.
The JFG considered the application and the evidence submitted. Whilst it is recognised that there is not expected to be significant amount of evidence in this patient cohort, it was felt that there was not sufficient evidence available to include this onto the formulary for routine prescribing in this patient cohort. It was felt that the use of timolol was more for cosmetic reasons and therefore it would be inequitable to include this on the formulary for these patients when there is a policy that says that BNSSG does not commission cosmetic procedures. It should also be noted, that there is the non-formulary one off prescription route within each acute trust that prescribers can access if it is felt to be appropriate to prescribe in one off cases.

**Action:**

1. **NB to inform applicant.**

4.2 **Anticoagulant solution – For use with Cell Saver**

This application was submitted by WL, Senior Perfusionist, UHBristol. Ian Channon, also a Senior Clinical Perfusion Scientist at UHBristol attended the meeting to present the application.

Please see application form for full details.

The application was for the inclusion of the ACD-A solution for use with the Cell saver which is used during cardiac surgery. The Cell saver is a machine that is used during surgery/trauma to save blood. The blood is washed, suspended in sodium chloride and then given back to the patient. Current practice is that the Sodium Chloride 0.9% 1L solution is injected with 15,000 units heparin by the perfusionist. There are potential problems with this method such as sterility issue, user error, and potential for needle stick injuries. The ACD-A solution is a ready made bag which therefore has the advantage of eradicating the potential for errors stated above, whilst having the same function of the saline solution with heparin. It will also be a quicker method, which is especially significant in an emergency situation. The submission is for the use in cardiac surgery, but there is potential interest in other areas where the Cell saver machine is used.

- **Patient safety** – Noting identified
- **Clinical effectiveness** – No trials, although this is to be expected.
- **Cost effectiveness or resource impact** – likely to be marginally more expensive than the heparin and sodium chloride.
- **Strength of evidence** - NA
- **Place in therapy relative to available treatments** - NA
- **National guidance and priorities** - The UK Cell Salvage Action Group has a factsheet which states that either a heparinised solution should be used, which would need to be made up, or the ACD-A solution can be used.
- **Local health priorities** - NA
- **Equity of access** – STMH have this already in use.

The JFG considered the application and evidence submitted. The JFG approved it for inclusion onto the formulary on the ground of the obvious advantages of using a pre-made bag compared to the addition of heparin to a litre bag of sodium chloride 0.9% without a significant increase in cost.

**Action:**

1. **NB to inform applicant.**
2. **NB to include on the formulary, TLS Red,**
3. KG to inform NB if divisional approval received
4. MP to investigate potential usage at NBT

4.2b Plasma-lyte 148 - A case for Formulary extension from UHBristol

Mr IC also discussed an extra paper regarding UHB’s wish to include Plasma-lyte 148 infusion on the formulary for use in UHB in addition to NBT. An application was made to the JFG by NBT on 14th May 2013 for use as an IV fluid replacement. This application was accepted. At this time, neither UHBristol nor Weston were interested in using the fluid. UHBristol are now requesting the restriction on the formulary ‘for use at NBT only’ to be removed. Mr Channon gave a brief presentation regarding its benefit – mainly that it is low in chloride (where high chloride levels have been associated with increased risk of renal replacement therapy and acute kidney injury); can avoid giving lactate which can confuse management as a normal lactate or falling lactate is a marker of clinical improvement; it does not include calcium to does not interfere with simultaneous blood and possibly bicarbonate administration; and it contains magnesium so may avoid having to separately infuse magnesium supplementation.

The JFG agreed for the restriction of ‘NBT only’ to be removed.

Action:
1. NB to inform applicant.
2. KG to inform NB if/when divisional approval received.
3. NB to update website

4.3 Memantine – Nystagmus

This application was submitted by Dr CG, Consultant Ophthalmic Physician, UHBristol and also attended the meeting to present the application.

Please see application form for full details.

CM presented a summary of the application and the evidence available. The application was for the inclusion of Memantine (at a dose of 20 - 40mg/day) to treat congenital or secondary nystagmus in patients with reduced vision who would like drug treatment and have failed on gabapentin. Nystagmus is typically challenging to treat, and the evidence available for any treatment is very limited. There are a number of small studies with short term follow up, however there is no evidence for the use of Memantine in this particular patient cohort i.e. failed on gabapentin. Nystagmus is very common, and it is difficult to ascertain the numbers that are at the severe end of the condition, and therefore may potentially warrant treatment. The literature suggests that the choice of treatment depends on the type of nystagmus. Concerns exist over the issues of long term treatment, as this is a drug used in dementia and long term data does not exist; and also there does not appear to be a standard pathway for the treatment of nystagmus. Not all studies looked at improvement in vision, and the clinical significance of improvement in vision is unclear. There is no data which empirically assess impact on activities of daily living or work, although it should be noted that, where assessed, patients reported significant improvements in their symptoms.

Discussion with Dr CG

The number of patients that have severe nystagmus that seek treatment are very few. These will be patients that the eye is moving and the image is degraded. A few cross over trials, including gabapentin and Memantine have been conducted. All report some
improvements in various symptoms in most patients. The numbers in these trials are low, and length of follow up was short. It is felt that this application fits those patients that could be considered exceptional, and therefore the merits of including a medicine for patients such as these was discussed.

Patients would be treated for however long they requested treatment, but potentially life long if it worked. To measure success, visual acuity and patient symptoms would be considered. Dr Guly has used gabapentin in one patient, and this hasn’t worked, which is why she is considering Memantine in this patient. There is no other alternative, although other areas have used baclofen.

The numbers of patients seeking treatment for nystagmus could potentially increase with self-help groups listing possible drug treatments available. The Neuro clinics will see more patients for the treatment of nystagmus, as these will be secondary to neurological or vestibular diseases. It is unknown how neurology would treat the nystagmus if the underlying cause cannot be rectified.

• **Patient safety** – Memantine is used in the treatment of Alzheimer’s and in most patients, side effects are mild and usually tolerable. However the dose suggested in nystagmus is higher than the licensed dose for Alzheimer’s, 20mg/day. There is also no long term data which could be significant when considering patient may be on this for a significant time period.

• **Clinical effectiveness** – A few controlled/crossover trials have been conducted involving patients with various types of nystagmus, both congenital and acquired. Also a few observational, non-comparative studies. These all report some improvements in various symptoms in most patients.

• **Cost effectiveness or resource impact** – Costs of drug treatment estimated to be £900 - £1800 per annum per patient.

• **Strength of evidence** – Small numbers of studies, mixed participants, length of follow up relatively short and methods of quantifying nystagmus and impact on vision not standardised across studies. Little data involving patients who have failed on gabapentin.

• **Place in therapy relative to available treatments** - unclear

• **National guidance and priorities** - none

• **Local health priorities** – NA

• **Equity of access** – One other local formulary was identified that included Memantine for the treatment of nystagmus refractory to gabapentin could be found.

The JFG considered the application and the evidence submitted. Whilst it is recognised that there is not expected to be significant amount of evidence in this patient cohort, it was felt that there was not sufficient evidence available to include this onto the formulary for routine prescribing in this patient cohort. It should also be noted, that there is the non-formulary one off prescription route within each acute trust that prescribers can access if it is felt to be appropriate to prescribe in one off cases.

**Action:**

1. **NB to inform applicant**

**4.4 Relvar (Fluticasone and vilanterol) – Asthma and COPD**

This application was submitted by Dr JC, Respiratory Consultant, NBT and Dr NJ, Respiratory Consultant, UH Bristol. No one was available to attend the meeting to present the application.
KG presented a summary of the application and the evidence available. The application was for the inclusion of Relvar (fluticasone (ICS – inhaled corticosteroid) and vilanterol (LABA – long acting beta agonist) in the formulary for the treatment of asthma or COPD. Fluticasone is an inhaled corticosteroid already on the formulary as Flixotide, and also in other combination products, such as Fostair, Symbicort and Flutiform and Seretide. Relvar is delivered in a dry powder inhaler device called Elipta. The lower strength inhaler is licensed for both the treatment of asthma and COPD, whilst the higher strength is only licensed for asthma. It is a once a day dosage, which is unique compared to the other LABA/ICS combinations, and a very easy to use design, especially significant for those with reduced hand mobility.

Fluticasone furoate 92 micrograms once a day is approximately equivalent to fluticasone propionate 250 micrograms twice a day and fluticasone furoate 184 micrograms once a day is approximately equivalent to fluticasone propionate 500 micrograms twice a day.

In terms of evidence for asthma, Relvar has been involved in two main RCTs. Woodcock et al. (n=806) found that there was no statistically significant difference between fluticasone furoate/vilanterol 92/22 micrograms once daily and fluticasone propionate/salmeterol 250/50 micrograms twice daily for the 0–24 hour weighted mean FEV1 week-24 change from baseline. The study was designed to show superiority of fluticasone furoate/vilanterol and powered to detect a difference of 80 ml in the serial weighted mean FEV1 between the 2 groups. At entry to the study (prior to a 4-week run-in period on ICS alone), 69% of participants were already using an ICS plus LABA (equivalent to step 3 or 4 of the British guideline on the management of asthma). Caution is needed in extrapolating the results of this study to people with less severe asthma.

Bateman et al. (n=2020) found that there was a statistically significant reduction from 15.9% to 12.8% in the risk of having a severe asthma exacerbation by 52 weeks with fluticasone furoate/vilanterol 92/22 micrograms once daily compared with fluticasone furoate 92 micrograms once daily. At entry to the study 60% of participants were already using an ICS plus LABA (equivalent to step 3 or 4 of the British guideline on the management of asthma).

In terms of evidence for COPD, there is one RCT(n = 266) which was a 12 week head to head study comparing Relvar (92/22) with twice daily Seretide (500/50). Relvar provided clinically meaningful improvements in lung function compared with baseline although superiority of weighted mean 24 hour FEV1 was not shown against Seretide 500. Both Relvar and Seretide improved QoL from baseline. Only Relvar exceeded the threshold for a clinically important difference however the difference compared with Seretide was not significant.

The available evidence was discussed at length. It has been shown that Relvar is neither superior nor inferior to Seretide. NB read out comments specifically from the applicants, and also that potentially Seretide could be removed for new patients for the treatment of COPD. A comment was also noted that ‘Relvar has a weak effect on exacerbations and on improvement of QoL - A maximum improvement of FEV1 of 40mls was seen with Relvar in one study that reduced to 10ml by the end of the first year, and actually those patients on vilanterol alone showed no improvement at all and were worse off at the end of the study.’ There was some debate over the perceived advance in device and once daily dosing and its significance in the holistic treatment of these patients. Relvar has been priced competitively in that it is the cheapest ICS/LABA combination on the market when comparing appropriate strengths and
licensing.

- **Patient safety** – The studies have shown that Relvar is generally well tolerated in asthma and COPD. In common with other ICS containing medicines there is an increased risk of pneumonia in patients with COPD who are treated with Relvar. Pneumonia occurred in 6% of patients receiving Relvar compared with 3% of patients receiving vilanterol alone. Also the number of non-traumatic fractures were seen more in the patients taking Relvar compared to those taking vilanterol alone. Cardiovascular events, particularly tachycardia, are known risks associated with LABAs. The summary of product characteristics states that fluticasone furoate/vilanterol should be used with caution in people with severe cardiovascular disease.

- **Clinical effectiveness** – Relvar has been shown to be as efficacious compared to Seretide in terms of improvement in lung function and improvement in the weighted mean 24 hours FEV1 from baseline at week 24 in the treatment of asthma. Relvar has been shown in a 12 week head to head study to be as efficacious as Seretide in terms of clinically meaningful improvements in lung function compared with baseline for the treatment of COPD.

- **Cost effectiveness or resource impact** – Relvar has been priced very competitively. Relvar 92/22 costs £27.80 and the higher strength costs £38.87. Therefore, compared with other mid dose ICS/LABA inhalers it is the cheapest and also compared to the higher dose combination inhalers it is the least expensive.

- **Strength of evidence** – There are various limitations with the studies, though also strengths. The asthma study by Woodcock et al was designed as a superiority study, though the findings were not consistent with this. There are no studies which compare Relvar with another combination ICS/LABA in terms of a patient orientated outcome such as exacerbation rate. There were also some methodological limitations in some of the COPD studies. However, generally the evidence was of sound quality.

- **Place in therapy relative to available treatments** - Relvar should be used for the treatment of asthma patients who are not adequately controlled on ICS alone, in line with the BTS-SIGN stepwise management guideline i.e. Step 4 (due to its steroid content). The evidence does not support it being any more efficacious than other step 4 inhaler. For COPD, the evidence suggests that it is similar in efficacy to Seretide and therefore could be placed alongside Seretide. It is licensed for use in patients with an FEV1 of less than 70% predicted normal. However NICE guidance 101 suggests that a LABA/ICS combination should be initiated in patients with a FEV1 of less than 50%.

- **National guidance and priorities** - none

- **Local health priorities** – Long term conditions

- **Equity of access** – NA

The JFG considered the application and the evidence and information submitted. Relvar has been approved for inclusion to the Joint Formulary for use in asthma and COPD (with a FEV1 of less than 50% predicted), TLS Green. The JFG once again noted that more inhalers are due on the market over the next 18 months, and a full review will be necessary once they have all been approved and available.

**Action:**

1. **NB to inform applicant.**
2. **NB to include on the formulary, TLS Green**
4.5 Ibopamine eye drops – Abnormally low intraocular pressure

This application was submitted by Mr RH, Consultant Ophthalmic Surgeon, UH Bristol. No one was available to attend the meeting to present the application.

Please see application form for full details.

CM presented a summary of the application and the evidence available. The application was for the inclusion of unlicensed Ibopamine eye drops to treat abnormally low intraocular pressure following retinal detachment or severe uveitis. It would be prescribed potentially indefinitely. There are no other treatment alternatives. It is predicted that up to 5 patients per year would be treated with Ibopamine eye drops. The group discussed what would happen without treatment i.e. what are the clinically meaningful benefits of treatment— is it just symptomatic relief or an improvement in vision? The literature suggests that chronic ocular hypotony is typically challenging to manage with very few therapeutic options with limited efficacy. There is not a significant amount of evidence available to consider… only 7 studies published between 1997 – 2014 were identified. Out of these 2 were abstract only as they were published in a foreign language. Most of the data comes from observational studies, and only 18 patients have been included in 2 comparative studies. All report some improvement in intraocular pressure (IOP). The clinical significance of an increase in IOP is unclear, and in fact the largest study that looked at improvement in vision found that no change in visual acuity was found.

- **Patient safety** – Side-effects, troublesome enough to warrant discontinuation of treatment, are relatively frequently reported in published studies. They include follicular conjunctivitis and irritation without conjunctivitis. Long term effects unknown.
- **Clinical effectiveness** – Lack of good quality trials. All studies reported improvements in IOP however it is difficult to ascertain the clinical significance of the increase in IOP.
- **Cost effectiveness or resource impact** – Costs have been estimated to be £336.70 per patient per 52 weeks.
- **Strength of evidence** – A lack of good quality evidence. Most data comes from observational studies. Length of follow up was generally short.
- **Place in therapy relative to available treatments** – No other treatment available.
- **National guidance and priorities** - none
- **Local health priorities** –
- **Equity of access** – No other local formulary found to include Ibopamine.

The JFG considered the application and the evidence submitted. Whilst it is recognised that there is not expected to be significant amount of evidence in this patient cohort, it was felt that there was insufficient evidence available to include this onto the formulary for routine prescribing in this patient cohort. It should also be noted, that there is the non-formulary one off prescription route within each acute trust that prescribers can access if it is felt to be appropriate to prescribe in one off cases.

**Action:**

1. *NB to inform applicant.*

5 Shared Care Protocols/TLS status
5.1 Ranolazine
This SCP has been written by LM, Respiratory Specialist Pharmacist at NBT. Prior to being presented here at the JFG it has been extensively reviewed across NBT and UHBristol by consultants, specialist nurses, and pharmacists. It has also been reviewed by GPs within BNSSG and comments acted upon. The JFG approved this SCP.

Action:
1. NB to upload SCP to the formulary website.

5.2 Lisdexamfetamine – Change in status request from Red to amber
The JFG discussed how the AWP and BNSSG formularies work together and the impact on the BNSSG formulary of a medicine being included on the AWP formulary. Lisdexamfetamine has been reviewed by the BNSSG JFG and included on the formulary for the treatment of ADHD in children and adolescents. It is not included currently on the adult formulary. It is licensed for continuation of treatment of ADHD into adulthood. It is included on the AWP formulary. The JFG agreed that before a TLS change could be discussed, it was necessary for the group to consider an application to ensure that the proper process of managing new drugs into the formulary was followed. During the application, the TLS status would be discussed.

Action:
1. NB to inform applicant that a NDR is required.

6 Individual Funding Requests
NB informed the group that via the IFR panels, it had been identified that a number of requests had been submitted for the use of Botulinum toxin for the treatment of urinary incontinence. Therefore the applicants have been contacted to request that they submit an application to the JFG for consideration as there is clearly a cohort.

7 Chapter review and formulary process
7.1 Chapter 11 chapter review progress
The review of chapter 11 presented at the last JFG has not been progressed further.

Action:
1. NB to review the comments received regarding chapter 11 and include information on current usage, whether the drug has been through MAG, if is specialised commissioning or not, and if it is PbR excluded or not.
2. NB to discuss with Tracey Williams.
3. NB to bring back to future JFG.

7.2 NDR form
NB stated that the revised NDR form was now available on the website and that all
applicants should now be directed to use this form from now on.

7.3 Chapter review

NB has altered the work plan for reviewing all of the chapters of the BNSSG Joint Formulary after the last meeting. NB will shortly send out the first chapters for review that will need to be sent out to the specialists within the trusts and CCGs for initial comments.

Action:
1. NB to send out chapters for review.
2. KG/MP/KH to send on chapters to appropriate specialists and collate comments to be sent back to NB at the end of the review period.

8 Specialised Commissioning Statements

None

9 MHRA Drug Safety Update

Nothing to discuss.

10 Items for Discussion

10.1 Primary Care Antibiotic Guidelines

NB reported that she had reviewed the recently updated BNSSG primary care antibiotic guidelines to ensure that they were in line with the formulary. There were a few minor changes required.

Action:
1. NB to amend formulary in line with antibiotic guidelines.

10.2 NDRs for April Meeting

NB stated that the NDRs for the following meeting were:
1. 1a. Dexmedetomidine for awake craniotomy, NBT submitted
   1b. Dexmedetomidine for sedation in PICU, UHBristol submitted
2. Colobreathe for non-CF bronchiectasis when nebuliser is not tolerated, NBT.
3. Regadenoson for stress myocardial perfusion imaging scans, NBT submitted. (TBC)
5. Alogliptin, Primary care submitted.
6. Lisdexamfetamine for ADHD in adults, AWP submitted. (TBC)

10.3 Metolazone Proposal (NBT)

Metolazone – MP presented a SBAR document on the issue of metolazone being only available as an unlicensed product. The reason for the discontinuation of metolazone is due to an inability to manufacture the previously licensed product. No generic company in the UK has a license, and therefore patients on metolazone will be required to be prescribed an unlicensed imported metolazone. Two products are
available for importation, one of which contains a colorant which is not permitted in the UK. This is not due to safety concerns, but due to lack of EU evaluation. Cardiologists' views have been sought and it is their opinion that metolazone still needs to remain on the formulary as it has a role in the treatment of severe heart failure. It has been requested that community pharmacists wherever possible obtain the Italian brand that does not include the colorant.

Action:

1. **NB to annotate formulary that metolazone is unlicensed.**

11 AOB

None

NB
Interface Pharmacist
6th March 2014
### BNSSG JFG

**Action Log for 4th March 2014**

<table>
<thead>
<tr>
<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
<th>RO (s)</th>
<th>Deadline</th>
<th>Date of Update</th>
<th>Update</th>
</tr>
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<tbody>
<tr>
<td>4.3.14</td>
<td>3.1</td>
<td>NICE TAs</td>
<td>NB/SB to add all positive NICE TAs to the JF website within 90 days of publication</td>
<td>NB/SB</td>
<td>31st March 2014</td>
<td>31st March 2014</td>
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<tr>
<td>4.3.14</td>
<td>4.1</td>
<td>Timolol for paediatric haemangioma NDR</td>
<td>Inform applicant of decision to reject application due to insufficient evidence base. Direct applicant to non-formulary one off request route within acute trust.</td>
<td>NB</td>
<td>31st March 2014</td>
<td>27th March 2014</td>
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<tr>
<td>4.3.14</td>
<td>4.2</td>
<td>Anticoagulant for Cell Saver NDR</td>
<td>Inform applicant of decision to include on the formulary. Update website.</td>
<td>NB</td>
<td>31st March 2014</td>
<td>27th March 2014</td>
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<tr>
<td>4.3.14</td>
<td>4.2b</td>
<td>Plasmalyte</td>
<td>Inform applicant of decision to include on the formulary. Update website</td>
<td>NB</td>
<td>31st March 2014</td>
<td>27th March 2014</td>
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<tr>
<td>4.3.14</td>
<td>4.3</td>
<td>Memantine for Nystagmus NDR</td>
<td>Inform applicant of decision to reject application due to insufficient evidence base. Direct applicant to non-formulary one off request route within acute trust.</td>
<td>NB</td>
<td>31st March 2014</td>
<td>27th March 2014</td>
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<tr>
<td>4.3.14</td>
<td>4.4</td>
<td>Relvar NDR</td>
<td>Inform applicant of decision to include on the formulary. Update website.</td>
<td>NB</td>
<td>31st March 2014</td>
<td>31st March 2014</td>
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<tr>
<td>4.3.14</td>
<td>4.5</td>
<td>Ibopamine eye drops NDR</td>
<td>Inform applicant of decision to reject application due to insufficient evidence base. Direct applicant to non-formulary one off request route within acute trust.</td>
<td>NB</td>
<td>31st March 2014</td>
<td>31st March 2014</td>
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<tr>
<td>4.3.14</td>
<td>5.1</td>
<td>Ranolazine SCP</td>
<td>Inform applicant of decision to sign off</td>
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<td>31st March 2014</td>
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<td>Date</td>
<td>Code</td>
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<tr>
<td>4.3.14</td>
<td>5.2</td>
<td>Lisdexamfetamine TLS Request</td>
<td>Inform applicant that a NDR is required initially and TLS status to be discussed</td>
<td>NB</td>
<td>31st March 2014 31st March 2014</td>
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<tr>
<td></td>
<td>7.1</td>
<td>Chapter 11 review</td>
<td>Review items requested for inclusion in terms of indication, and whether they are NHSE commissioned or not. Bring back to JFG.</td>
<td>NB</td>
<td>22nd April 2014 Not complete</td>
<td></td>
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<tr>
<td></td>
<td>7.3</td>
<td>Chapter review</td>
<td>Send out first chapters for Specialist review</td>
<td>NB and MP/KG/MG/JH/MG/DC</td>
<td>31st March 2014 25th March 2014 Chapters sent out</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>10.1</td>
<td>Primary Care Antibiotic guidelines</td>
<td>Amend website in line with new primary care antibiotic guidelines</td>
<td>NB</td>
<td>17th March 2014 10th March 2014 Discussion with microbiologists re: Nystatin vs miconazole first line</td>
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<td></td>
<td>10.3</td>
<td>Metolazine</td>
<td>Amend website to state that it is unlicensed</td>
<td>NB</td>
<td>31st March 2014 17th April 2014</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RO – Responsible Officer
**MEETING DATES 2014**

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SPCs</th>
<th>Time</th>
<th>Venue</th>
</tr>
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<tbody>
<tr>
<td>Tuesday 21st January 2014</td>
<td>3rd December 2013</td>
<td>10 am to 1pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<tr>
<td>Tuesday 4th March 2014</td>
<td>21st January 2014</td>
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<td>Bevan Room South Plaza</td>
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<tr>
<td>Tuesday 22nd April 2014</td>
<td>11th March 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 3rd June 2014</td>
<td>22nd April 2014</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room South Plaza</td>
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<td>Tuesday 15th July 2014</td>
<td>3rd June 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
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<td>Tuesday 2nd September 2014</td>
<td>22nd July 2014</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room South Plaza</td>
</tr>
<tr>
<td>Tuesday 14th October 2014</td>
<td>2nd September 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 25th November 2014</td>
<td>14th October 2014</td>
<td>9am to 12pm</td>
<td>Boardroom South Plaza</td>
</tr>
</tbody>
</table>

**NB.** The times of the morning meetings have changed so that the meetings now start at 9am and finish at 12 midday.
BNSSG Joint Formulary Group
Meeting held on: Tuesday 22nd April 9am – 12 midday
Venue: Seminar Room, Pharmacy Department, Southmead Hospital

Minutes

Present:

Public Health Consultant, Bristol City Council (Chair)
Interface Pharmacist, NHS Bristol CCG
Interface Pharmacist, NHS Bristol CCG
Clinical Effectiveness Research Lead, Bristol City Council
HoMM, NHS North Somerset CCG
Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust
Public Health Registrar
Deputy Head of Medicines Management, NHS South Gloucestershire CCG
Medicines Management Pharmacist, NHS Bristol CCG
Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust
Joint D&TC Chair, North Bristol NHS Trust

Apologies:

Consultant in Emergency Medicine, UHBristol NHS Foundation Trust and Associate Director of Patient Safety, and Chair of UHB Medicines Advisory Group
GP, Bristol and member of Bristol CCG Board
HoMM, NHS Bristol CCG
Formulary Pharmacist, AWP
GP, North Somerset
Joint D&TC Chair, North Bristol NHS Trust
Chief Pharmacist, AWP
Nurse Prescriber, Bristol
Nurse Prescriber, Bristol
Director of Pharmacy Weston Area Health NHS Trust
HoMM, NHS South Gloucestershire CCG

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest
None
The meeting was not quorate. In accordance with the ToR of this group, the Chair of the group determined that the meeting should continue and the Formulary Pharmacist will secure endorsement of any decisions ex-committee via email. Therefore decisions taken during this meeting will need to be ratified and actioned once approved.

2 Minutes of the meeting of 4th March 2014 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 4th March 2014 had been circulated by NB following the meeting. No further comments had been submitted regarding the decisions made. The decision regarding the application for the drug Relvar was to be discussed in ‘Matters arising.’ The minutes of this meeting were approved.

Matters arising from March 2014 meeting

Relvar NDR
Following the JFG March meeting, where the decision to include Relvar for the treatment of COPD and Asthma was made, the Midlands Therapeutics and Advisory Committee (MTRAC) considered and reported on Relvar in the treatment of COPD. In its review, it stated that ‘The fluticasone furoate/vilanterol (FF/VIL) dry powder inhaler cannot be recommended for prescribing for the treatment of chronic obstructive pulmonary disease (COPD), due to the potential safety risk associated with the similarity of the inhaler colour to a reliever inhaler; and the possibility of accidental steroid overdose.’ Therefore it was necessary to bring the decision back to the group to confirm that the group are still happy with the original decision. Comments have been sought from the whole group prior to this meeting.

LM (Respiratory Specialist Pharmacist, NBT) attended the meeting. The group felt that whilst the colour of the inhaler is not ideal, it was felt that there were a growing number of different inhaler types on the market now, and that prescribers and patients, are familiar with other inhalers than just the MDIs. KG confirmed that the respiratory nurses at UHB were not concerned with the colour of the inhaler. Lloyd felt that the MTRAC review provided a timely reminder for prescribers to counsel patients appropriately, and to not rely on the colour of inhalers. The SMC have also since reported on Relvar for the treatment of COPD (7th April 2014). It states that (Relvar Ellipta®) is accepted for restricted use within NHS Scotland - in patients with severe COPD (FEV1 <50% predicted normal).’ The SMC is due to issue advice on asthma in June 2014.

The group felt happy to uphold the decision made at the last JFG, and that colour alone was not a reason to reject the application. Patients should be counselled effectively to ensure that they are aware of the different inhalers and when to use them.

Ibopamine NDR
At the March JFG, the group discussed an application for Ibopamine eye drops in the treatment of abnormally low intraocular pressure. This application was rejected on the grounds of insufficiently robust evidence available in this patient cohort to be able to make this available for routine prescribing. The applicant had been informed of the decision and was made aware of the non-formulary one off prescription route, which the group felt would be an appropriate route for these patients. The applicant has since responded:

‘This is a very disappointing decision as the numbers of patients involved is small, the cost is low and the patients are usually in a pretty desperate position (as is the 16 year old girl who is facing a cosmetically unacceptable shrunken eye due to low pressure on top of the psychological trauma of losing the vision).’

It was requested that Dr H comments were shared with the group. Dr H has been made aware of
the process within UHB to prescribe non-formulary medicines for one off patients.

3 NICE New Technology Appraisals Published

3.1 Visual impairment caused by macular oedema secondary to central retinal vein occlusion – Aflibercept solution for injection **TA305**

3.2 Multiply relapsed or refractory aggressive non-Hodgkin’s B cell lymphoma - Pixantrone monotherapy **TA306**
- BNSSG TLS status to be Red.

No TAs adopted into the BNSSG Joint Formulary in March 2014

4 New Drug Requests (NDRs)

SUMMARY

4.1 **Dexmedetomidine** – Awake Craniotomy (NBT)  
Approved for inclusion onto the formulary, on the grounds of the clinical benefits demonstrated using dexmedetomidine in these patients – anxiolytic, analgesic and does not cause respiratory depression and thus an increase in intracranial pressure. TLS Red.

4.2 **Dexmedetomidine** – For sedation in Paediatric Intensive Care (PICU, UHB)  
Approved for inclusion onto the formulary on the grounds of the clinical benefits demonstrated in these patients. TLS Red.

4.3 **Colobreathe Inhaler** – Non Cystic Fibrosis Bronchiectasis  
Approved for inclusion onto the formulary on the grounds of a logical pathway demonstrated for those patients who require prescription of colistimethate but are unable to tolerate or comply with nebulisers. TLS Red.

4.4 **Botulinum toxin (Botox)** – Urinary Incontinence  
Clinically accepted, costs of current and proposed pathways need demonstrating and agreeing by CCG boards. TLS Red. Will remain non-formulary until CCG boards have signed off the application.

4.5 **Alogliptin** – Type 2 diabetes  
Decision deferred. More information needed regarding the drug class, the ‘gliptins’ to enable the JFG to identify which gliptins should be included on the formulary.

4.6 **Dapoxetine** – Premature ejaculation  
Application rejected. Although licensed, no cost-effectiveness versus other unlicensed but standard practice treatments had been demonstrated.

4.7 **Regadenoson** – For use in stress myocardial perfusion imaging scans (NBT)  
Approved for inclusion onto the formulary in line with UHB MAG decision.

4.8 **Linaclotide** – IBS with Constipation
Approved for inclusion onto the formulary once shared care protocol has been developed.

Decision Criteria used by JFG for NDR

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

Full Discussion

4.1 Dexmedetomodine – Awake Craniotomy (NBT)

This application was submitted by Dr PK, Consultant Anaesthetist, NBT. Dr PK attended the meeting to present the application.

Please see application form for full details.

NB presented a summary of the application. The application was for the inclusion of dexmedetomidine for use in awake craniotomies, which would be an off-label use. The JFG approved the inclusion of dexmedetomidine onto the formulary on the 15th October 2013, for a specific cohort – ‘For those patients failing to wean from invasive ventilation with traditional management due to agitation. UHB only.’

Both SMC and AWMSG have approved dexmedetomidine for use but in the licensed indication of sedation in adult intensive care units, in patients requiring a sedation level not deeper that arousal in response to verbal stimulation.

The current regime being used is propofol and remifentanil and both these agents are not licensed for use in awake craniotomies. There are currently no agents specifically licensed for this indication. There is limited evidence available, but this is not surprising given the specialist indication.

Dexmedetomidine has the advantage that it doesn’t cause respiratory depression compared to propofol and remifentanil and therefore the risk of a rise in intracranial pressure is reduced. A rise in intracranial pressure could lead to the procedure being abandoned. It induces reversible sedation during which the patient can easily be aroused, and also has anxiolytic and analgesic properties. Dexmedetomidine will allow patients to respond to verbal stimulation which is necessary during these procedures. The evidence although weak (case reports, small open label studies), does support these advantages. Dexmedetomidine would cost more than propofol and/or remifentanil though this cost is proposed to be offset by a reduction in theatre time, which is costed to be approximately £20 per minute. The application has been supported by the Clinical Director, MM for this indication only. It is in-tariff. It would only be used at NBT for this indication and not UHB or Weston.

Dr PK has used it once in a patient, with a very good outcome; he would now like to increase usage, in same manner that the unit in Salford Royal do.

Discussion with Dr PK

Dr PK would like to use Dexmedetomidine for awake craniotomies, due to it having no respiratory effects compared to propofol. It is causes a dose dependent sedation, from
which it is easy to rouse patients. It has been used extensively in Europe and the USA, but only just beginning to be used in the UK (Dexmedetomidine has been around in the USA since 2009, but only introduced into the UK from 2011). Salford Royal have been using this technique successfully; other centres are also using it. Patients are put to sleep and then are woken up for the surgery for which they need to be awake to ensure the best preservation of the eloquent areas of the brain. The problems with the current regime used (propofol and remifentanly) are pain and that the patients are difficult to rouse. Experience has shown that by using dexmedetomidine patients wake up quicker, as the ‘sleep’ is more natural. When using propofol, rousing patients is more unpredictable and can take up to 20 -25 mins. When using propofol, the patients seem to be awake, but they do not understand everything. Propofol and remifentanly both have a respiratory depressive effect – this can be a problem because as soon as the respiratory rate decreases, the levels of CO2 increase, which causes an increase in the intraocular pressure, and subsequently the dura cannot be opened, which would lead to the procedure being abandoned.

Hypotension and bradycardia are side effects associated with dexmedetomidine, which would have to be managed. It is a more selective alpha2 agonist compared to clonidine, and Dr PKs opinion is that side effects are not as marked with dexmedetomidine compared to clonidine.

- **Patient safety** – Hypotension and bradycardia are side effects associated with dexmedetomidine, which would have to be managed. Patients appear to tolerate the procedure with dexmedetomidine with no major complications.
- **Clinical effectiveness** – No agent is specifically licensed for awake craniotomies. The evidence included in the application indicates that dexmedetomidine has anxiolytic and analgesic properties in addition to sedation without causing respiratory depression, and thus a rise in intracranial pressure. It is suggested that lower doses than those used in intensive care for sedation.
- **Cost effectiveness or resource impact** – Dexmedetomodine is in-tariff. The application has been signed off by the clinical director. It has an increased cost compared to the current regime, though this increase is proposed to be offset by a reduction in theatre time. It has been estimated to cost NBT an additional £416.36 - £2,379.20 of drug costs based on the predicted numbers.
- **Strength of evidence** – No RCTs have been included as part of the application – all the papers are small scale studies or case reports but provide weak evidence for its use and the dosing. Considering the small number of patients involved, it is not surprising that large RCTs do not exist for this indication.
- **Place in therapy relative to available treatments** – Dexmedetomidine would be used in all patients undergoing awake craniotomies, who currently are treated with propofol and remifentanly. It is not licensed, however no agent is specifically licensed in this indication.
- **National guidance and priorities** – No National guidance exists
- **Local health priorities** – NA
- **Equity of access** – Salford currently use it in these patients. Difficult to identify other areas that include it on their formulary for this indication.

The JFG considered the application and the evidence submitted. Whilst there is no strong evidence in this patient cohort, the JFG recognised that this is not to be unexpected due to the specific indication and numbers of patients. Dexmedetomidine has anxiolytic and analgesic properties without an effect on respiratory rate, and subsequent rise in intracranial pressure, therefore it is a suitable agent for use in this cohort. The evidence (small studies and case reports) supports this. The JFG have approved the inclusion of dexmedetomidine onto the formulary for patients undergoing awake
craniotomies, TLS Red.

**Action:**

1. **NB to inform applicant.**
2. **NB to include on the formulary**

### 4.2 **Dexmedetomidine** – For sedation in Paediatric Intensive Care (PICU, UHB)

This application was submitted by Professor AW and Dr IJ, Consultants in Paediatric Anaesthesia and Intensive Care, UHBristol. Dr Ian Jenkins attended the meeting to present the application.

Please see application form for full details.

The application was for the inclusion of dexmedetomidine for sedation in paediatric intensive care at UHB, specifically in those patients who have difficult sedation in long stay paediatric patients. It would only be used when all other classic sedation drugs have failed and will be specifically considered in infants with life threatening pulmonary hypertension or intractable withdrawal from sedation/analgesic drugs. It would not be used as routine.

The JFG approved the inclusion of dexmedetomidine onto the formulary on the 15th October 2013, for a specific cohort – ‘For those patients failing to wean from invasive ventilation with traditional management due to agitation. UHB only.’ Therefore the cohort suggested in this application is very similar, except paediatric.

It is not licensed in the paediatric population, though this is not unexpected. Paediatric experiences in the literature are in the form of small studies and case reports. It suggests the potential use of dexmedetomidine as an adjunctive agent to other sedatives during mechanical ventilation and opioid withdrawal.

**Discussion with Dr IJ**

Dr IJ acknowledged the lack of evidence, but as discussed, this is not to be unexpected. Dexmedetomidine would only be used in patients with difficult sedation in long term PICU patients. It is proposed that it is more effective than the current agents used, clonidine - it is a more selective alpha 2 agonist, and has analgesic, anxiolytic properties, along with no effect on respiratory rate. There is limited evidence (1 study) which has ‘proved’ that dexmedetomidine does not cause respiratory depression.

The cardiovascular events noted with dexmedetomidine in one study was discussed – in this study, cardiovascular events were shown to be three times more likely with dexmedetomidine compared to chlorpromazine, midazolam and fentanyl. Most agents used will have a degree of cardiovascular effects, but these patients are on PICU and will be closely monitored. It is more cardiovascularly stable with a more effective sedating action compared to clonidine.

- **Patient safety** – It has been shown that in paediatric patients who received dexmedetomidine following cardiothoracic or heart transplantation surgery that adequate sedation and analgesia was provided without compromising haemodynamic or respiratory status.

- **Clinical effectiveness** – Much of the data that currently exists is based on small case reports that have looked at dexmedetomidine in other clinical settings and not just the PICU setting. It has shown to reduce the dose or discontinuation of other sedative agents. Dexmedetomidine produces sedation, a mild degree of analgesia and anxiolytic effects without significant respiratory depression.

- **Cost effectiveness or resource impact** – It is more expensive than the
alternative agent currently used – clonidine. It would be used in a small refined cohort and so increase in drug costs are likely to be small. It is suggested that the increase in drug costs may be off-set by a decrease in the number bed days with successful weaning.

- **Strength of evidence** – Weak evidence, small case reports, used in other settings and indications though in the paediatric environment.
- **Place in therapy relative to available treatments** - To be used if all classic sedative agents have failed.
- **National guidance and priorities** - None.
- **Local health priorities** – NA
- **Equity of access** – Approved for adults in patients failing to wean from invasive ventilation with traditional management due to agitation.

The ward pharmacist can monitor the use of dexmedetomidine to ensure that it is in line with the formulary and the proposed pathway, and indication.

The JFG considered the application and evidence submitted. Whilst there is no strong evidence in this patient cohort, the JFG recognised that this is not to be unexpected due to the specific indication and numbers of patients. There are proven advantages of dexmedetomidine compared to other agents, making it a consideration in those patients in whom sedation is proving difficult. The JFG has approved the inclusion of dexmedetomidine onto the formulary for long stay paediatric patients on PICU who are experiencing difficult sedation – specifically those with life threatening pulmonary hypertension or intractable withdrawal from sedation/analgesic drugs, TLS Red.

**Action:**

1. **NB to inform applicant.**
2. **NB to include on the formulary, TLS Red,**
3. **KG to inform NB if divisional approval received**

**4.3 Colobreathe inhaler** – Non Cystic fibrosis bronchiectasis when nebuliser is not appropriate (off label use).

This application was submitted by Dr MP, Respiratory Consultant, NBT. LM (Specialist Respiratory Pharmacist, NBT) attended the meeting to present the application.

Please see application form for full details.

CM presented a summary of the application and the evidence available. The application was for the inclusion of Colobreathe inhaler for the treatment of chronic pulmonary infection caused by pseudomonas aeruginosa in patients with non CF bronchiectasis where the patient would benefit from continued colistimethate sodium but does not tolerate it in its nebulised form, or is unable to comply with the process of reconstitution and nebulisation of colistimethate despite appropriate training and support, and thus nebulised tobramycin would otherwise be considered.

There are currently no licensed colistimethate products for the treatment of non-CF bronchiectasis; use of nebulised or inhaled colistimethate sodium for treating non-CF bronchiectasis is off label. The main issues in this application is how appropriate is it to extrapolate data from patients with CF to those with non-CF bronchiectasis. There is very small evidence for the nebulised form in non-CF bronchiectasis, let alone the dry powder inhalers. The disease itself is under-researched making evidence based decision making difficult. Authors talk about how valid it is to extrapolate evidence from the CF population to the non-CF bronchiectasis population.
It is clear that the cohort identified in this NDR is just those who can't tolerate the nebulisers and therefore this is proposed to be very small numbers – less than 5 in BNSSG.

Discussion with LM

LM acknowledged that there was a potential issue in extrapolating results from studies involving CF patients to those with non-CF bronchiectasis. Bronchiectasis is very under researched. A lot of decision making is based on anecdotal evidence. Currently, if you have a patient who is experiencing multiple exacerbations, they would be initiated on treatment to reduce these. Options suggested for P. aeruginosa are gentamycin, tobramycin and colistimethate. Due to a lack of treatment options, established clinical practice has been to use colistimethate in a similar way for non-CF bronchiectasis caused by P. aeruginosa to how it is used in people CF, despite lack of marketing authorisation. In response to this practice, NICE have recently published an ESUOM outlining the evidence base for the off-label use of colistimethate in this population. No case series used the inhaled colistimethate. Tobramycin is also available as an inhaler.

NBT currently have 4 patients who they have concerns about complying with nebulisers. Of these, 2 have tried an inhaler and have been successful – one patient who was having exacerbations every 6 weeks is now at week 19 without a further exacerbation after the introduction of the inhaler. The other 2 patients discontinued treatment with the inhaler.

It is logistically more difficult for the department to initiate a patient on an inhaler compared to the nebulisers as they use homecare for the delivery of the nebulisers, whereas they would have to supply the inhalers from secondary care.

Gentamicin and colistimethate are first line options, and most patients will improve with these. For those who are still experiencing exacerbations, the third line option is tobramycin.

It was questioned why inhalers aren’t first line over the nebulisers, given that this would be easier for all patients. The inhalers are not without problems – occasionally the capsules for the inhaler break, there is an increase in the frequency of sore throats, and nasal problems. The colobreathe inhaler is similar in price to nebulised tobramycin, but more expensive than gentamicin or colistimethate. They have not considered an application for inhaled tobramycin due to the increased incidence of sore throats particularly with this.

They would always prescribe for a maximum of 3 months, and then review, and stop if there is no change in exacerbation rate.

- **Patient safety** – Currently already on the formulary for the treatment of CF patients.
- **Clinical effectiveness** – Non-CF bronchiectasis is an under-researched condition with the evidence base for treatment having largely been extrapolated (validity unclear) from studies in CF or based on consensus expert opinion. Current BTS guidelines state that patients having >3 exacerbations per year requiring antibiotic therapy or patients with fewer exacerbations that are causing significant morbidity should be considered for long-term nebulised antibiotics. The NICE evidence summary on non-CF bronchiectasis and colistimethate considered inhaled colistimethate, however no case series used the inhaler, just the nebuliser.
- **Cost effectiveness or resource impact** – Costs of drug treatment estimated to be £900 - £1800 per annum per patient.
- **Strength of evidence** – No published RCTs have investigated nebulised or inhaled colistimethate for non CF bronchiectasis. The NICE summary conclude by saying that there are 4 case series that provide weak evidence for the safety and effectiveness of nebulised colistimethate sodium for treating non CF
bronchiectasis. ? Difficult to extrapolate to inhaler.

- **Place in therapy relative to available treatments** – To be only used in those patients in whom nebuliser treatment is not appropriate/failed.
- **National guidance and priorities** - none
- **Local health priorities** – NA
- **Equity of access** –

The JFG considered the application and the evidence submitted. The JFG acknowledged that this disease area is under researched, and therefore decisions have to be made by extrapolating evidence. It is clear that there is a logical pathway for these patients to follow, and whilst there is not a strong evidence base, the inhaled route would only be used in those patients in whom nebulisers are not appropriate, and essentially there are no other options to treat a rise in exacerbation rate. The JFG approved the inclusion on the formulary of Colobreath only for patients in whom nebulisers were inappropriate.

The JFG discussed whether the BNSSG Non-CF bronchiectasis guidelines needed updating to accommodate this – it was decided that the guidelines cover the wider bronchiectasis population and that the patients on colobreath would be those considered exceptional.

**Action:**

1. **NB to inform applicant**
2. **MP to confirm directorate approval**
3. **NB to include on the formulary, TLS Red**

Post meeting note – MP confirmed directorate approval.

**4.4 Botulinum toxin A, Botox – Urinary Incontinence**

This application was submitted by Mr MD, Consultant Urologist, NBT, and he attended the meeting to present the application.

Please see application form for full details.

NBT were asked to submit a NDR to the JFG after applications to the IFR panel had identified a cohort. NB presented a summary of the application and the evidence available. The application was for the inclusion of Botox for the treatment of urinary incontinence; specifically patients will be adults with symptoms of urgency urinary incontinence (UUI) due to overactive bladder (OAB) or neurogenic detrusor overactivity (NDO) in patients with multiple sclerosis and spinal cord injury, who are not adequately managed with antimuscarinics. A proposed pathway for the introduction of Botox in this indication was presented along with the application. NICE, SMC, AWMSG and Cochrane have all recently reported on the use of Botox in these indications (although in differing indications across OAB).

11 RCTs in total were included in the NICE clinical guidance on the management of urinary incontinence in women, comparing Botulinum toxin A 200U versus placebo, Botulinum toxin A 200 U versus 100 U and Botulinum toxin A versus placebo. On the basis of a favourable clinical efficacy and the health economic profile, the CDG felt that on balance the evidence justified the recommendation to offer Botulinum toxin A as the first intervention to be routinely offered to women who have had unsuccessful conservative treatment (including antimuscarinic drugs) and have proven detrusor overactivity. NICE have also published clinical guidance on *Urinary incontinence in neurological disease. Management of lower urinary tract dysfunction in neurological disease* issued August 2012. Within this guidance, it states that bladder wall injection with Botulinum toxin type A should be offered to adults with spinal cord disease, with symptoms of an
overactive bladder and in whom antimuscarinic drugs have proved to be ineffective or poorly tolerated. It should also be offered to adults with spinal cord disease, and with urodynamic investigations showing impaired bladder storage and in whom antimuscarinic drugs have proved to be ineffective or poorly tolerated.

SMC and the AWMSG conclude that Botox should be an option for the management of urinary incontinence in adult patients with neurogenic detrusor overactivity due to subcervical spinal cord injury or multiple sclerosis who are not adequately managed with anticholinergics. This is based on 2 phase III double blind, placebo controlled studies.

Cochrane have also reported on Botulinum toxin injections for adults with overactive bladder syndrome. The evidence was up to date to February 2010. Participants had either neurogenic OAB or idiopathic OAB with or without stress incontinence. 19 studies met the inclusion criteria, most patients had neurogenic OAB but some included patients with idiopathic OAB. The authors concluded that intravesical Botulinum toxin appears to be an effective therapy for refractory OAB but as yet little controlled trial data exist on benefits and safety compared to other interventions or with placebo. Further robust data are required on long term outcomes, safety and optimal dose of Botulinum toxin for OAB.

Botox is a PbR excluded medicine, and urinary incontinence is a CCG commissioned service. With the proposed number of 100 patients, the CCG boards would be required to sign off the application, as this could equate to £115,940 per year in terms of drug costs and hospital attendance costs. There would be cost savings associated with this if the treatment is successful in terms of reduction in OAB drug cost, reduction in pads and reduction in GP visits. To date, cost-effectiveness data are not currently available from RCTs.

Discussion with Mr MD

Overactive bladder (OAB) associated with urinary incontinence (UI) is very common. It is initially managed by fluid restriction and behavioural modifications such as reduction in caffeine. Bladder training will treat 50% of patients successfully. The next line of treatment is to offer overactive bladder drugs, and then if these are unsuccessful, Mirabegron. These resistant cases can demonstrate such urgency that the patient are unable to get to the toilet in time, and this has a major impact on work and quality of life. It is this cohort that Botox is aimed at.

There are 2 large phase III trials involving Botox, and is supported by NICE, and therefore as a regional unit, would like to be able to offer this treatment – especially given that other areas in the region are already offering Botox in this cohort – Dorset, Somerset, and Gloucestershire, Exeter and Devon (though the last three not confirmed). Being a regional unit, NBT should have access to be able to use this treatment.

The other options for patients are major reconstruction surgery, which is associated with an increased risk of cancer, infections and renal failure. An alternative is sacral nerve stimulation which requires funding to be agreed, which costs £13,000 per patient. There are currently 65 patients waiting for this.

The current pathway/proposed pathway…
The intention is that those patients suitable for Botox would be offered repeat injections at around 6 – 8 months. Generally, those patients with idiopathic OAB generally need a further injection at 6-9 months, and those with neurogenic OAB find that the injection lasts a little longer, on average 12 months.

There is a 15% failure rate with botox for this indication. Generally, a patient would be offered a repeat injection to rule out any administration error that may have resulted in treatment failure. If a second injection proves ineffective, then no subsequent injections would be offered.

- **Patient safety** – The most frequently reported adverse events demonstrated in the trials are urinary tract infections and urinary retention.
- **Clinical effectiveness** – There are a number of well-designed trials evaluating botox in the treatment of neurogenic and idiopathic over active bladder. On the basis of these, NICE, SMC and AWMSG have all indicated that Botox should be offered as a possible intervention to patients with OAB with proven detrusor overactivity who have failed conservative treatment.
- **Cost effectiveness or resource impact** – To date, cost effectiveness data are not available from RCTs. The potential costs to the BNSSG CCGs to treat 100 patients could be £115,940, which includes drug costs and clinic costs. This needs to be considered against the costs of treating these patients without access to Botox i.e. the costs of continuing to fail (pads/drugs/GP visits)/nerve stimulation/surgery. Potentially introducing botox may be a cost saving to the CCG when taking all options into account.
- **Strength of evidence** – Small, short term RCTs, which have been appraised by NICE/SMC/AWMSG and Cochrane. There is a lack of long term efficacy data and
limited information on repeat injections.

- **Place in therapy relative to available treatments** – There are limited treatment options for patients with severe symptoms not responding to behavioural/lifestyle interventions and drug treatments. The alternatives include invasive surgical intervention. Should be offered to patients, once proven detrusor overactivity has been established, in those patients with severe UI (idiopathic/neurogenic OAB) who have failed with conservative treatment. See proposed pathway.

- **National guidance and priorities** – NICE/SMC/AWMSG all recommend it in different cohorts – Idiopathic and Neurogenic OAB. The Royal College of Obstetricians and Gynaecologists state that ‘current evidence suggests that Botox may be effective for the symptomatic treatment of detrusor overactivity and OAB. Its use should however be reserved for patients who fail to improve with conservative treatment and medical management with two different anticholinergic drugs.’

- **Local health priorities** – Long Term conditions
- **Equity of access** – Many other CCGs have considered Botox in this area and have included it on their formulary e.g. Nottinghamshire, East Kent, Hertfordshire and York. Some are funded based upon criteria based access.

The JFG considered the application and the evidence and information submitted. Botox has been considered clinically appropriate for inclusion to the Joint Formulary in those patients with severe UI who have proven detrusor overactivity and have failed conservative treatment. TLS Red. As Botox is a PbR excluded medicine, and UI is CCG commissioned, the inclusion of Botox for this indication requires to be agreed by the CCG boards.

**Action:**

1. **NB to inform applicant.**
2. **NB and SB to meet Mr Drake to finalise figures comparing costs of the current treatment pathway with the proposed costs of the new treatment pathway.**
3. **To present to each CCG board the proposal. The JFG to be informed of the final outcome.**

### 4.5 Alogliptin – Management of Type 2 diabetes

This application was submitted by Dr FF, GP North Somerset and also supported by Dr PS, Senior Consultant in Diabetes and Endocrinology, Weston Area Health Trust. Dr FF attended the meeting to present the application.

Please see application form for full details.

NB presented a summary of the application and the evidence available. The application was for the inclusion of alogliptin to manage type 2 diabetes in combination with other glucose lowering medicinal products including insulin when these, together with diet and exercise do not provide adequate glycaemic control. NICE guidance 87 on the management of type 2 diabetes outlines when introducing gliptin is appropriate. Alogliptin was not available when this guidance was published and therefore is not included; however it is assumed that it would be included in their conclusions on the class of gliptins. The SMC reviewed Alogliptin and concluded that it was not recommended for use within Scotland. This was based on there being no clinical studies of alogliptin as triple therapy in combination with metformin and a sulfonylurea; the EMA did not consider the non-inferiority (as add on to metformin) of alogliptin to glipizide to be demonstrated; the submitting company did not present a sufficiently robust clinical and economic analysis to gain acceptance.

The AWMSG have received a submission but have not reviewed it as yet.
Currently on the BNSSG formulary, we Saxagliptin is our recommended gliptin with Sitagliptin and Linagliptin as alternatives. Prescribing data in Bristol shows that each three gliptins are being prescribed in fairly equal amounts. Alogliptin is approximately 15 -20% cheaper than the other gliptins available.

Alogliptin does have data showing that in patients who are at high risk of cardiovascular disease, with inadequate glycaemic control the introduction of alogliptin did not significantly affect cardiovascular events compared to placebo.

In the Endure study, which was a large multinational, randomised, double blind controlled study, comparing alogliptin to glipizide, although it was found that alogliptin changed HbA1c by 0.72% compared to 0.59% with glipizide, the dose of glipizide being 5mg was considered low and many type IIs would be on higher doses.

MP confirmed that NBT Endocrinology were not looking to introduce this particular gliptin.

Discussion with Dr FF

Dr FF confirmed that that this was a medicine that could potentially realise a significant saving to the CCGs. However it should be noted that significant education would have to take place in order for the proposed savings to be realised as the work in the NDR has demonstrated that there is no particular first line gliptin currently being prescribed within BNSSG. Essentially this is a gliptin offering the same advantages compared to the other agents, with additional safety data in terms of cardiovascular events in high risk patients, at a cheaper acquisition cost. There are no issues with this gliptin as far as he is aware of.

The SMC report was highlighted, and his opinion was that comparing alogliptin to another gliptin was unlikely to have occurred, and that the other gliptins do not have head to head studies either. Dr FF does not feel alogliptin is inferior. There is no evidence as triple therapy, but no evidence that it would be contra-indicated either. Dr Faheem felt that all of the gliptins should be available on the formulary.

- **Patient safety** – The EXAMINE study showed that alogliptin did not have a negative effect on cardiovascular events in patients at high risk of these. In general the safety profile of alogliptin plus metformin was similar to that of placebo plus metformin. In combination with a sulfonylurea, a slighter higher proportion of patients in the alogliptin group presented at least one adverse event during the study compared to placebo. Treatment adverse events were experienced in 18% of alogliptin 25mg, 15% of alogliptin 12,5mg and 10% of placebo patients.  
- **Clinical effectiveness** – Alogliptin in combination with metformin or sulfonylurea was associated with a modest, but clinically significant improvement in glycaemic control.
- **Cost effectiveness or resource impact** – This is not a new cohort of patients, as it is 15-20% lower than the other available gliptins, cost savings could be realised.
- **Strength of evidence** – Evidence for alogliptin as dual therapy in combination with metformin of sulfonylurea included three RCTs, phase III. No evidence as triple therapy; no comparative data against other gliptins; the dose of glipizide used in the trial was considered low.
- **Place in therapy relative to available treatments** – Should be prescribed in accordance with NICE Clinical Guideline 87. However it should be noted, that although may be considered licensed, there is no data available for use as triple therapy in combination with metformin and gliclazide.
- **National guidance and priorities** – NICE, as general Glipitin use. SMC have rejected it, and AWMSG yet to report.
- **Local health priorities** – Long term conditions.
- **Equity of access** – Unable to identify other formularies that include alogliptin as
The JFG considered the application and the evidence submitted. Whilst there is evidence showing the beneficial effects of alogliptin in terms of reduction in HbA1c in the management if type 2 diabetes, there are no head to head trials against the other gliptins, and no trials involving alogliptin as part of triple therapy i.e. in combination with metformin and a sulfonylurea. There are limitations to the studies, and the SMC state that the non-inferiority to glipizide was not shown in the trial as the dose used of glipizide was too low. However, it does have a lower acquisition cost compared to the other gliptins. At this stage, the group could not identify which gliptins should remain on the formulary without a thorough review of each agent in terms of evidence and licensing – the JFG were unclear whether alogliptin was comparable to the other gliptins. Alogliptin was not approved for addition to the formulary at this stage until a review of the class could be undertaken and considered.

Action:

1. NB to inform applicant.
2. NB to arrange a drug class review of the gliptins to consider during the chapter review (chapter 7)

4.6 Dapoxetine – Premature ejaculation. Dr SS, Speciality Doctor in Sexual Health and psychosexual medicine, UH Bristol.

This application was submitted by Dr SS, Speciality Doctor in Sexual Health and psychosexual medicine. Dr SS also attended the meeting to present the application.

Please see application form for full details.

NB presented a summary of the application and the evidence available. The application was for the inclusion of dapoxetine for the treatment of premature ejaculation (PE). This is the first and only licensed medicine for PE. There are 5 RCTs that show that dapoxetine increases the time from penetration to ejaculation by between 1 and 2 minutes. It is convenient and well tolerated. Adverse effects are in line with the other SSRIs. A comparison of the treatments for PE (unlicensed) published in the International Society for Sexual Medicine’s Guidelines for the diagnosis and treatment of premature ejaculation suggested that the improvement in intravaginal ejaculatory latency time (IELT) was the least for dapoxetine (2.5 – 3 times improvement) compared to daily dose of paroxetine (8 times) and topical lignocaine (4 – 6 times). The alternatives whilst being used off label, but accepted standard practice are significantly less expensive.

Discussion with Dr SS

There are no licensed treatments available to treat PE. It is a significant problem and causes a high degree of distress. Currently they use off label SSRIs, which are more effective if used on a daily basis however patients will often not want to take an antidepressant daily, with the side effects that come with this. Dapoxetine has been specifically designed being short acting and cleared quickly, and therefore to be used on a when required basis. The current treatment pathway involves general and psycosexual treatment. Medicinal treatments include clomipramine, SSRIs and Emla cream. The mainstay of treatment is behavioural exercises in order to improve the confidence.

There is no evidence that this is a cost effective treatment; however this is a small cohort of patients that are high users of the NHS, and therefore if treatment is successful, there is a potential that the resources used by these patients will decrease. Dr Soodeen was asked, that apart from the fact that it is licensed, what are the advantages for dapoxetine over other treatment – it has a rapid onset of action and it is short acting. It is
acknowledged that this is an area where there is a high degree of anxiety and there is a significant placebo effect. Dr SS did not feel that there would be capacity issues with the introduction of being able to prescribe dapoxetine.

- **Patient safety** – The most frequent reported adverse events were nausea, diarrhoea, headache, dizziness, insomnia, somnolence, fatigue and nasopharyngitis. Most adverse events were mild to moderate in severity. Syncope occurred in 0.05%, 0.06% and 0.23% of participants receiving placebo, dapoxetine 30mg and dapoxetine 60mg respectively.

- **Clinical effectiveness** – Pooled analyses of data from 4 of the 5 trials showed that increases in mean IELT were significantly greater with both doses of dapoxetine compared with placebo. After 12 weeks' treatment, from a baseline of 0.9mins, mean IELT had increased to 3.1 and 3.6mins with dapoxetine 30mg and 60mg respectively vs placebo 1.9mins.

- **Cost effectiveness or resource impact** – Significant acquisition cost compared to the off label options. The cost of a year's treatment based on three times a week usage would be £764.92. The number of patients in BNSSG is estimated to be 50, and therefore total drug costs for these patients could be up to £38,246.

- **Strength of evidence** – 5 RCTs, placebo controlled. All trials had similar designs.

- **Place in therapy relative to available treatments** – No other licensed treatment available.

- **National guidance and priorities** – Mentioned in the BASHH guidelines.

- **Local health priorities** – NA

- **Equity of access** – Other local formularies checked. 15 had considered and concluded that dapoxetine would be non-formulary. 2 have included it on their formulary (Coventry and Barts).

The JFG considered the application and the evidence submitted. This is the first agent to be specifically licensed for PE. There is evidence to show that dapoxetine does improve the IELT, compared to placebo. It is effective in many, convenient and well tolerated. There is however no comparative data against alternative treatments. When compared to the relatively efficacious other available treatments, although unlicensed for this indication, they are accepted best practice, dapoxetine does not appear to be as efficacious. It has a significant acquisition cost. The JFG therefore did not consider dapoxetine to be appropriate for inclusion on the formulary as it did not demonstrate cost effectiveness in comparison with other available treatments.

**Action:**

1. **NB to inform applicant.**

4.7 **Regadenoson (Rapiscan)** – for use in stress myocardial perfusion imaging scans.

This application was submitted by NBT. Regadenoson is a medicinal agent used in myocardial perfusion imaging. It is not listed in the BNF, and these agents do not appear on the BNSSG formulary, however it is a medicinal product. UHB MAG considered a request to use Regadenoson in January 2013 and approved its use. Therefore the application brought to the JFG was for information to approve its use at NBT in addition to UHB.

**Action:**

1. **NB to inform applicant.**

2. **NB to add to the formulary.**
4.8 Linaclotide – Presentation of IBS-C pathway written by Dr AB (Gastroenterologist, NBT) and Dr MC (GPwSI, Bristol)

Linaclotide was considered at the JFG back in September and October 2013. It was rejected for the treatment of IBS-C. *The JFG felt that the clinical evidence did not support inclusion into the JF. It is a novel agent, but this not sufficient to accept it on to the formulary. The JFG would reconsider the use of this drug within BNSSG if the evidence base changes.* In October it was further discussed, and minuted that ‘more evidence is needed, and if submitted the group would reconsider.’

Dr AB and Dr MC have therefore worked on a pathway to ensure that there is a clear treatment pathway to enable only a specific cohort of patients would be initiated on linaclotide.

It was confirmed that the JFG does not look at drugs just in the context of the primary care drugs budget but to the local NHS as a whole, including other services. The introduction of linaclotide is hoped to reduce the number of scopes being performed (for which it is over capacity currently). There is good evidence that patients are taking up out-patient appointments and endoscopies with IBS-C symptoms, which could be reduced by introducing linaclotide. 58% of patients who have endoscopies conclude with no other action. This costs around £400, and in comparison, linaclotide is relatively inexpensive.

It has been accepted and classified as Green in Gloucester and Cheltenham since January – there have been 39 patients in 4 months.

In Doncaster there have been 80 prescriptions in 8 months.

In Wales and Scotland, most areas have included it as green, though some amber.

This drug is not to be considered first line, but third line.

The pathway was discussed. The group felt that it should include other formulary options for the treatment of IBS-C prior to considering linaclotide. The pathway could then be considered for the GP population. It would be prescribed for 1 month and reviewed for efficacy. If there has been no effect, a repeat prescription would not be issued.

Dr MC has used it in 3 patients – 1 stopped due to severe diarrhoea (which is expected with treatment, and therefore patients need to be counselled appropriately to persist with treatment), and the other 2 are significantly better. Dr AB has prescribed it twice – again one stopped with diarrhoea and the other patient improved.

The JFG was presented with another CCG IBS-C pathway which included other treatment options, and it was felt that the pathway should be similar to this.

The JFG considered the pathway and concluded that linaclotide could be included on the formulary as amber 1 month. A SCP would need to be developed. This would allow the Community Gastro clinic to prescribe, and other specialists, and then GPs to maintain prescription if patient is stable. After 6 months of being included on the formulary, prescribing data would be reviewed by the JFG to ascertain numbers being prescribed and Dr MC and Dr AB to report back to the JFG. At this time, if the JFG agree for linaclotide to remain on the formulary, the pathway should be revised to include formulary options, and then linaclotide could be considered Green.

*Action:*

1. *NB to inform applicant.*
2. **NB to liaise with Dr Cohen/Dr Beale to write SCP.**

## 5 Shared Care Protocols/TLS status

5.1 **Rasagline – Change in status request from amber 3 months to green**

This change in status request was submitted by NBT for the treatment of Parkinson’s Disease. The JFG did not feel that it should be made Green, as GPs are not familiar with dose adjustments especially for newly diagnosed patients. A SCP allows for better support and care of patients. The JFG did agree for the SCP to be amended and Rasagline to be changed to amber 1 month.

**Action:**

1. **NB to inform applicant**
2. **NB to liaise with NBT to amend SCP.**
3. **NB to update website with revised SCP.**

5.2 **Stalevo - Change in status request from amber 3 months to green**

As above

**Action:**

1. **NB to inform applicant**
2. **NB to liaise with NBT to amend SCP.**
3. **NB to update website with revised SCP.**

5.3 **Entacapone – Change in status request from amber 3 months to green**

As above

**Action:**

1. **NB to inform applicant**
2. **NB to liaise with NBT to amend SCP.**
3. **NB to update website with revised SCP.**

5.4 **Rufinamide – Change in status request from Red to amber and SCP**

SCP submitted for the treatment of epilepsy. There are minimal monitoring requirements. GPs have been asked for comments prior to the meeting – none submitted. The JFG agreed to the TLS change and the introduction of the SCP with a few amendments relating to monitoring.

**Action:**

1. **NB to inform applicant**
2. **NB to liaise with NBT to amend SCP.**
3. **NB to update website with SCP.**

5.5 **Perampanel – Change in status request from Red to amber and SCP**

SCP submitted for the treatment of epilepsy. There are minimal monitoring requirements.
GPs have been asked for comments prior to the meeting – none submitted. The JFG agreed to the TLS change and the introduction of the SCP with a few amendments relating to monitoring.

**Action:**
1. **NB to inform applicant**
2. **NB to liaise with NBT to amend SCP.**
3. **NB to update website with SCP.**

### 6 Individual Funding Requests

None.

### 7 Chapter review and formulary process

#### 7.1 Chapter review progress

Chapters 6 and 7 have been sent out for Specialist Comments. NB confirmed what was expected during this process. NB to arrange future meetings to discuss comments.

**Action:**
1. **NB to progress chapter review.**

### 8 Specialised Commissioning Statements

None

### 9 Items for Discussion

#### 9.1 NDRs for June Meeting

Post meeting NB confirmed the NDRs to be discussed in June

1. Lisdexamfetamine for ADHD in adults, AWP.
2. Ibandronic acid for treatment of osteoporosis in postmenopausal women, Bristol CCG submitted.
3. Colesevelam for bile acid malabsorption, NBT submitted.
4. Oxandrolone as an adjunct to nutritional support in severe burns in children, UHB

### 10 AOB

None

**NB**

Interface Pharmacist

23rd April 2014
## Action Log for 22<sup>nd</sup> April 2014

<table>
<thead>
<tr>
<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
<th>RO (s)</th>
<th>Deadline</th>
<th>Date of Update</th>
<th>Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.4.14</td>
<td>2.1</td>
<td>Relvar NDR from March 2014</td>
<td>Inform applicant to include on the BNSSG formulary and include on the formulary</td>
<td>NB</td>
<td>16&lt;sup&gt;th&lt;/sup&gt; May 2014</td>
<td>NB</td>
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<tr>
<td>22.4.14</td>
<td>3.1</td>
<td>NICE TAs</td>
<td>NB/SB to add all positive NICE TAs to the JF website within 90 days of publication</td>
<td>NB/SB</td>
<td>31&lt;sup&gt;st&lt;/sup&gt; April 2014</td>
<td>NB/SB</td>
<td></td>
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<tr>
<td>22.4.14</td>
<td>4.1</td>
<td>Dexmedetomidine for awake craniotomy NDR</td>
<td>Inform applicant of decision. Update website</td>
<td>NB</td>
<td>16&lt;sup&gt;th&lt;/sup&gt; May 2014</td>
<td>NB</td>
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<tr>
<td>22.4.14</td>
<td>4.2</td>
<td>Dexmedetomidine for PICU NDR</td>
<td>Inform applicant of decision to include on the formulary. Update website.</td>
<td>NB</td>
<td>16&lt;sup&gt;th&lt;/sup&gt; May 2014</td>
<td>NB</td>
<td></td>
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<tr>
<td>22.4.14</td>
<td>4.3</td>
<td>Colobreathe for non-CF bronchiectasis NDR</td>
<td>Inform applicant of decision to include on the formulary. Update website.</td>
<td>NB</td>
<td>16&lt;sup&gt;th&lt;/sup&gt; May 2014</td>
<td>NB</td>
<td></td>
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<tr>
<td>22.4.14</td>
<td>4.3</td>
<td>Botox for UI NDR</td>
<td>Inform applicant of next steps – to prepare financial case to present to CCG boards</td>
<td>NB</td>
<td>31&lt;sup&gt;st&lt;/sup&gt; May 2014</td>
<td>NB</td>
<td></td>
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<tr>
<td>22.4.14</td>
<td>4.5</td>
<td>Alogliptin NDR</td>
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<td>NB</td>
<td>16&lt;sup&gt;th&lt;/sup&gt; May 2014</td>
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<td>4.6</td>
<td>Dapoxetine NDR</td>
<td>Inform applicant of decision to reject application.</td>
<td>NB</td>
<td>16&lt;sup&gt;th&lt;/sup&gt; May 2014</td>
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<td>4.8</td>
<td>Linaclotide pathway for IBS-C</td>
<td>Inform applicant that a SCP required, and when added to the formulary, to report back to the JFG with patient numbers and experience.</td>
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RO – Responsible Officer
MEETING DATES 2014

<table>
<thead>
<tr>
<th>Date</th>
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<th>Time</th>
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<tr>
<td>Tuesday 21st January 2014</td>
<td>3rd December 2013</td>
<td>10 am to 1pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<tr>
<td>Tuesday 4th March 2014</td>
<td>21st January 2014</td>
<td>1.30 – 4.30pm</td>
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<td>11th March 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<tr>
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<td>22nd April 2014</td>
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<tr>
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<td>3rd June 2014</td>
<td>9am to 12pm</td>
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<td>22nd July 2014</td>
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<td>2nd September 2014</td>
<td>9am to 12pm</td>
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<td>Tuesday 25th November 2014</td>
<td>14th October 2014</td>
<td>9am to 12pm</td>
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NB. The times of the morning meetings have changed so that the meetings now start at 9am and finish at 12 midday.
**BNSSG Joint Formulary Group**

Meeting held on: Tuesday 3rd June 1.30pm – 4.30pm

NHS Bristol CCG, Bevan Room, South Plaza

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**Minutes**

**Present:**

- Public Health Consultant, Bristol City Council (Chair)
- Interface Pharmacist, NHS Bristol CCG
- Interface Pharmacist, NHS Bristol CCG
- Clinical Effectiveness Research Lead, Bristol City Council
- HoMM, NHS North Somerset CCG
- Consultant in Emergency Medicine, UHBristol NHS Foundation Trust and Associate Director of Patient Safety, and Chair of UHB Medicines Advisory Group
- Deputy Head of Medicines Management, NHS South Gloucestershire CCG
- Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust
- HoMM, NHS Bristol CCG
- Specialist Pharmacist, UHBristol NHS

**Apologies:**

- Joint D&TC Chair, North Bristol NHS Trust
- Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust
- GP, Bristol and member of Bristol CCG Board
- Formulary Pharmacist, AWP
- GP, North Somerset
- Joint D&TC Chair, North Bristol NHS Trust
- Chief Pharmacist, AWP
- Nurse Prescriber, Bristol
- Nurse Prescriber, Bristol
- Director of Pharmacy Weston Area Health NHS Trust
- HoMM, NHS South Gloucestershire CCG

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1. **Welcome, Apologies and Declaration of Interests**

   **Declarations of Interest**
   
   None
The meeting was not quorate. In accordance with the ToR of this group, the Chair of the group determined that the meeting should continue and the Formulary Pharmacist will secure endorsement of any decisions ex-committee via email. Therefore decisions taken during this meeting will need to be ratified and actioned once approved.

NB informed the group that TO (Nurse prescriber) is moving to a new role outside of the BNSSG area and will therefore no longer continue to be part of the group. We will look for another member to fill this role for the group.

2 Minutes of the meeting of 22nd April 2014 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 22nd April 2014 had been circulated by NB following the meeting. No further comments had been submitted regarding the decisions made. The minutes of this meeting were approved.

Matters arising from April 2014 meeting

2.1 Botulinum toxin for urinary incontinence NDR
The JFG discussed the above NDR at the April meeting, and the group were satisfied that botulinum toxin should be available for the treatment of urinary incontinence. However it was necessary to show that the use of botulinum toxin would either be cost neutral or cost saving otherwise a business case would have to be submitted to the CCG boards. Since the meeting, SB has met with Mr MD, and has started to look at the costs of the current treatment pathway, comparing this with the costs of the proposed treatment pathway which includes botulinum toxin. This should be ready for presentation at the July JFG. Providing this shows cost neutral/cost savings botulinum toxin will be added to the formulary.

2.2 Gliptin class review
The alogliptin NDR was discussed at the April meeting. The group felt that it was necessary to look at the gliptin class as a whole so that we could rationalise our gliptin choices. This work is currently being undertaken and will be presented during the chapter 6 review which is currently in progress.

3 NICE New Technology Appraisals Published

3.1 Vasculitis (anti-neutrophil cytoplasmic antibody- associated) – rituximab (with glucocorticoids) TA308
3.2 Lung cancer (non-small cell, EGFR mutation positive) – afatinib TA310
3.3 Multiple myeloma – bortezomib (induction therapy) TA311
   • BNSSG TLS status to be Red.

TAs adopted into the BNSSG Joint Formulary April 2014

   • TA303 Multiple Sclerosis (relapsing) – teriflunomide, TLS RED

4 New Drug Requests (NDRs)
SUMMARY

4.1  **Lisdexamfetamine – Adult ADHD.**

Approved for inclusion onto the formulary, on the grounds of additional benefits compared to dexamfetamine – once daily dosing, longer duration of action and reduced street abuse potential. TLS Red – to review TLS status in line with paediatric review, October 2013.

4.2  **Ibandronic acid – Osteoporosis**

Approved for inclusion onto the formulary as a second line option for post-menopausal osteoporosis if generic bisphosphonates (alendronate and risedronate) are not tolerated. TLS Blue.

4.3  **Colestevlam – Bile acid malabsorption.**

Approved for inclusion onto the formulary, as a second line option for those patients with confirmed bile acid malabsorption and they are unable to tolerate colestyramine. There is currently there is no alternative option on the formulary. TLS Red

4.4  **Oxandrolone – Adjunct to nutritional support in severe burns.**

Deferred decision. The guidelines that were submitted to the group need to be reviewed and approved within the Bristol Children’s Hospital. Once these have been approved and there is Trust support for the use of oxandrolone in this patient cohort, the JFG have agreed for inclusion to the formulary to enable the Joint Formulary to be consistent. TLS Red.

4.5  **Review of Bevacizumab in the treatment of non-ischaemic central retinal vein occlusion BNSSG Policy**

The JFG have agreed to decommission the use of bevacizumab in this patient cohort in line with the NICE TA 283 involving ranibizumab.

4.6  **Review of Bevacizumab for patients with macular oedema secondary to central or branch retinal vein occlusion BNSSG Policy**

The JFG have agreed to decommission the use of bevacizumab in this patient cohort in line with the NICE TA 283 involving ranibizumab.

**Decision Criteria used by JFG for NDR**

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

**Full Discussion**

4.1  **Lisdexamfetamine – Adult ADHD (AWP)**

This application was submitted by Dr OB, Consultant Psychiatrist, AWP, and he also attended the meeting to present the application.
CM presented a summary of the application having completed an evidence appraisal. The application states Lisdexamfetamine (LD) would be a second line treatment for use in adults with ADHD. This would be for treatment initiation, and this would therefore be off label use. Shire has a licence for continuation of treatment of ADHD symptoms into adulthood but is currently in the process of applying for a license for initiation in adults. Methylphenidate and dexamfetamine are also unlicensed in adults; atomoxetine does have a licence for use in adults. There is evidence that the condition does persist into adulthood, and the condition itself is becoming more frequently diagnosed in adults, it is also felt that there are many people who are currently undiagnosed.

It appears from the application form that the applicant wishes to replace dexamfetamine with LD. It is a pro-drug which is hydrolysed to dexamfetamine. There is evidence showing that it does have a longer duration of action.

In terms of evidence of efficacy there is data in the adult population which would be transferable to our patient population. There is placebo controlled comparator data, but no active comparator data. It is short term but the treatment effects are large and consistent. There is longer term data, which is open label and randomised.

There are advantages of LD compared with dexamfetamine; it is once a day, and they duration of action is longer, and there is less street abuse potential.

There was a brief discussion about the cardiovascular adverse events that may be related to LD treatment, and the incidence of these. This was to be picked up further with the applicant.

**Discussion with Dr OB**

LD is a stimulant that is part of an established package of treatment for ADHD. There are currently 480 adult ADHD patients within Bristol. Out of these, there are currently 21 that are on LD; methylphenidate MR is the most effective first line agent in the majority of patients. Within BNSSG there is currently an agreed Shared Care Protocol which assists GPs to take over the care of adult ADHD patients when they are being treated with methylphenidate MR. LD fits as an appropriate 2nd line agent. NICE state that Methylphenidate should be a first line agent for adult ADHD patients, and that atomoxetine and dexamethasone should be second line (LD was not available at the time of publication). Dr Badat states that if methylphenidate is effective but not tolerated he would then initiate another stimulant i.e. dexamfetamine/Lisdexamfetamine. However, if methylphenidate is not effective he would consider atomoxetine as an alternative. Dr OB ad however has not initiated a patient on dexamfetamine in the last 2 years, and would not be looking for shared care for this. LD is more useful in patients who need a longer duration of action: its clinical effect is evident for 14 hours, which is the longest of all the ADHD medications. In terms of efficacy, in meta-analyses, LD is as efficacious compared to the other medications. The NNT for stimulants in the treatment of ADHD is 1.2.

In terms of licensing, methylphenidate and dexamfetamine are not licensed for use in adults, however it is accepted practice and it is not envisaged that these companies are going to extend their licenses.

If LD were to be included in the formulary Dr OB would expect some growth in prescribing, as the main bar to it being prescribed currently is that GPs cannot take over the care of these patients. However, he would not expect a huge increase. The monitoring for LD is as the other stimulants, and the side effects are similar to dexamfetamine. In terms of the safety profile and cardiovascular disease, Dr Badat confirmed that if a patient has a positive cardiac history, the patient would be referred to the GP for management. Actual cardiovascular events were extremely rare in trials, and estimated to be 1 in 10,000.
These adverse events could be anything from a one off tachycardia to something more serious.

- **Patient safety** – Cardiovascular events: Sudden death in patients with pre-existing structural cardiac abnormalities or other serious heart problems.

- **Clinical effectiveness** – In all trials, the differences from placebo are highly statistically significant and robust to choices of analysis and handling of missing data.

- **Cost effectiveness or resource impact** – In terms of acquisition cost, LD is more than methylphenidate; however it is comparable to dexamfetamine and atomoxetine, and therefore would not present a cost pressure. If this were to be included on the formulary potentially, more patients may be prescribed it in primary care under shared care guidance, and less prescribed dexamfetamine and atomoxetine.

- **Strength of evidence** – Evidence of effectiveness of LD in the treatment of adult ADHD patients comes from a 4 week placebo controlled RCT and a 10 week pivotal RCT. Longer term data come from an open label extension study, and improvement in core symptoms were maintained for up to 12 months. There are no data directly comparing LD with dexamfetamine or any other second line agents.

- **Place in therapy relative to available treatments** – It would not be appropriate as a first line agent, but a second line agent if methylphenidate fails i.e. not tolerated or not effective. It is proposed that dexamfetamine may be removed from the formulary and lisdexamfetamine added

- **National guidance and priorities** – None found that related to lisdexamfetamine.

- **Local health priorities** – Mental Health delivery theme, Bristol CCG – increased quality of service and improved access to mental health interventions.

- **Equity of access** – Salford currently initiate LD in adult ADHD patients. Difficult to identify other areas that include it on their formulary for this indication.

The JFG considered the application and the evidence submitted. The JFG agreed that lisdexamfetamine does offer advantages compared to dexamfetamine and it has been shown to be efficacious and well tolerated in adults. It was agreed to add it to the formulary, as TLS Red. It was felt that GPs would not be familiar with this drug currently. The JFG agreed for lisdexamfetamine to be included, TLS Red for use in children in October 2013. At this time we agreed to review the TLS status in 1 year. The JFG therefore agreed to consider changing to TLS amber with shared care protocol in October this year. Ongoing discussions are required including with the paediatric team in relation to removing dexamfetamine off the formulary.

**Action:**

1. NB to inform applicant.
2. NB to include on the formulary, TLS Red
4.2 Ibandronic acid – Osteoporosis

This application was submitted by LR, Medicines Management Pharmacist, NHS Bristol CCG. NB presented the application on her behalf. The application was also supported by Dr SC, Rheumatologist, UHBristol.

Please see application form for full details.

The application was for the inclusion of ibandronic acid 150mg once a month tablet for postmenopausal women who require treatment of osteoporosis with a bisphosphonate in whom the first line choice is not appropriate. This was in direct response to the MHRA’s restriction on the use of strontium. Strontium is currently on the BNSSG formulary as a second line agent. In March 2014, the MHRA issued advice in Drug Safety Update that stated that ‘Strontium ranelate is now restricted to the treatment of severe osteoporosis in postmenopausal women and adult men at high risk of fracture who cannot use other osteoporosis treatments due to, for example, contraindications or intolerance.’ This therefore now restricts the number of oral options that are available for patients before being referred to secondary care for denosumab/iv zoledronic acid.

Ibandronic acid 150mg tablets have been available since 2006 for the treatment of osteoporosis in postmenopausal women. SMC reviewed it back in 2006 and at the time considered it suitable for prescribing as it has proven efficacy in terms of reducing vertebral fractures. It was noted that compared with other bisphosphonates, evidence had not be shown that it reduced the risk of femoral neck fractures. MTRAC in 2006 stated that the evidence for comparative efficacy of oral ibandronate was considered to be weak as only one published trial included the licensed dose. This trial did not use fracture incidence as the primary outcome and the comparator was oral ibandronate 2.5mg daily. Ibandronate had not been compared with other bisphosphonates or other existing osteoporosis treatments. It was considered to have a low place in therapy.

The reason that Ibandronic acid is currently non-formulary within BNSSG is due to lack of robust efficacy compared to other bisphosphonates and its elevated cost. The acquisition cost of Ibandronic acid has recently dropped due to generics being available, and now it is only just over double the cost of alendronic acid, and significantly less than strontium.

The National Osteoporosis Guideline Group (2014) showed that Ibandronic acid does not have evidence showing a reduction in hip fracture, and that in terms of non-vertebral fracture, this has only been shown in post hoc analysis. It is therefore considered further down in the treatment pathway. Strontium is also considered second line treatment.

Direct comparison of the efficacy of different bisphosphonates in reducing fractures is not possible, as trial populations and designs in pivotal clinical trials have differed and head to head studies with fracture as the primary endpoint have not been performed.

A review in 2013 looked at the anti-fracture efficacy of ibandronate over time. A large amount of data from randomized, controlled fracture trials, bridging studies using surrogate end points, meta-analyses, and observational studies based on a clinical setting is available to suggest that ibandronate has sustained vertebral and non-vertebral anti-fracture efficacies in women with osteoporosis.

Ibandronic acid has the potential advantage that it is only administered once a month and therefore where compliance is an issue this could be useful.

- **Patient safety** – As a group, the bisphosphonates are generally well tolerated. They have a well-documented adverse effect profile and gastrointestinal effects are a known issue. Evidence has shown that ibandronic acid is as well tolerated as
the other bisphosphonates.

- **Clinical effectiveness** – Ibandronic acid has been shown to reduce the risk of vertebral fractures in postmenopausal women. Efficacy in reducing femoral neck fractures and other non-vertebral fractures has not been established.

- **Cost effectiveness or resource impact** – The acquisition cost of ibandronic has recently reduced significantly due to generics being available. It now costs just over £3 per month per patient, compared to alendronic acid £0.90 and risedronate £1.16 per month. Strontium costs £27.08 per month per patient. Therefore there would be a cost saving realised if all patients that were prescribed strontium were switched to ibandronic acid.

- **Strength of evidence** – The evidence that was reviewed in 2006 by MTRAC was considered to be weak at the time, as only one trial included the licensed dose. A review in 2013 looked at the anti-fracture efficacy of ibandronate over time – this considered information from randomised, controlled fracture trials, bridging studies using surrogate end points, meta analyses, and observational studies. This concluded that ibandronate had sustained vertebral and non-vertebral anti-fracture efficacies in women with osteoporosis.

- **Place in therapy relative to available treatments** – This would not be considered first line therapy as the evidence is stronger for the generic bisphosphonates. It would only be appropriate for those patients in whom generic bisphosphonates are not appropriate or not tolerated. It would be necessary to make this clear on the formulary if the application is successful.

- **National guidance and priorities** – The National Osteoporosis Guideline Group (2014) showed that Ibandronic acid does not have evidence showing a reduction in hip fracture, and that in terms of non-vertebral fracture, this has only been shown in post hoc analysis. It is therefore considered further down in the treatment pathway. Strontium is also considered second line treatment.

- **Local health priorities** –

- **Equity of access** – Other areas are considering including ibandronic acid in their formularies given the drop in acquisition cost, and restrictions on strontium prescribing. The Greater East Midlands Commissioning Support recommended including ibandronic acid in their formulary for the reasons outlined above.

The JFG considered the application and evidence submitted. The JFG approved the addition of ibandronic acid to the formulary as a second line option if first line generic bisphosphonates are inappropriate or not tolerated. TLS Blue.

**Action:**

1. **NB to inform applicant.**
2. **NB to include on the formulary, TLS Blue,**

4.3 **Colesvelam** – Bile acid malabsorption (off label use).

This application was submitted by Dr RP, Gastroenterologist, NBT. Dr RP also attended the meeting to present the application.
Please see application form for full details.

MP presented a summary. The application is for colesevelam for the treatment of bile acid malabsorption (BAM), second line if colestyramine treatment is not tolerated/failed. NICE have published an evidence summary review for colesevelam in the treatment of BAM. Within this, there were RCTs involving small numbers, but mostly they were case studies. 70% respond to colestyramine. Currently, the BNSSG formulary does not have an alternative agent for those patients that don't respond to colestyramine or can't tolerate it, and therefore there does not appear to be a formulary approved pathway for BAM patients. The case studies showed that there was improvement in BAM after using colesevelam. A systematic review which was published after the NICE evidence summary concluded that colesevelam could be considered an appropriate second line agent. It is a tablet compared to a sachet therefore this offers some advantages for some patients.

ER to check with the Gastroenterologists at UHB to ascertain their views and if it is something that they would like to prescribe.

A one month trial has been discussed with Dr RP and seems appropriate; if the patient hasn’t responded in this time frame, then treatment should be stopped.

**Discussion with Dr RP**

BAM – there are susceptible individuals who don’t reabsorb bile and they develop profuse diarrhoea. For some, this can completely incapacitate the individual. These patients don’t always come to secondary care as the symptoms can be disguised by other causes. The existing standard of care is that patients would be given colestyramine and the response to treatment will be quick. Within 1 week, most patients will respond and will carry on treatment. If the patient can’t tolerate the treatment, but get better (vomiting is usually the main side effect), this is the role for colesevelam. This would be a minority group of patients.

There are 3 papers that involve colesevelam. All three papers were small in design. One (n= 45) was a pre and post observational study. Patients had an intolerance to colestyramine, and the study showed that colesevelam had significant benefits. The other study (n = 5) was a case series, involving patients who had SeCHAT proven BAM, and all 5 were given colesevelam and improved.

NBT had presented a paper at the European Gastroenterology Conference that involved patients with terminal ileal Crohns disease who were treated with colesevelam, and it was shown to have significant benefit in these patients.

A one week trial would be sufficient to ascertain whether a patient can tolerate it and is responding. The numbers involved is suggested to be 10 -15 for Dr Prezemioslo, and 30 in total for NBT. The alternative to using colestyramine is for the patient to continue to fail, or potentially lead to the need for an end ileostomy, though no patient in NBT has been operated on for BAM. Currently, Dr RP is filing out non-formulary one off requests for these patients to have treatment with colestyramine. It may be reasonable for a GP to prescribe once stable, though this is not being requested at this state.

- **Patient safety** – The evidence has shown that it appears to be better tolerated with regards to vomiting when compared to colestyramine. Flatulence and constipation appears to affect 1 in 10 people who take it. No patients in the n = 5 study withdrew due to adverse effects, however 5 out of 45 patients withdrew in the other study due to adverse effects.

- **Clinical effectiveness** – There is not a significant amount of data to support the application, but this is to be expected. In one case series, colesevelam was shown to improve diarrhoea frequency and urgency of defecation, steatorrhoea,
abdominal pain and faecal incontinence, in all patients. In the other case series, diarrhoea resolves with colesevelam in all 5 patients with BAM.

- **Cost effectiveness or resource impact** – The acquisition cost of colesevelam compared to colestyramine is only marginally more - £43.68 compared to £38.74.

- **Strength of evidence** – No RCTs were identified that compared colesevelam with placebo or other treatments in people with bile acid malabsorption. One RCT compared colesevelam with placebo in women with diarrhoea predominant IBS, and two case series were identified that reported on the efficacy of colesevelam for BAM.

- **Place in therapy relative to available treatments** – This would only be used in patients who are intolerant of colestyramine. It is unlicensed for the treatment of BAM.

- **National guidance and priorities** – None.

- **Local health priorities** –

- **Equity of access** – There is currently no alternative treatment on the formulary for patients who have failed/intolerant of the first line agent colestyramine.

The JFG considered the application and the evidence submitted. The JFG acknowledged that this disease area is under researched, and therefore this makes it challenging to make evidence based decisions. The limited data available shows that colesevelam can be useful in the treatment of BAM and is generally well tolerated. The JFG approved the inclusion on the formulary of colesevelam in patients with proven BAM who have failed or intolerant of the first line agent colestyramine. NBT have already had directorate approval for this application.

**Action:**

1. **NB to inform applicant**
2. **ER to confirm UHB Gastroenterologist opinion.**
3. **Include on the formulary, TLS Red**

### 4.4 Oxandrolone – Adjunct to nutritional support in severe burns (paediatric)

This application was submitted by Dr AU, Consultant Paediatric Anaesthetist, NBT/Bristol Children’s Hospital. No one was available to attend the meeting to present the application.

Please see application form for full details.

NB/MP gave a brief summary of the application. All Children’s services have now moved from NBT to The Bristol Children’s Hospital. At the time that this application was written, and the guidelines the services will still based at NBT. This application was for oxandrolone to be used as an adjunct to nutritional support in severe burns. A NDR was requested as it had been recognised that a cohort of patients existed and therefore a review was required. Guidelines had also been written in NBT, although unclear as to what route that these had been approved by. All the references and dosages in the guidelines have been checked through NBT Medicines Information. Some inconsistencies
with the formulary application and guidelines were identified. This is an in-tariff medication and therefore the cost of treatment would lie with secondary care.

ER raised the issue of which governance route the guidelines had been through and what processes were put in place for the transfer of services from NBT to the Children’s Hospital, in relation to transfer of guidelines.

This would be a very small cohort of patients – n = 1 or 2. National guidance from ESPEN recommends the use of oxandrolone. Apparently this drug has already been used in NBT patients using individual non-formulary one off requests.

The JFG considered the application and the evidence and information submitted. The group felt that it would be necessary to have trust support by endorsing the guidelines prior to the JFG accepting its use to include on the formulary. Once the guidelines have been approved in The Bristol Children’s Hospital, the JFG will accept Oxandrolone onto the formulary.

**Action:**
1. **NB to inform applicant to request information on whether the guidelines are being endorsed by the Children’s Hospital.**

**4.5 Bevacizumab in the treatment of non-ischaemic central retinal vein occlusion**

**BNSSG Policy**

Dr SB, Public Health registrar has reviewed the existing (out of date) BNSSG policies. These were approved at the Commissioning Advisory Forum prior to the Joint Formulary being in existence. Following these policies being agreed, NICE have published technology appraisal 283. This involves licensed ranibizumab for these indications and NICE have approved its use. Bevacizumab is not licensed for these indications. The NICE technology appraisal therefore supersedes the CAF policy, and bevacizumab should be decommissioned for these indications. Dr SB has been in contact with the ophthalmologists at UHB and they are in agreement.

The JFG have agreed to decommission the policy.

**Action:**
1. **SB/NB to action decommissioning the policies.**

**4.6 Bevacizumab for patients with macular oedema secondary to central or branch retinal vein occlusion BNSSG policy**

As above.

**5 Shared Care Protocols/TLS status**

**5.1 Ulipristal – Change in status request from Red to amber 3 months**

This change in status request was submitted by Dr VM who had put in the original application to the JFG for the drug to be included in the formulary. Ulipristal was agreed for inclusion into the formulary in October 2012, for the treatment fibroids. A TLS status was given as Red as treatment could only be continued for a maximum of 3 months and therefore there was no benefit in the drug being amber 3 months. Ulipristal now has a license for a further treatment course of up to 3 months, and therefore may now allow GPs
to prescribe ulipristal and potentially reduce the need hospital out-patient appointments.

The JFG was concerned that if this was prescribed in primary care, that it could end up being added to a patient’s repeat prescription list, and carried on indefinitely without review. The actual treatment and management pathway for uterine fibroids was unclear. It was assumed that the patient would be reviewed by secondary care prior to a second course of ulipristal was initiated. It was therefore felt that if this was the case, that secondary care should still maintain the prescribing. It was not felt to be a priority for prescribing in primary care. It will therefore remain red until further information is provided.

**Action:**

1. **NB to inform applicant**

5.2 **Riluzole – Review and update of expired existing SCP**

The SCP was agreed.

**Action:**

1. **NB to inform applicant**
2. **NB to add new SCP to the formulary website.**

5.3 **Linaclotide – New SCP for amber 1 month post NDR decision April 14**

Following the decision at the April JFG for linaclotide to be added to the formulary, a SCP was prepared. The SCP was discussed. More detail is required within the SCP in terms of what defines improvement. It was decided that the GP will be able to do the review providing the SCP is sufficiently detailed to enable the GP to determine if the linaclotide has improved symptoms. The words ‘re-examine patient’ will be taken out of the SCP. Once the SCP has been uploaded and linaclotide added to the formulary, we will review the prescribing trends within BNSSG after 6 months.

**Action:**

1. **NB to alter SCP**
2. **NB to inform applicant**
3. **NB to add linaclotide to the formulary and upload the SCP.**

6 **Individual Funding Requests**

North Somerset have had an exceptional funding request for ustekinumab for childhood eczema. To continue to monitor requests.

7 **Chapter review and formulary process**

7.1 **Chapter review progress**

Chapters 6 and 7 have been sent out for Specialist Comments. NB confirmed what was expected during this process. NB to arrange future meetings to discuss comments.

**Action:**
1. **NB to progress chapter review.**

8 **Specialised Commissioning Statements**

None. This section of the agenda was agreed that it could be removed from a standing item for future meetings. It had been included during the NHS Structure changes, however since then we have robust procedures in place to ensure that any new NHS England policy that is published will be included onto the BNSSG Joint Formulary website, and a link to the policy included.

9 **Items for Discussion**

9.1 **NDRs for July Meeting**

NB confirmed the NDRs to be discussed in July

1. Artiss, surgical glue (NBT) re-discussion from 2013, with applicant present.
2. Melatonin for prevention of delirium in ICU (NBT)

NDR for September – Anoro (Umeclidinium and vilanterol)

10 **AOB**

None

**NB**

*Interface Pharmacist*

*10th June 2014*
<table>
<thead>
<tr>
<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
<th>RO (s)</th>
<th>Deadline</th>
<th>Date of Update</th>
<th>Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.6.14</td>
<td>2.1</td>
<td>Botulinum toxin in urinary incontinence</td>
<td>Liaise with Mr Drake and bring costings back to the JFG July 2014</td>
<td>NB/SB</td>
<td>July 2014</td>
<td></td>
<td>Awaiting report back from MR Drake</td>
</tr>
<tr>
<td>3.6.14</td>
<td>2.2</td>
<td>Gliptin class review</td>
<td>Ensure that the review is included in the chapter 6 review.</td>
<td>NB/SB</td>
<td>July 2014</td>
<td></td>
<td>Review complete – added to chapter 6 review</td>
</tr>
<tr>
<td>3.6.14</td>
<td>3</td>
<td>NICE TAs</td>
<td>NB/SB to add all positive NICE TAs to the JF website within 90 days of publication</td>
<td>NB</td>
<td>30th June 2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6.14</td>
<td>4.1</td>
<td>Lisdexamfetamine NDR</td>
<td>Inform applicant of decision to include on the formulary, TLS red. To review TLS status in October 2014. Update website.</td>
<td>NB</td>
<td>30th June</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6.14</td>
<td>4.2</td>
<td>Ibandronic acid NDR</td>
<td>Inform applicant of decision to include on the formulary. Update website</td>
<td>NB</td>
<td>30th June</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6.14</td>
<td>4.3</td>
<td>Colesevelam NDR</td>
<td>Inform applicant of decision to include on the formulary, TLS Red. Update website.</td>
<td>NB</td>
<td>30th June</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6.14</td>
<td>4.4</td>
<td>Oxandrolone NDR</td>
<td>Inform applicant of decision – to ascertain if guidelines have been approved through The Children’s Hospital. Once they have to include on the formulary.</td>
<td>NB</td>
<td>30th June</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6.14</td>
<td>4.5 and 4.6</td>
<td>Bevacizumab policy review</td>
<td>Decommission use of bevacizumab in these indications</td>
<td>NB/SB</td>
<td>30th June</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6.14</td>
<td>5.1</td>
<td>Ulipristal TLS change in status request</td>
<td>Inform applicant of decision for ulipristal to remain as red.</td>
<td>NB</td>
<td>30th June 2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6.14</td>
<td>5.2</td>
<td>Riluzole SCP review</td>
<td>Inform applicant. Upload new SCP to website</td>
<td>NB</td>
<td>30th June 2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6.14</td>
<td>5.3</td>
<td>Linaclotide SCP</td>
<td>Inform applicant. Amend SCP to add detail around improvement to enable GP to assess patient. Upload to website</td>
<td>NB</td>
<td>30th June 2014</td>
<td>SCP needs updating then to add to website</td>
<td></td>
</tr>
<tr>
<td>3.6.14</td>
<td>7.1</td>
<td>Chapter review</td>
<td>Progress process</td>
<td>NB</td>
<td>30th June 2014</td>
<td>NB</td>
<td></td>
</tr>
</tbody>
</table>

RO – Responsible Officer
## MEETING DATES 2014

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SPCs</th>
<th>Time</th>
<th>Venue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuesday 21st January 2014</td>
<td>3rd December 2013</td>
<td>10 am to 1pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 4th March 2014</td>
<td>21st January 2014</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room South Plaza</td>
</tr>
<tr>
<td>Tuesday 22nd April 2014</td>
<td>11th March 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 3rd June 2014</td>
<td>22nd April 2014</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room South Plaza</td>
</tr>
<tr>
<td>Tuesday 15th July 2014</td>
<td>3rd June 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Brunel Building Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 2nd September 2014</td>
<td>22nd July 2014</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room South Plaza</td>
</tr>
<tr>
<td>Tuesday 14th October 2014</td>
<td>2nd September 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Brunel Building Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 25th November 2014</td>
<td>14th October 2014</td>
<td>9am to 12pm</td>
<td>Boardroom South Plaza</td>
</tr>
</tbody>
</table>

NB. The times of the morning meetings have changed so that the meetings now start at 9am and finish at 12 midday.
BNSSG Joint Formulary Group  
Meeting held on: Tuesday 15th July 2014 9am – 12midday  
Pharmacy Seminar Room, Pharmacy Department, Brunel Building, Southmead Hospital

Minutes

Present:

Interface Pharmacist, NHS Bristol CCG (Chair)  
Deputy HoMM, NHS Bristol CCG  
HoMM, NHS North Somerset CCG  
Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust  
HoMM, NHS South Gloucestershire CCG

Apologies:

Public Health Consultant, Bristol City Council (Chair)  
Clinical Effectiveness Research Lead, Bristol City Council  
Joint D&TC Chair, North Bristol NHS Trust  
Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust  
Consultant in Emergency Medicine, UHBristol NHS Foundation Trust and Associate Director of Patient Safety, and Chair of UHB Medicines Advisory Group  
GP, Bristol and member of Bristol CCG Board  
HoMM NHS Bristol CCG  
Formulary Pharmacist, AWP  
GP, North Somerset  
Joint D&TC Chair, North Bristol NHS Trust  
Chief Pharmacist, AWP  
Director of Pharmacy Weston Area Health NHS Trust

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest  
None

The meeting was not quorate. In accordance with the ToR of this group, the Chair of the group determined that the meeting should continue and the Formulary Pharmacist will secure endorsement of any decisions ex-committee via email. Therefore decisions taken during this meeting will need to be ratified and actioned once approved.
Minutes of the meeting of 3rd June 2014 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 3rd June 2014 had been circulated by NB following the meeting. No comments had been received that required further discussion.

Matters arising from June 2014 meeting

2.1 Botulinum toxin for urinary incontinence NDR
Following the NDR application discussed at the April meeting SB has met with Mr MD to investigate the costs of the current treatment pathway compared to the cost of the proposed treatment pathway which includes botulinum toxin. We are still awaiting final figures from the trust to present to the JFG. Providing this shows cost neutral/cost savings botulinum toxin will be added to the formulary.

NB and MP to chase Mr MD and Mrs KM (Deputy General Manager for Surgery, NBT) for the information.

2.2 Ulipristal TLS decision
The TLS status for ulipristal was discussed at the June meeting. The group were unclear of the treatment pathway for the management of uterine fibroids and therefore unable to agree to a TLS change at this stage. NB has been made aware of a potential extension of the license during 2015 which will be for the medical management of uterine fibroids. It therefore may be more appropriate at this stage to consider it appropriate for primary care prescribing. Currently across BNSSG there are some GPs that are being asked and taking on the prescribing – 27 items prescribed within Bristol (May 13 – April 14) and 9 items prescribed within North Somerset (April 13 – May 14). The decision remains that Ulipristal should remain Red.

NICE New Technology Appraisals Published

3.1 Canagliflozin in combination therapy for treating type 2 diabetes TA315
• Post meeting note: BNSSG TLS status to be Blue in line with dapagliflozin and NICE guidance.
• To be included in the formulary with immediate effect.

TAs adopted into the BNSSG Joint Formulary May and June 2014
• TA305 Aflibercept for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion, TLS RED
• TA306 Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin’s B-cell lymphoma, TLS RED
• TA308 Rituximab in combination with glucocorticoids for treating anti-neutrophil cytoplasmic antibody-associated vasculitis, TLS RED

New Drug Requests (NDRs)

SUMMARY
4.1 Melatonin – Prophylaxis of delirium in adult intensive care units.
Deferred decision until next meeting when further information can be provided and with the applicant in attendance.

4.2 Artiss – Surgical Glue for plastic surgery procedures
Deferred decision until the next meeting when further information can be provided.

Decision Criteria used by JFG for NDR

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

Full Discussion

4.1 Melatonin – Prophylaxis of delirium in adult intensive care units (NBT submission).

This application was submitted by Dr MT, Consultant Anaesthetist, NBT. No one was available to attend the meeting to present the application.

Please see application form for full details.

CM had conducted a public health evidence review of the application. NB presented a summary of the application and appraisal of evidence. The application was for the inclusion of melatonin in the BNSSG Joint formulary for the prophylaxis of delirium in those patients who are at high risk in intensive care. The JFG discussed how patients would be identified as being at high risk. There is evidence to suggest that there are four baseline risk factors which are positively and significantly associated with the development of delirium in the ICU: pre-existing delirium, high severity of illness upon admission, but mechanisms for identifying those at high risk are not stated in the application. It appears that the application could be for all patients on ITU to reduce the risk of delirium by attempting to simulate normal circadian rhythm whilst sedated. This would be an off label use of melatonin. It is currently being prescribed in NBT ICU and when patients are transferred from ITU the melatonin is being discontinued. The only suggested alternatives are the benzodiazepines, haloperidol and drugs such as zopiclone, however these are not really suitable alternatives.

Delirium and sleep disruption are recognised complications in the ICU setting. No other local formulary has melatonin listed for this indication, however it is our impression that other centres are prescribing it in this manner, or to improve sleep in ICU settings. It is known that sleep disruption and delirium in ICU are associated with abnormal patterns of melatonin secretion and therefore theoretically there should be an improvement by using melatonin. No good quality evidence was able to be found that compared the effectiveness of melatonin with any other intervention designed to prevent delirium. There is limited evidence for effectiveness of melatonin (or melatonin agonist) in the prevention of delirium but these studies are limited in their generalizability to an ICU population as they have predominantly been conducted in the elderly population, not within an ICU setting. There is tentative evidence for the effectiveness of melatonin to increase sleep duration in an ICU setting; however significant study limitations make these findings highly uncertain.
NICE guidance (2010) for the general prevention of delirium recommends non-pharmacological interventions, and does not recommend any preventative pharmacological intervention, stating that evidence is limited and whilst pharmacological agents may be a simple preventative treatment for delirium, there is uncertainty about effectiveness and side effects and so should be used with caution. Furthermore, recent guidelines (2013) on delirium in ICU also do not mention melatonin and no recommendation is provided for using pharmacological or a combined non-pharmacological and pharmacological delirium protocol in adult ICU patients.

ER had already contacted NB to confirm that she was happy with the application.

- **Patient safety** – Melatonin is generally accepted as safe and no adverse effects were reported in the studies reviewed in the evidence appraisal. Safety data underpinning the licence indicate that there are no serious adverse effects associated with use of melatonin at its licensed dose. However, the effect of any stage of renal insufficiency on melatonin pharmacokinetics has not been studied and there is no experience of the use of melatonin in patients with liver impairment or in patients with auto-immune disease.

- **Clinical effectiveness** – There is no good quality evidence that compared the effectiveness of melatonin with any other intervention designed to prevent delirium. There is limited evidence for effectiveness of melatonin (or melatonin agonist) in the prevention of delirium but these studies are limited in their generalizability to an ICU population as they have predominantly been conducted in the elderly not within an ICU setting. There is tentative evidence for the effectiveness of melatonin to increase sleep duration in an ICU setting; however significant study limitations make these findings highly uncertain.

- **Cost effectiveness or resource impact** – This would not present a significant cost pressure if this were to be included on the formulary – suggested £2,790 per year for approx. 300 patients. However there is no data that examines the cost effectiveness of this intervention. Delirium and sleep disturbances are recognised as significant management complications in the ICU setting, and therefore any intervention that improves the management of these could have a significant impact on ICU length of stay.

- **Strength of evidence** – The studies which considered melatonin in the prevention of delirium are limited in their generalisability as they were not conducted in the ICU setting and nearly all carried methodological flaws.

- **Place in therapy relative to available treatments** – There is no other pharmacological treatment that would be used in the prophylaxis of delirium in ICU. Sleep disturbances may be treated with benzodiazepines and zopiclone. Melatonin would be used as a preventative measure along with a bundle of non-pharmacological interventions.

- **National guidance and priorities** – None found that related to melatonin. NICE guidance (2010) for the general prevention of delirium recommends non-pharmacological interventions.

- **Local health priorities** –

- **Equity of access** – It is currently being prescribed in the ICU as non-formulary. Other areas are believed to be using it in this manner, although we have not been able to identify a particular area to discuss this with.

The JFG considered the application and the evidence submitted. It was not possible to fully ascertain exactly which patients would be prescribed melatonin in ICU. There is no
evidence to suggest that this is an effective treatment, although there is theoretical potential. The use of melatonin in this cohort appears to be more experimental at this stage. The JFG acknowledged that it was unlikely that a large RCT would be undertaken in this particular cohort, and therefore it may be that local research/audit may be required. At this current time, the JFG was not able to make a definitive decision and therefore the decision will be deferred until next meeting when the information can be obtained and the applicant can attend the meeting.

Action:

1. **MP to contact the applicant to discuss the issues outline above and to invite to a future JFG meeting.**
2. **NB to include on a future agenda.**

4.2 Artiss – Surgical glue (NBT submission)

This application was submitted by Mr PW, Plastic Surgeon, North Bristol NHS Trust. No one was able to attend the meeting to present the application.

Please see application form for full details.

This application was originally submitted and discussed in the JFG in September 2013. At this time, it was minuted that…

‘The JFG was unable to consider the application fully as
- the applicant was unable to attend the meeting to present the application
- the application lacked the financial impact of using this drug i.e. the number of patients it would be used on
- the application lacked sufficient clinical evidence.
- the application lacked an appraisal of the evidence to supports its use’

Although this meeting had been identified as an appropriate time for the applicant to attend, unfortunately Mr PW was now not able to attend. MP had considered the application in more detail and had had discussion with the pharmaceutical rep. Essentially, Artiss is a diluted form of Tisseel, which is already on the formulary. Tisseel sets too quickly and therefore is not suitable for use during plastic surgery procedures as it does not allow manipulation of the skin flap. Baxter therefore developed Artiss specifically for this reason, and it contains less thrombin.

The JFG was still not able to ascertain an estimate of the number of patients that it would be used in and what currently is used – is it staples or is Tisseel being currently used diluted? Artiss is a PbR excluded drug and therefore secondary care will invoice the CCG for the drug costs which are incurred. The expected numbers are required to determine how much a cost pressure this could pose to the CCG. If it is identified that this is a new cost then it may be that this change in practice would need to be submitted to the CCG during the annual planning round.

It appears to be clinically acceptable, and there is evidence to suggest that a surgical glue is more favourable than staples/sutures.

- **Patient safety** – As it is a diluted form of Tisseel, it is not expected to have any more issues compared with Tisseel.

- **Clinical effectiveness** – Two RCTs support the use of artiss for skin grafts and flap attachment. In the first study, artiss was compared with staples and artiss was found to be non-inferior. In addition, there were significantly less haematomas and seroma formations in the artiss group. In the second study using facelift patients, there were statistically significant reductions using fibrin sealant in the volume of serous fluid output.
- **Cost effectiveness or resource impact** – At this current time it is not possible to suggest what the resource impact would be – there are no indications of potential numbers involved, and no indication of what the current procedure is e.g. replacing Tisseel with artiss or replacing staples with artiss. Fibrin Sealants are PbR excluded and therefore any increase in costs may have to be considered by the CCG board in year.

- **Strength of evidence** – Two RCTs.

- **Place in therapy relative to available treatments** – Unable to ascertain.

- **National guidance and priorities** – None available.

- **Local health priorities** –

- **Equity of access** – Tisseel has been included on the formulary for non-plastic procedures. Other plastic centres are currently using Artiss.

The JFG considered the application and evidence submitted. The JFG was still unable to approve the inclusion of Artiss. Whilst it is accepted that there appears to be evidence that artiss would be beneficial in this patient cohort, the JFG had no indication of what potential cost pressure that this could pose to the CCG due to the lack of information included regarding patient numbers and the current practice at NBT. If this is a new development, it may be that this should be taken forward during the annual planning round which will begin in October.

**Action:**

1. **NB to inform applicant.**
2. **MP to contact applicant to try and acquire the information**
3. **NB to agenda at a further meeting.**

5  **Shared Care Protocols/TLS status**

5.1 **No new SCPs for discussion**

5.2 **Neurology SCPs**

SCP for Rasagiline (amber 1 month), Stalevo (amber 1 month), Entacapone (amber 1 month), Rufinamide (amber 3 months) and Perampanel (amber 3 months) had all been discussed at the April 2014 JFG. Minor alterations were required. These alterations had been made and were back with NBT for agreement. Once these amendments have been agreed the new versions of the SCPs will be included on the website.

**Action:**

1. **NB to upload the SCPs once agreement from NBT has been confirmed.**

6  **Individual Funding Requests**

A general discussion took place regarding recent IFRs in each CCG. To continue to monitor
requests.

7 Chapter review and formulary process

7.1 Chapter 6 Specialist Comments

The comments relating to the current Chapter 6 were discussed and agreed.

Action:

1. *NB to update spread sheet and to email out to rest of the group for e-approval.*
2. *NB to alter chapter with agreed changes and to send out for general consultation*

7.2 Chapter 11 Specialist Comments

The comments relating to the current Chapter 11 were discussed and agreed.

Action:

1. *NB to update spread sheet and to email out to rest of the group for e-approval.*
2. *NB to alter chapter with agreed changes and to send out for general consultation*

7.3 Chapter 7 Specialist Comments

There was insufficient time to discuss the comments relating to chapter 7.

7.4 Chapter 1 Specialist Comments

There was insufficient time to discuss the comments relating to chapter 7.

7.5 Chapter 13 Specialist Comments

There was insufficient time to discuss the comments relating to chapter 7.

Action:

1. *NB to update organise a meeting in August to discuss comments received on the chapters so far.*
2. *NB to review work plan for chapter review.*

8 Joint Formulary End of Year report

Insufficient time to discuss.

Action:

1. *NB to include on agenda for September meeting.*

9 Items for Discussion

9.1 NDRs for July Meeting
NB confirmed the NDRs to be discussed in September:

1. Anoro (Umeclidinium and vilanterol) for COPD maintenance. Joint NBT and UHB submission
2. Molludab (Potassium Hydroxide 5%) for Molluscum contagiosum. UHB submission
3. Striverdi Respimat (Olodaterol) for COPD maintenance. Joint NBT and UHB submission

9.2 Magnesium Supplementation

The current Magnesium guidance on the formulary needs review. There are currently a number of different magnesium salts on the formulary for different indications. This piece of work needs to be conducted across BNSSG.

Action:

1. AS at North Somerset to lead on updating the guidance.
2. NB to add to JFG agenda once draft revision has been submitted

9.3 Primary Care BNSSG Sip Feed formulary

NB informed the group that the Bristol CCG Medicines Management dietitian had undertaken an exercise to compile a list of oral nutritional supplements for primary care use. She is due to meet with South Glos and North Somerset later in the week. Once this is final, NB will send around to the JFG for e-approval and then this will be added to the JFG website.

Action:

3. NB to send around final document for e-approval
4. NB to add to JF website following e-approval

9.4 Suboxone NDR

NB informed the group that she had a further application for Suboxone (buprenorphine and naloxone) from a Consultant Psychiatrist in Addictions from Addaction, North Somerset. The JFG considered an application from AWP back in February 2013. The group considered this application but unfortunately rejected its inclusion onto the formulary ‘due to the benefits over buprenorphine being theoretical with no evidence and RCTs to support them.’ It was therefore difficult to justify the increased acquisition cost compared to buprenorphine. Therefore the consultant was informed that the group would not reconsider this unless there was any new evidence. However, the Consultant wished for the chance to be able to personally discuss the application with the group, believing that there would be a niche group of patients where Suboxone would be useful and that the additional costs required could be found by reducing the spend on branded Subutex.

The JFG discussed the merits of re-discussing an application. It was the opinion of the group that unless there was any new evidence than a re-discussion should not occur.

Action:

1. NB to find out if there is any new evidence – if there is, NB to agenda the NDR at the September meeting.
2. NB to inform the applicant of the outcome.
10 AOB

None

NB
Interface Pharmacist
21st July 2014
### Action Log for 15th July 2014

<table>
<thead>
<tr>
<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
<th>Responsible Officer</th>
<th>Deadline</th>
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<tr>
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<td>Botulinum toxin in urinary incontinence</td>
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<td>NB/SB</td>
<td>September 2014</td>
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<td></td>
</tr>
<tr>
<td>15.7.14</td>
<td>3.1</td>
<td>Positive NICE Technology Appraisals</td>
<td>Add positive NICE TAs to the JF website.</td>
<td>NB/SB</td>
<td>July 2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.7.14</td>
<td>4.1</td>
<td>Melatonin for prevention of delirium NDR</td>
<td>Inform applicant that JFG unable to make decision. More information required (MP to gather). To add to a future agenda.</td>
<td>NB/MP</td>
<td>September 2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.7.14</td>
<td>4.2</td>
<td>Artiss NDR</td>
<td>Inform applicant that JFG unable to make decision. More information required (MP to gather). To add to a future agenda</td>
<td>NB/MP</td>
<td>September 2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.7.14</td>
<td>5.2</td>
<td>Neurology SCPs</td>
<td>To add Rasagiline, Entacapone, Stalevo, Rufinamide and Perampanel SCPs to the website once agreement from NBT has been obtained.</td>
<td>NB</td>
<td>22nd July 2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.7.14</td>
<td>7.1</td>
<td>Chapter 6 specialist review</td>
<td>Update spread sheet with agreed actions. Email to rest of JFG for agreement, make changes to chapter. Send chapter out for general consultation.</td>
<td>NB</td>
<td>30th July</td>
<td>Send chapter 6 out for general consultation in accordance with work plan</td>
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<tr>
<td>15.7.14</td>
<td>7.2</td>
<td>Chapter 11 specialist review</td>
<td>Update spread sheet with agreed actions. Email to rest of JFG for agreement, make</td>
<td>NB</td>
<td>30th July</td>
<td>Send chapter 11 out for general consultation in</td>
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<tr>
<td>Date</td>
<td>Item</td>
<td>Description</td>
<td>Responsible</td>
<td>Due Date</td>
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<td>15.7.14</td>
<td>7.3</td>
<td>Chapter 7: Arrange a further meeting to discuss comments.</td>
<td>NB/SB</td>
<td>30&lt;sup&gt;th&lt;/sup&gt; June</td>
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<td>7.4</td>
<td>Chapter 1: Arrange a further meeting to discuss comments.</td>
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<td>30&lt;sup&gt;th&lt;/sup&gt; June 2014</td>
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<td>7.5</td>
<td>Chapter 13: Arrange a further meeting to discuss comments.</td>
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<td>15.7.14</td>
<td>8</td>
<td>JFG End of Year Report: Add to a future agenda.</td>
<td>NB</td>
<td>30&lt;sup&gt;th&lt;/sup&gt; July</td>
<td>SCP needs updating then to add to website</td>
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<td>15.7.14</td>
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<td>Magnesium Supplementation guidance: North Somerset to lead on review of guidance</td>
<td>NB/AS</td>
<td>Decemb er</td>
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<td>15.7.14</td>
<td>9.3</td>
<td>Primary Care Sip feed formulary: To send out to JFG for e-approval.</td>
<td>NB</td>
<td>22&lt;sup&gt;nd&lt;/sup&gt; July</td>
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<td>15.7.14</td>
<td>9.4</td>
<td>Suboxone NDR discussion: To inform applicant of decision not to reconsider an application</td>
<td>NB</td>
<td>30&lt;sup&gt;th&lt;/sup&gt; July</td>
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### MEETING DATES 2014

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SPCs</th>
<th>Time</th>
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<tbody>
<tr>
<td>Tuesday 21st January 2014</td>
<td>3rd December 2013</td>
<td>10 am to 1 pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 4th March 2014</td>
<td>21st January 2014</td>
<td>1.30 – 4.30pm</td>
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<tr>
<td>Tuesday 22nd April 2014</td>
<td>11th March 2014</td>
<td>9am to 12 pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 3rd June 2014</td>
<td>22nd April 2014</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room South Plaza</td>
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<tr>
<td>Tuesday 15th July 2014</td>
<td>3rd June 2014</td>
<td>9am to 12 pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 2nd September 2014</td>
<td>22nd July 2014</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room South Plaza</td>
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<tr>
<td>Tuesday 14th October 2014</td>
<td>2nd September 2014</td>
<td>9am to 12 pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 25th November 2014</td>
<td>14th October 2014</td>
<td>9am to 12 pm</td>
<td>Boardroom South Plaza</td>
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NB. The times of the morning meetings have changed so that the meetings now start at 9am and finish at 12 midday.
BNSSG Joint Formulary Group
Meeting held on: Tuesday 2\textsuperscript{nd} September 2014 1.30pm – 4.30pm
Bevan Room, South Plaza, NHS Bristol CCG

Minutes

Present:

Interface Pharmacist, NHS Bristol CCG (Chair)
Deputy HoMM, NHS Bristol CCG
HoMM, NHS North Somerset CCG
Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust
Medicines Management Pharmacist, South Gloucestershire CCG
Public Health Consultant, Bristol City Council (Chair)
Clinical Effectiveness Research Lead, Bristol City Council
Consultant Renal Physician, and Joint D&TC Chair, North Bristol NHS Trust

Apologies:

Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust
Consultant in Emergency Medicine, UHBristol NHS Foundation Trust and Associate Director of Patient Safety, and Chair of UHB Medicines Advisory Group
GP, Bristol and member of Bristol CCG Board

HoMM NHS Bristol CCG
Formulary Pharmacist, AWP
GP, North Somerset
Joint D&TC Chair, North Bristol NHS Trust
Chief Pharmacist, AWP
Director of Pharmacy Weston Area Health NHS Trust

1 Welcome, Apologies and Declaration of Interests

\textbf{Declarations of Interest}

None

The meeting was not quorate. In accordance with the ToR of this group, the Chair of the
group determined that the meeting should continue and the Formulary Pharmacist will secure endorsement of any decisions ex-committee via email. Therefore decisions taken during this meeting will need to be ratified and actioned once approved.

2 Minutes of the meeting of 15th July 2014 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 15th July 2014 had been circulated by NB following the meeting. No comments had been received that required further discussion.

Matters arising from July 2014 meeting

2.1 Botulinum toxin for urinary incontinence NDR
Following the NDR application discussed at the April meeting SB has met with Mr MD to investigate the costs of the current treatment pathway compared to the cost of the proposed treatment pathway which includes botulinum toxin. We are still awaiting final figures from the trust to present to the JFG. Providing this shows cost neutral/cost savings botulinum toxin will be added to the formulary.

NB and MP to chase Mr MD and Mrs KM (Deputy General Manager for Surgery, NBT) for the information.

Post meeting note: The figures should be available for presentation at the October meeting.

2.2 Primary Care Sip Feed formulary
The Bristol CCG Medicines Management dietitian had coordinated the compilation of a primary care Sip feed formulary, which has been agreed across BNSSG. This was sent around the JFG for e-approval, and this is now on the formulary website. HW requested that a further document that had been produced which includes more detailed prescribing information for GPs to be also included on the website. This document has only been agreed within Bristol and therefore this needs to be agreed within South Gloucestershire and North Somerset before it can be added to the website. More information has been included within section 9.4 on the formulary detailing how to deal with patients who are discharged from hospital on sip feeds.

Action:
1. NB to liaise with dietitian re prescribing advice document
2. NB to include prescribing advice document on the website once agreed across BNSSG.

3 NICE New Technology Appraisals Published

3.1 Enzalutamide for metastatic hormone – relapsed prostate cancer previously treated with docetaxel containing regimen. TA316

Agreed TLS Red

3.2 Prasugrel with percutaneous coronary intervention for treating acute coronary syndromes (review of technology appraisal guidance 182) TA317

Currently TLS Amber 1 month on the BNSSG formulary. Review of the changes in the new appraisal required.

3.3 Lubiprostone for treating chronic idiopathic constipation TA318

TLS Blue suggested in line with prucalopride on the BNSSG formulary. NB to
contact GP members of the group to confirm that this is acceptable.

**3.4** Ipiilmumab for previously untreated advanced (unresectable or metastatic) melanoma **TA319**

TLS Red

TAs adopted into the BNSSG Joint Formulary July and August 2014

- Lung cancer (non-small cell, EGFR mutation positive) – afatinib **TA310**. TLS Red
- Multiple myeloma – bortezomib (induction therapy) **TA311**. TLS Red
- Alemtuzumab for treating relapsing-remitting multiple sclerosis **TA 312**. TLS Red
- Canagliflozin in combination therapy for treating type 2 diabetes **TA 315**. TLS Blue

**4 New Drug Requests (NDRs)**

**SUMMARY**

**4.1** Potassium Hydroxide 5% (Molludab) – Molluscum contagiosum

Approved for inclusion onto the BNSSG formulary only for patients who are immunocompromised or immunosuppressed, who have other dermatological symptoms, who have extensive coverage, or where it is causing serious distress. TLS Blue

**4.2** Umeclidinium and vilanterol (Anoro) – COPD maintenance.

Approved for inclusion onto the BNSSG formulary in place of Ultibro as this is still not available within the UK, TLS Blue.

**4.3** Olodaterol (Striverdi) – COPD maintenance.

Rejected for inclusion onto the BNSSG formulary on the grounds of insufficient evidence placing it above the current formulary approved long acting beta agonists. This will be reviewed when the combination LAMA/LABA inhaler is available in 2015.

**4.4** Melatonin – Prophylaxis of delirium in adult intensive care units.

Deferred decision until a future meeting when further information can be provided and with the applicant in attendance.

**4.5** Artiss – Surgical Glue for plastic surgery procedures

Deferred decision until a future meeting when further information can be provided.

**Decision Criteria used by JFG for NDR**

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
• Place in therapy relative to available treatments
• National guidance and priorities
• Local health priorities
• Equity of access

Full Discussion

4.1 Potassium Hydroxide 5% (Molludab) – Molluscum contagiosum. Dr CK, Consultant Dermatologist, UHBristol.

Dr CK attended the meeting to present the application. Please see application form for full details.

NB presented a summary of the application; the critical appraisal had been completed by HC at UHBristol. Molluscum contagiosum (MC) is a common and relatively harmless (but highly contagious) viral infection of the skin. The maximum incidence occurs in pre-schoolers aged 1-4 years. The most common approach is to do nothing as the condition often disappears on its own within 12 -18 months; treatment is generally reserved for older children and adults in cases where the spots are particularly unsightly and affect the quality of life. Some patients are referred into secondary care for severe cases and treatment is recommended, which is currently liquid nitrogen, or Imiquimod. Imiquimod is not licensed for the treatment of MC and is considerably more expensive than Molludab. There is currently no formulary choice for the treatment of MC.

Discussion with Dr CK

Dr CK re-confirmed that MC is a common virus which is harmless but a nuisance. Occasionally children may get more than 100 spots, and can cause a degree of morbidity. They can be near the face or the body folds, or if the patient has eczema this can complicate the condition. In the majority of cases, no treatment is necessary. If treatment is required in severe cases, this would be either liquid nitrogen which does work but is painful and leaves scars, or off label Imiquimod. There is not a significant amount of evidence for this, and it is expensive.

There are a few medium sized, placebo controlled trials which show that potassium hydroxide 10% is efficacious and tolerated. More recently, smaller studies have shown that 5% is as efficacious as 10%. It has been shown that it is comparable to Imiquimod and liquid nitrogen. Molludab has been shown not to be painful.

Generally the referrals that are made to secondary care are appropriate and secondary care only see the severe cases.

• Patient safety – Molludab is generally well tolerated with the main adverse effects being stinging and some irritation. Some trials have demonstrated that Molludab has less adverse effects than other treatments e.g. cryotherapy. It has been shown to have similar tolerability to Imiquimod, but more adverse events compared to tretinoin cream. The Cochrane review found that no treatments were associated with adverse effects.

• Clinical effectiveness – Trials have shown that Molludab is as efficacious as other treatments for treating MC. No trial has demonstrated superiority. Trials have demonstrated that potassium hydroxide provides a good response to treatment, and a faster response than its comparators.

• Cost effectiveness or resource impact – It has a relatively low cost - £13.50 per bottle,
which is considerably less expensive compared to Imiquimod (£113.00/28 sachets). It also should be considered that this is a treatment that is relatively easy to administer in the home. It should be noted however that this would be an additional cost if it were to be used on all MC cases.

- **Strength of evidence** – Trials have been small in numbers (n = 30, n = 50, n = 30) and in some trials, patients have been lost to follow up. Some studies did not take in to consideration spontaneous clearing.

- **Place in therapy relative to available treatments** – MC for the majority of patients is self-limiting, although can take up to 18 months to clear completely. Therefore for the majority of patients, the current recommendation of no treatment should continue. However Molludab does offer a licensed treatment for those particular patients in whom the virus is severe and causing serious distress. Currently, in secondary care, these patients are offered liquid nitrogen or Imiquimod which can be more painful and more expensive than Molludab.

- **National guidance and priorities** – The British Association of Dermatologists have produced a patient information leaflet for MC. It states for treatment:

  "This depends partly on the age of the person who has it. Many of the treatments are painful and often it is best not to treat since the spots will eventually go away on their own. It is almost always better to avoid painful non-essential treatment in children since a child hurt by active treatment may be frightened of doctors for life.

  If active treatment is needed, there are several possibilities:

  The spots can be frozen with liquid nitrogen (cryotherapy) at intervals until they are clear.

  Some simple measures cause the spots to become inflamed and then to go away. These include squeezing the spots out with a pair of forceps, and piercing them with a small sharp object such as a clean cocktail stick. A local anaesthetic cream, applied to the area and left on under a plastic film for one hour before the procedure, will help to reduce the pain.

  The spots can be scraped off with a sharp instrument (curettage) after local anaesthetic injection.

  An eye specialist should deal with spots on the eyelids.

  A cream containing a chemical that affects the immune system (imiquimod) has recently had some success, but should be avoided in pregnancy. Imiquimod is not licensed for treating molluscum contagiosum, although it is often prescribed for this condition."

- **Local health priorities** – Not listed as a high priority locally.

- **Equity of access** – No other formulary could be identified that included Molludab within it. Patients are able to purchase this treatment from a pharmacy.

The JFG felt that the clinical case had been presented sufficiently for Molludab to be available for the treatment of MC in those severe cases, those patients who are immunocompromised/immunosuppressed, those with other dermatological conditions, or where the condition is causing serious distress. The pros and cons were discussed regarding the possibility of it being available for these patients in the community. If it were to be classified as Red, it would be necessary for a GP to refer into secondary care for this treatment (which is also available to purchase from pharmacies). If it were to be classified as blue, and therefore able to be prescribed in primary care, suitable patients would have access to this treatment which could subsequently reduce the number of referrals.
Concern was raised over the possibility of patients being inappropriately prescribed the treatment if it were included on the formulary i.e. those in whom no treatment is currently recommended. The niche cohort should be clearly identified on the website, and GPs appropriately educated about which patients should be treated with Molludab.

The JFG considered the application and the evidence submitted. Molludab should be approved for inclusion onto the formulary, TLS Blue, for those patients who are immunocompromised/immunosuppressed, those with other dermatological conditions, or where the condition is causing severe distress. This should be reviewed in 12 month’s time.

Action:

1. NB to confirm with Dr Kennedy the appropriate wording for the cohort of patients that should be prescribed Molludab.

2. NB to confirm with the GP members of the group that a TLS of Blue is appropriate.

3. NB to inform applicant and include on the formulary

4. NB to include on list of medicines which require review post inclusion on the formulary

4.2 Umeclidinium and vilanterol (Anoro) – COPD maintenance. Dr JC, Respiratory Consultant, NBT and Dr NJ, Respiratory Consultant, UHBristol

LM (Specialist Respiratory Pharmacist, NBT) and Dr NJ, Respiratory Consultant UHBristol attended the meeting to present the application. Please see application form for full details.

No additional critical appraisal had been completed as the SMC had recently reported their recommendation in August 2014. The SMC stated that Anoro is not recommended for use within NHS Scotland. This is due to the company not presenting a sufficiently robust clinical and economic analysis. There were three randomised controlled studies within the review and that these showed that after 24 weeks of treatment Anoro significantly improved lung function compared to a long acting antimuscarinic in patients with moderate to very severe COPD. However there was no difference between treatments in dyspnoea or health status. The evidence therefore shows an improvement in clinical measures, but not patient orientated outcomes.

Anoro is available in the Elipta device and therefore is useful for those patients who have low respiratory flow.

Discussion with Dr NJ and LM

Anoro is a LABA/LAMA combination inhaler. The studies involving Anoro showed an improvement in lung function but did not reduce the number of exacerbations. Am improvement was seen in the dyspnoea index but this improvement was not clinically meaningful. The clinical trial data is consistent with the data that was available for Ultibro (indacaterol/glycopyrronium). Anoro is priced as cheaper than tiotropium (LAMA) and significantly cheaper than the only other LAMA/LABA combination, Ultibro - £32.50 compared to £44.55. Ultibro was agreed for inclusion onto the formulary in December 2013, however it is still not available for prescription in the UK. We are unaware of when this agent is likely to be available, and so currently we are still without a dual bronchodilator for COPD. Dual bronchodilation with a LABA and LAMA is expected to set a new standard of care in the management of COPD and will help to reduce the need/prolong the need to initiate inhaled steroids i.e. it will primarily used in those patients needed combination bronchodilation prior to introducing steroids. The existing pathway for COPD involving an inhaled
steroid in the routine management of COPD is not now the preferred pathway, and a combination LABA/LAMA inhaler would assist in this. The treatment pathway for new COPD patients would need to be changed, and the BNSSG COPD guidelines need to be updated to include these agents. Being in one device this should help to improve compliance.

If Anoro was not accepted onto the formulary, more patients would remain on seretide and tiotropium. This has safety implications (risk of pneumonia) and cost implications. At this current time, there is no evidence to suggest that the use of Anoro in place of seretide would be more beneficial.

Despite the SMC advice, Portsmouth and South East Kent have accepted it onto their formulary.

The SMC acknowledged the data the GSK had presented, but were not satisfied with the cost model. GSK are getting ready to re-submit to the SMC and the expectation is that it will be accepted by the SMC at this point. The major issue with the studies was that there were no improvements seen in the patient orientated outcomes and that you would expect quality of life data for COPD trials.

From a patient compliance point of view, having a dual LABA/LAMA in the one inhaler will improve patient compliance.

- **Patient safety** – Safety concerns for Anoro include cardiac effects such as arrhythmias e.g. atrial fibrillation and tachycardia and an increased risk of vascular events. Long term safety data for the licensed dose are not yet available.

- **Clinical effectiveness** – Three randomised controlled studies demonstrated that after 24 weeks of treatment, umeclidinium/vilanterol statistically significantly improved lung function compared with tiotropium monotherapy in patients with moderate to very severe COPD. The improvement was clinically significant in two of the three studies. There was no difference between umeclidinium/vilanterol and tiotropium monotherapy in dyspnoea or health status. It is unclear how the efficacy of Anoro compares to existing LABA/LAMA therapy.

- **Cost effectiveness or resource impact** – A cost utility analysis was presented to the SMC comparing Anoro with tiotropium monotherapy. However, the main issue with this is that the comparison with tiotropium alone was considered less appropriate at this time – dual therapy would have been more appropriate. Owing to the uncertainties surrounding the clinical evidence, the economic case was not demonstrated.

- **Strength of evidence** – The European Medicines Agency recommends that lung functions parameters alone are insufficient to assess therapeutic effect and that if selected as a primary endpoint, additional evidence of efficacy must be demonstrated through the use of a co-primary endpoint, which should either be a symptom based endpoint or a patient related endpoint. The only direct comparative evidence is against tiotropium monotherapy which is not considered as a relevant comparator to dual LABA/LAMA therapy. Despite the expectation that dual therapy with Anoro would be superior to tiotropium monotherapy, the differences were not always significant in terms of the important patient related outcomes.

- **Place in therapy relative to available treatments** – In general, clinical experts consulted by SMC consider that the pace of Anoro in treatment is as an alternative to separate inhalers of tiotropium and a LABA with the potential advantage of improving compliance.

- **National guidance and priorities** – SMC advice as detailed above. The manufacturers have resubmitted an application to the SMC and this advice is due February 2015. The All Wales Medicines Group have received a submission but as yet it is not timetabled for when the appraisal will be presented.
• **Local health priorities** – Long term conditions.

• **Equity of access** – Unable to find many inclusions on local formularies. It is included in the Portsmouth and South East Hampshire Prescribing formulary. The JFG agreed for the inclusion of the only other LABA/LAMA combination, Ultibro however this is still not available. Whilst Anoro has not been compared with Ultibro, these are both LABA/LAMA combination inhalers.

The JFG considered the application and evidence submitted. The JFG acknowledged that the SMC did not recommend it for use within Scotland. However, it is also recognised that the LABA/LAMA combination is being used earlier in the management of COPD patients and a combination inhaler will aid compliance. The first combination LABA/LAMA inhaler was agreed for inclusion on the formulary (Ultibro) however this is still not available for prescription. The JFG agreed for its inclusion onto the formulary, TLS blue.

**Action:**

1. **NB** to inform applicant

2. **NB** to add to the formulary, TLS Blue.

4.3 **Olozaterol (Striverdi)** – COPD maintenance. *Dr James Calvert, Respiratory Consultant, NBT and Dr Nabil Jarad, Respiratory Consultant, UHBristol.*

LM (Specialist Respiratory Pharmacist, NBT) and Dr NJ, Respiratory Consultant UHBristol attended the meeting to present the application. Please see application form for full details.

No additional critical appraisal had been completed as the SMC had recently reported their recommendation in August 2014. The SMC stated that Striverdi is not recommended for use within NHS Scotland. This was due to the company not presenting a sufficiently robust clinical and economic analysis. In trials, it has been compared against formoterol and shown to be equally as efficacious in terms of lung function.

Striverdi is delivered via the Respimat device.

**Discussion with Dr NJ and LM**

Olozaterol is a LABA which has shown modest improvement in lung function in the clinical studies. The studies were well designed and consistent with the other LABAs. The question remains whether all LABAs are equal in terms of clinical efficacy. Olozaterol has been compared to placebo and formoterol in the studies, and it has been shown to be superior placebo, and no different to formoterol.

This would really be a niche group of patients who would be prescribed olozaterol – those that are on a LAMA e.g. tiotropium and require a LABA to reduce exacerbation frequency or improve breathlessness.

A combination of olozaterol and tiotropium is to be launched at some point in 2015, and it will be interesting to assess the clinical efficacy for this combination.

The question of removing indacaterol in place of olozaterol was put to Dr NJ. Dr NJ felt that he would not support this as his experience is that the patients like the Breezehaler device (indacaterol). Lloyd suggested that Dr JC would support this change.

• **Patient safety** – In trials, discontinuation emergent AE occurred in 71%, 69% and 71% of
patients in the olodaterol 5microgram, formoterol and placebo groups respectively.

- **Clinical effectiveness** – In pivotal studies, olodaterol was significantly superior to placebo for the primary end points of FEV1 AUV and for trough FEV1. In two 48 week studies, there was no significant difference between olodaterol 5 microgram and another long acting beta2 agonist for the primary endpoints of trough FEV1 and FEV1 area under the curve at week 24.

- **Cost effectiveness or resource impact** – The economic case could not be demonstrated in the submission to the SMC. However it does have a lower acquisition cost compared to indacaterol, and salmeterol but a slightly higher cost compared to formoterol.

- **Strength of evidence** – There have been no head-to-head studies between olodaterol and indacaterol or other LABA. There was no significant difference between olodaterol and placebo in terms of secondary endpoint – time to exacerbation. Whilst indacaterol may be considered the most appropriate comparator as it is once a day, the other LABAs are prescribed in higher volumes in COPD. The exclusion of comparisons to appropriate alternative treatments is a major weakness.

- **Place in therapy relative to available treatments** – Olodaterol would provide clinicians and patients with an alternative to indacaterol and to twice daily LABAs and LAMAs as well as a different inhaler device.

- **National guidance and priorities** – NICE advises using LABA alone for the symptomatic treatment of COPD in patients with stable disease and FEV1 >50%, who remain breathless or have exacerbations despite the use of SABAs when required. Also, the use of a LAMA in addition to a LABA is noted in situations where an ICS is declined or not tolerated.

- **Local health priorities** – Long term conditions.

- **Equity of access** – Unable to find any instances of it being included on a local formulary. Many have not yet even reviewed olodaterol and therefore is non-formulary by default.

The JFG considered the application and evidence submitted. The JFG was unable to approve the inclusion of olodaterol to the BNSSG formulary due to a lack of comparative efficacy data against other LABAs. There are also no other unique factors supporting olodaterol over existing formulary LABAs.

**Action:**

1. **NB** to inform applicant

**4.4 Melatonin** – Delirium in Intensive Care. Dr MT, Consultant Anaesthetist, NBT. Re-discussion

This NDR was first discussed at the July JFG. A few questions remained which meant that the JFG were unable to make a decision at the time. No further progress has been made on the application.

**Action:**
1. **MP** to contact applicant to try and acquire the information

2. **NB** to agenda at a further meeting.

### 4.5 Artiss – Surgical Glue. Mr PW, Plastic Surgeon, North Bristol NHS Trust. Re-discussion

This NDR was first discussed at the back in 2013, and again in July 2014. A few questions still remained which meant that the JFG were unable to make a decision at the time. No further progress has been made on the application.

**Action:**

1. **MP** to contact applicant to try and acquire the information

2. **NB** to agenda at a further meeting.

### 5 Shared Care Protocols/TLS status

#### 5.1 Methylphenidate MR

The current SCP had been reviewed and updated by BS at AWP. Some minor changes had been made but the majority had remained. A few minor alterations were suggested and once these have been made, this will be signed off.

**Action:**

1. **NB** to make alterations and liaise with BS

2. **NB** to upload new SCP to website

#### 5.2 Denosumab (oncology)

A SCP had been submitted by UHB for denosumab in the prevention of skeletal related events in adults with bone metastases from breast cancer and from solid tumours other than prostate. This is currently classified as TLS Red within BNSSG. Further work is required around the administration and the costs associated with this, in primary and secondary care. There are potential options to potentially improve the administration for the patient and to save costs. The GP views that have been sought initially are not supportive of taking on the administration for these patients as it stands, and further work in terms of costing is required.

**Action:**

1. **NB/SB** to progress investigating the denosumab pathway

#### 5.3 Rifampicin Change in status request

NBT had submitted a request to change Rifampicin for indications other than TB to amber no shared care. The JFG were supportive of this change, recognising the need for GPs to
prescribe this for patients who have been discharged from hospital and also potentially being able to prescribe for a patient that isn't in hospital. The need for some prescribing guidance was discussed and the JFG felt that some areas would need written guidance about potential monitoring and therefore we will request that this is written. This will be uploaded onto the website.

**Action:**

1. **MP** to inform applicant of need for prescribing guidance

2. **NB** to upload prescribing guidance and change TLS status on website

### 5.4 Finasteride and Dutasteride Change in status request

A GPwSI from North Somerset has suggested changing the finasteride and dutasteride to Green/Blue respectively. The JFG agreed that there is no guidance suggesting that these should be commenced and monitored in secondary care. Potentially if GPs prescribe these to the right patients, it may reduce the number of referrals into secondary care. Finasteride would remain as first line (green), with dutasteride as second line (blue) for those patients intolerant of finasteride.

**Action:**

1. **NB** to change TLS status on website

### 6 Individual Funding Requests

A general discussion took place regarding recent IFRs in each CCG. To continue to monitor requests. The need for a better way to monitor these was discussed. A list of all IFRs and their outcome is required, and October would be a good time for this.

**Action:**

1. **SB/NB** to progress IFR monitoring

### 7 Chapter review and formulary process

#### 7.1 Chapter 13 Specialist Comments

NB stated that a few members of the JFG had met since the last meeting to discuss the comments on chapters 7, 1 and 13. The chapter review process needs reviewing. Chapter 13 comments to be held, and to organise further meetings for the chapter review.

**Action:**

1. **NB** to review chapter review process.

### 8 Joint Formulary End of Year report

The report was briefly discussed and some amendments were suggested.

**Action:**
1. **NB** to amend the end of year report and to send it around the group for e-approval.

9 **Items for Discussion**

9.1 **NDRs for October Meeting**

Currently the NDRs for discussion at the October meeting are:

1. **Co-enzyme Q10** for mitochondrial disease. NBT submission, CM to do critical appraisal.
2. **Paliperidone** for schizophrenia. AWP submission, NB to do critical appraisal.
3. **DuoResp Spiromax** (**Budesonide and formoterol**) for asthma and COPD, NB to do critical appraisal.
4. **TO CONFIRM** Umeclidinium for COPD. NB SMC due to report on 8th December 2014, therefore may postpone this until the January meeting.

9.2 **Review of Angiotensin II receptor antagonists**

The cardiac specialist pharmacist had been in contact regarding our formulary choices as now telmisartan has become generic, it has a cheaper acquisition cost. It was decided that this would be taken up within the chapter review process.

9.3 **Colecalciferol licensed vs unlicensed products**

The section on the formulary relating to the colecalciferol products has been amended so that it is formatted better, and now includes the licensed products Desunin, Fultium and InVita D3 as green products, with the unlicensed products as blue.

9.4 **Discontinued products on the formulary**

NB presented a list of medicines which have been removed from the formulary as they had now been discontinued:

- Piperazine
- Otosporin
- Liquid paraffin

9.5 **NICE Clinical Guideline 181, updated from 67**

The updated clinical guideline re Lipid modification states that atorvastatin should be used first line now. The BNSSG lipid guidelines are being updated by RB. It was agreed to move atorvastatin up to first line with simvastatin in the first instance.

9.6 **Implications of removal of generic sildenafil from schedule 2**

The SLS criteria do not now have to be fulfilled to enable generic sildenafil to be prescribed on the NHS. There was a discussion as to how this would impact our formulary. It was felt that a NDR would be needed for indications outside the existing SLS criteria if prescribers within BNSSG wanted to use this within this cohort of patients. This needs further discussion at the BNSSG D&TC.

9.7 **Removal of UHB restriction only for posaconazole**

NBT had been in contact regarding formulary use within NBT of posaconazole. It was agreed to remove the UHB restriction.

9.8 **Silicone dressings**

There was a brief discussion regarding where these dressings are best placed with regards to formulary i.e. dressings formulary or the BNSSG medicines formulary. NB to investigate further.
10 AOB

None

NB
Interface Pharmacist
10th September 2014
**BNSSG JFG**

**Action Log for 2nd September 2014**

<table>
<thead>
<tr>
<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
<th>Responsible Officer</th>
<th>Deadline</th>
<th>Date of Update</th>
<th>Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.9.14</td>
<td>2.1</td>
<td>Botox for urinary incontinence</td>
<td>Chase Mr Marcus Drake for figures</td>
<td>NB</td>
<td>Sept</td>
<td></td>
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<tr>
<td>2.9.14</td>
<td>2.2</td>
<td>Sip Feed formulary</td>
<td>Liaise with Bristol dietitian re: prescribing advice for the formulary website</td>
<td>NB</td>
<td>Sept</td>
<td></td>
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<tr>
<td>2.9.14</td>
<td>3</td>
<td>NICE TA’s</td>
<td>Add positive NICE TA’s to the website</td>
<td>NB</td>
<td>August/sept</td>
<td></td>
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<tr>
<td>2.9.14</td>
<td>3</td>
<td>NICE TA’s</td>
<td>Review TA 317 for changes that would implicate formulary in BNSSG</td>
<td>NB</td>
<td>End sept</td>
<td></td>
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<tr>
<td>2.9.14</td>
<td>4.1</td>
<td>Molludab</td>
<td>Liaise with Cameron Kennedy and GPs re formulary wording and TLS status. Add to the formulary once agreed</td>
<td>NB</td>
<td>End sept</td>
<td></td>
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<tr>
<td>2.9.14</td>
<td>4.2</td>
<td>Anoro</td>
<td>Inform applicant and add to the formulary</td>
<td>NB</td>
<td>End sept</td>
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<tr>
<td>2.9.14</td>
<td>4.3</td>
<td>Striverdi</td>
<td>Inform applicant of decision to reject inclusion</td>
<td>NB</td>
<td>End sept</td>
<td></td>
<td></td>
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<tr>
<td>2.9.14</td>
<td>4.4</td>
<td>Melatonin</td>
<td>Follow up unanswered questions with applicant</td>
<td>MP</td>
<td>December</td>
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<tr>
<td>2.9.14</td>
<td>4.5</td>
<td>Artiss</td>
<td>Follow up unanswered questions with applicant</td>
<td>MP</td>
<td>December</td>
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<tr>
<td>2.9.14</td>
<td>5.1</td>
<td>Methylphenidate MR SCP</td>
<td>Liaise with Bethan Shepherd re minor changes, upload new SCP to website</td>
<td>MP</td>
<td>End sept</td>
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<tr>
<td>Date</td>
<td>Area</td>
<td>Description</td>
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<tr>
<td>2.9.14</td>
<td>5.2</td>
<td>Denosumab (oncology) Further work required to investigate full implications and costings</td>
<td>NB/SB</td>
<td>December</td>
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<tr>
<td>2.9.14</td>
<td>5.3</td>
<td>Rifampicin change in status request Change TLS. Ask for written guidance from NBT and add to website</td>
<td>NB/MP</td>
<td>End sept</td>
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<tr>
<td>2.9.14</td>
<td>5.4</td>
<td>Finasteride and dutasteride change in status request Change TLS</td>
<td>NB</td>
<td>End sept</td>
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<tr>
<td>2.9.14</td>
<td>6</td>
<td>Individual Funding requests Improve reporting mechanisms for all IFRs within BNSSG to identify potential cohorts</td>
<td>NB/SB</td>
<td>October</td>
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<tr>
<td>2.9.14</td>
<td>8</td>
<td>JFG End of year report Make minor amendments and for each organisation to send on further</td>
<td>NB/SB/MP/KG/KH/MG/DC</td>
<td>October</td>
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<tr>
<td>2.9.14</td>
<td>9.5</td>
<td>NICE Clinical Guideline 181 Ensure update of BNSSG lipid guidelines are taking place</td>
<td>NB</td>
<td>October</td>
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<tr>
<td>2.9.14</td>
<td>9.6</td>
<td>Removal of SLS criteria for generic sildenafil Discuss at BNSSG D&amp;TC</td>
<td>NB</td>
<td>September</td>
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<tr>
<td>2.9.14</td>
<td>9.8</td>
<td>Silicone dressings Investigate dressings formulary and impact on BNSSG Medicines formulary</td>
<td>NB</td>
<td>December</td>
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</tbody>
</table>
MEETING DATES 2014

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SPCs</th>
<th>Time</th>
<th>Venue</th>
</tr>
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<tbody>
<tr>
<td>Tuesday 21st January 2014</td>
<td>3rd December 2013</td>
<td>10 am to 1pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 4th March 2014</td>
<td>21st January 2014</td>
<td>1.30 – 4.30pm</td>
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<tr>
<td>Tuesday 22nd April 2014</td>
<td>11th March 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 3rd June 2014</td>
<td>22nd April 2014</td>
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</tr>
<tr>
<td>Tuesday 15th July 2014</td>
<td>3rd June 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Brunel Building Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 2nd September 2014</td>
<td>22nd July 2014</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room South Plaza</td>
</tr>
<tr>
<td>Tuesday 14th October 2014</td>
<td>2nd September 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Brunel Building Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 25th November 2014</td>
<td>14th October 2014</td>
<td>9am to 12pm</td>
<td>Boardroom South Plaza</td>
</tr>
</tbody>
</table>

NB. The times of the morning meetings have changed so that the meetings now start at 9am and finish at 12 midday.
BNSSG Joint Formulary Group
Meeting held on: Tuesday 14th October 2014 9.00am -12midday
Seacole Conference room, Southmead Hospital, Brunel Building

Minutes
Present:

Interface Pharmacist, NHS Bristol CCG (Chair)
Deputy HoMM, NHS Bristol CCG
Deputy HoMM, NHS North Somerset CCG
Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust
Head of Medicines Management, South Gloucestershire CCG
Public Health Consultant, Bristol City Council (Chair)
Consultant Renal Physician, and Joint D&TC Chair, North Bristol NHS Trust
Deputy HoMM, NHS Bristol CCG
Care of the elderly Pharmacist, North Somerset Community Partnership
Formulary Pharmacist, AWP (from 10.45am)

Apologies:

Clinical Effectiveness Research Lead, Bristol City Council
Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust
GP, Bristol and member of Bristol CCG Board
GP, North Somerset
Joint D&TC Chair, North Bristol NHS Trust
Chief Pharmacist, AWP
Director of Pharmacy Weston Area Health NHS Trust
GP, Bristol

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest
None

The meeting was not quorate. In accordance with the ToR of this group, the Chair of the group determined that the meeting should continue and the Formulary Pharmacist will secure endorsement of any decisions ex-committee via email. Therefore decisions taken during this meeting will need to be ratified and actioned once approved. It was also
decided to look at the Terms of Reference in relation to quoracy.

2  Minutes of the meeting of 2nd September 2014 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 2nd September 2014 had been circulated by NB following the meeting. NB had received comments relating to the Molludab NDR that needed further discussion (see matters arising).

Matters arising from September 2014 meeting

2.1 Molludab NDR
Following the NDR application discussed at the September meeting NB had received comments regarding the decision. The comments related to the potential for creep in prescribing if Molludab was included on the formulary. The group made the decision to include Molludab on the formulary, TLS Blue, for those patients who are immunocompromised, immunosuppressed, those with other dermatological conditions and those in whom the condition is causing significant distress. The group discussed the TLS status again and felt that they were still happy with the decision made at the September meeting. It is important to make the niche group clear on the formulary website and also to provide significant education for the GPs so that it is not inappropriately prescribed. NB confirmed her intention to send out a Joint Formulary Newsletter in the near future that would highlight this.

Action:

1. NB to add Molludab to the formulary website as above, TLS Blue
2. NB to send out a JF Newsletter highlighting Molludab.

3  NICE New Technology Appraisals Published

3.1 Dimethyl fumarate for treating relapsing remitting multiple sclerosis. TA320
   TLS Red

3.2 Lenalidomide for treating myelodysplastic syndrome associated with an isolated deletion 5q cytogenetic abnormality TA322
   TLS Red

There were no TAs adopted into the BNSSG Joint Formulary in September 2014

4  New Drug Requests (NDRs)

SUMMARY

4.1 Ubidecarenone (Co-enzyme Q10) – Mitochondrial disease

Needs financial sign off from the neurosciences directorate at NBT. Once this has been confirmed, ubidecarenone has been approved for inclusion onto the BNSSG formulary for patients with mitochondrial disease who have skeletal myopathy with symptoms of pain and fatigue under the care of Dr Merrison. TLS Red.

4.2 DuoResp (Budesonide and formoterol) – COPD maintenance and
asthma. Approved for inclusion on the BNSSG formulary due to it being cost effective. TLS Green.

4.3 **Botulinum toxin** – urinary incontinence.

This is proposed to be put into the annual commissioning round.

4.4 **Paliperidone (depot)** – Schizophrenia.

Agreed for inclusion onto the BNSSG formulary due to the practical advantages that it offers compared to risperidone depot, TLS Red.

**Decision Criteria used by JFG for NDR**

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

**Full Discussion**

4.1 **Ubidecarenone (Co-enzyme Q10)** – Mitochondrial disease. *Dr AM, Consultant Neurologist, NBT.*

Dr AM attended the meeting to present the application. Please see application form for full details.

NB presented a brief summary of the application; the critical appraisal had been completed by CM. The group had an in-depth discussion regarding commissioning of mitochondrial disease and where a decision to include or not to include ubidecarenone should be made. Mitochondrial disease is commissioned by Specialised Commissioning (NHS England). Ubidecarenone (Co-Q10) is an in-tariff medication and there is no mechanism for NHS E to assess in-tariff medications, unless there is a listed policy. Ubidecarenone is listed within the Manual for Prescribed Specialised Services 2013/3014 within Section 62 Highly specialist metabolic disorders and it states that NHS E commissions it for those patients who are registered inherited metabolic disorder patients. It is not listed within the mitochondrial disease section. It was therefore felt that it needed to be brought to the BNSSG JFG for discussion from a governance point of view, though financial acceptance will be down to the neurosciences directorate within NBT. There is currently no formulary choice for the treatment of mitochondrial disease.

**Discussion with Dr AM**

Dr AM explained the commissioning arrangements regarding the Neuromuscular disease services that NBT provide. She confirmed that back in 2010, the whole NMD service was commissioned by Specialised Commissioning. Prior to this there were no adult services at all in the South West which brought about a very fragmented level of care. The service serves approximately 3000 adult patients, and there is a continuing need for more resources. Dr AM provides clinics in NBT, Taunton, Gloucester and UHBristol. NBT applied and were awarded the Operational Delivery Network and therefore is a specialist clinical and support service for children and adults living with a neuromuscular condition in the South west. The network covers amongst others… many neuropathies and mitochondrial disorders. Currently, this network is the only network that is funded directly from Specialised Commissioning.
Dr AM explained that the maximum number of patients with mitochondrial disease in the area would be 150, but she actually only sees about 30. She has prescribed ubidecarenone in only a handful of patients, although she will discuss the potential benefits with patients and some choose to purchase it. Some patients do not have the funds to be able to continually buy it and if it is effective then all patients should be able to have access to it. Most patients treated in London and Oxford will have tried it or will be taking it and it is estimated that about one third of patients respond to it. Dr AM has not prescribed it in isolated symptoms, but in patients where fatigue, pain and perceived proximal weakness are issues. Other medications which are tried are gabapentin and pregabalin for the pain, however these don’t always work. She is aware that there may be a placebo element to it but also there is a physiological element too. The patients that are suitable for a trial of 3-6 months are those with skeletal myopathy with symptoms of pain and fatigue that have become difficult to manage. After 3-6 months, if it hasn’t worked, she would not continue the prescription. Dr AM would suggest that she sees about a quarter of patients receiving benefit from taking ubidecarenone. The disease itself is progressive over many years and does not fluctuate.

The following information was all contained in the NDR application form, although not discussed in depth at the meeting.

- **Patient safety** – No serious adverse events have been associated with the use of CoQ10. There are reports of wakefulness and sleep disruption.

- **Clinical effectiveness** – A 2012 Cochrane SR assessed a range of treatments for mitochondrial diseases tested in 12 robust studies but concluded that there was no clear robust evidence supporting the use of any intervention in mitochondrial diseases. Innumerable individual case studies and other small case series of patients with definite coenzyme Q10 deficiency (either primary or secondary) show variable responses to CoQ10 treatment. However, it appears that clinical improvement has been documented in many patients. Some studies appear to clearly demonstrate that treatment with CoQ10 significantly alters the course of the disease and can be lifesaving, however treatment protocols have not been standardised and results have not been uniform. Evidence suggests that whilst the muscle symptoms associated with CoQ10 deficiency have been reported to improve in many cases, neurological symptoms appear to be only partially ameliorated. Additionally evidence suggests early CoQ10 supplementation is crucial for success of the therapy.

- **Cost effectiveness or resource impact** – The applicant has indicated a cost of £40 a month per patient and therefore £480 per year. CoQ10 is in tariff and therefore the resource impact would be on secondary care, NBT. A GP would not be expected to take on the prescription. It would therefore be necessary to ensure agreement has been confirmed from the neurosciences directorate.

- **Strength of evidence** – With a limited evidence-base (mostly confined to case series and reports and little data from randomised trials, the treatment of mitochondrial diseases is largely anecdotal. Generation of level I evidence is always going to be problematic – owing largely to the diverse range of conditions with different symptoms, each with small numbers; the range of outcome measures (many of which are proxy with unclear clinical significance) and the unwillingness of industry to invest research and development monies in a product considered to be a food supplement.

- **Place in therapy relative to available treatments** – There is no other formulary option for the treatment of mitochondrial diseases. It would only be tried in patients experiencing fatigue and muscle pain.

- **National guidance and priorities** – None relevant. We have made contact with the 3
specialist centres for advice. They have all confirmed that CoQ10 is on their formulary but as yet have not been able to furnish us with information as to how this decision was made.

- **Local health priorities** – Not listed as a high priority locally.

- **Equity of access** – Other formularies list Co-Q10 on their formularies, including the 3 specialist centres for mitochondrial disease. Patients would/should not be referred to a specialist centre just for a trial of Co-Q10. Ubidecarenone is listed in the 2014-2015 BNF for children, specifically for mitochondrial disorders.

The JFG considered the application and the evidence submitted. Most of the discussion centred on the commissioning arrangements for these patients. NBT are directly commissioned by NHS E SC to provide treatment for NMD patients, mitochondrial patients included. Co-Q10 is listed within the Manual for Prescribed Specialised Services 2013/2014 within Section 62 Highly specialist metabolic disorders and it states that NHS E commissions it for those patients who are registered inherited metabolic disorder patients; however it is not listed within the mitochondrial disease section. Therefore there is no policy that currently states whether Co-Q10 is commissioned for these patients. It has therefore been considered by the JFG from a governance point of view, but the neurosciences directorate are required to confirm that they are happy with the application prior to this being included on the formulary. As it is listed on the 3 specialist centres formularies, and NBT are commissioned to provide services for these patients as an Operational Delivery Network, it should be available locally on the formulary for these patients. Once the Neurosciences directorate have signed off the application this will be included on the formulary for patients with mitochondrial disease with skeletal myopathy with symptoms of pain and fatigue that are difficult to manage under the care of Dr Merrison, TLS Red.

**Action:**

1. **MP** to contact the Neurosciences directorate to sign off the application.

   **POST MEETING NOTE:** Neurosciences directorate have signed off the application and accept financial responsibility.

2. **NB** to inform applicant and include on the formulary, TLS Red

4.2 **DuoResp (Budesonide and formoterol)** – COPD maintenance and asthma. *Dr JC, Respiratory Consultant, NBT and Dr NJ, Respiratory Consultant, UHBristol*)

There was no one available to attend the meeting to present the application. Please see application form for full details.

DuoResp is a combination inhaler containing budesonide and formoterol indicated for the treatment of asthma and COPD in adults. It is comparable to the current formulary option Symbicort. There is no low strength inhaler and it is only licensed in adults. The high dose and medium dose of DuoResp have been conclusively shown to be equivalent in adults to the reference Symbicort. The low dose DuoResp inhaler has not been conclusively shown to be equivalent and hence cannot be authorised at present. Symbicort is currently in the BNSSG COPD and Asthma guidelines. DuoResp would be able to replace Symbicort; it is an easy to use breath actuated dry powder inhaler. It is considerably cheaper than Symbicort currently: £29.97 vs £38.00 per device.

The JFG considered the application and information submitted. DuoResp has been shown
to be equivalent to Symbicort. There have been no head to head trials, though this is not unexpected. The JFG agreed for DuoResp to be included on the formulary due to its lower acquisition cost compared to Symbicort, TLS green. The BNSSG COPD and Asthma guidelines will need to be updated to accommodate this; however this may be delayed until more of the new inhalers have been considered by the JFG.

Action:

1. NB to inform applicant

2. NB to add to the formulary, TLS Green.

4.3 Botulinum toxin – urinary incontinence. Presentation of financial planning of current and proposed pathways.

The NDR for Botox for the treatment of UI was considered back in April 2014. The decision at this meeting was ‘...the group were satisfied clinically that botulinum toxin should be available for the treatment of urinary incontinence. However it was necessary to show that the use of botulinum toxin would either be cost neutral or cost saving otherwise a business case would have to be submitted to the CCG boards. Providing this shows cost neutral/cost savings botulinum toxin will be added to the formulary.’

Since this meeting, SB and NB have worked with MD and KM (Deputy General Manager - Surgery and Interim Urology Service Manager) to obtain figures for the proposed introduction of Botox in the UI treatment pathway compared to the current treatment pathway. NB presented a brief overview of the costs, though a full Business case had been submitted to the group. The JFG discussed the costs presented. It was felt that whilst the group acknowledged acceptance that Botox is effective and relatively safe in this patient cohort especially compared to the alternatives e.g. major surgery, the costs involved by introducing this to the treatment pathway were largely difficult to predict. Potentially, the threshold for surgical intervention will reduce. If the treatment is successful repeat injections are required resulting in an accumulating secondary care population. The JFG did not feel confident that based on the figures presented, that this would result in cost savings.

The group agreed that NBT should put this application through the annual commissioning rounds for agreement. The Commissioning Intention letters are being written currently.

Action:

1. NB to inform applicant

2. SB to link with CCG colleagues to ensure that Botox for UI is picked up during the annual commissioning round and CCG boards.

3. MP to link with the NBT finance team to arrange input into the annual commissioning round.

4.4 Paliperidone (depot) – Schizophrenia. BS Formulary Pharmacist, AWP Mental Health Trust
BS, Formulary Pharmacist at AWP attended the meeting to present the application. Please see application form for full details.

Paliperidone is an atypical antipsychotic depot injection indicated for maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone. It was agreed to be included on the AWP formulary earlier this year. Risperidone depot is on the BNSSG formulary, TLS Red. Paliperidone has demonstrated efficacy in long term placebo controlled studies and short term studies compared with risperidone. The results demonstrate superior efficacy compared with placebo and durable treatment effects and similar efficacy and adverse effect profiles compared with risperidone.

Compared with risperidone injection, paliperidone injection offers several practical advantages: greater licensed dose range of four compared to three doses, reduced dose frequency with monthly vs fortnightly injections, less time consuming and complex dose preparation, easier storage requirements which could reduce wastage, dose interval flexibility and no requirement for additional oral antipsychotic drugs during initiation.

Paliperidone injection is more expensive compared to risperidone – depending on the dose, it is estimated that paliperidone would cost between £2,207 and £4,711 per year compared to risperidone £2,072 and £3,712 per patient per year.

There are BNSSG patients being treated in AWP who are currently being prescribed paliperidone. GPs should not be currently asked to take on the continuing prescription. The typical antipsychotic depots are currently amber on the formulary. It was felt that GPs do not currently have the capacity to absorb an increase in workload that would be involved if paliperidone was to be made amber. It was felt that this should remain in secondary care where they have the appropriate expertise to monitor these high risk patients.

- **Patient safety** – The safety profile of paliperidone injection is consistent across the shorter phase studies. The most common adverse effects included insomnia, anxiety, headache, restlessness and weight gain. These adverse effects are common to atypical antipsychotic drugs.

- **Clinical effectiveness** – The key study of paliperidone injection in schizophrenia is a randomised double blind comparison against risperidone. It has shown sustained and similar efficacy compared to risperidone injection.

- **Cost effectiveness or resource impact** – Due to its higher acquisition cost compared to risperidone, there could be an impact on the primary care prescribing budget if this were to be made amber. The decision to initiate compared to risperidone will be made by the specialist. However, it should be considered that there is anticipated a reduction in the number of clinic visits due to the reduction in dosage frequency and also a projected reduction in waste. It is difficult to predict the net savings/costs from using paliperidone rather than risperidone. It is likely to increase net drug expenditure compared with risperidone, however it may yield overall savings in healthcare costs as detailed above. These savings maybe difficult for commissioners to realise.

- **Strength of evidence** – Three key studies in adult patients: Long term placebo controlled and short term trials compared with risperidone. Double blind.

- **Place in therapy relative to available treatments** – Paliperidone injection would be used in patients in whom risperidone would have been considered in the past. These are patients in whom compliance with oral therapy is unreliable but are responsive to paliperidone or risperidone.

- **National guidance and priorities** – The SMC accepted paliperidone for use within NHS
Scotland.

- **Local health priorities** – Not listed as a high priority locally.

- **Equity of access** – AWP includes paliperidone on its formulary, and there are multiple examples of paliperidone being included on other formularies. Different areas have classified it as Red or amber.

The JFG considered the application and evidence submitted. Evidence has shown that it has similar efficacy compared to risperidone and it has practical advantages compared to risperidone: mainly a reduction in the frequency of administration and the lack of a need to store in a fridge. It is however more expensive compared to risperidone, though these additional costs maybe slightly off set by a reduction in clinic visits. It was felt that it should be included on the formulary however it should remain TLS Red for the current time so that patients can be monitored appropriately.

**Action:**

1. **NB** to inform applicant

2. **NB** to add to the formulary TLS Red

5  **Shared Care Protocols/TLS status**

5.1  **Acamprosate (Review of expired SCP)**

The current SCP had been reviewed and updated by BS at AWP. The SCP has been put onto the new BNSSG SCP template, however the content has generally remained the same. The dosing in renal impairment has been updated according to The Renal Drug Handbook. The group reviewed the wording in the SCP regarding blood tests and agreed that the lines of responsibilities are clear.

This was signed off.

**Action:**

1. **NB** to upload new SCP to website

5.2  **Depakote (Valproate semisodium) (Review of expired SCP)**

The current SCP had been reviewed and updated by BS at AWP. The SCP has been put onto the new BNSSG SCP template, however the content has generally remained the same. The group reviewed the wording in the SCP regarding blood tests and agreed that the lines of responsibilities are clear.

The SCP was signed off.

**Action:**

1. **NB** to upload the new SCP to the website
5.3 Apomorphine change in status request

NBT had submitted a request to change Apomorphine from Red to amber. Apomorphine is used for Parkinson disease patients and is delivered via subcutaneous infusion and injection. It has been used in the treatment of PD since the 1990s. The application states that the dose titration and training will continue in secondary care, and they will still be responsible for any dose changes but GPs could write prescriptions in between clinic appointments. This will ensure that a patient does not run out of medication. There are low numbers of patients who are currently receiving apomorphine – only 3 in the past year. It was therefore discussed that on the one hand, moving this to amber would not impose a significant amount of work, but it also means that a GP would not see many patients at all on apomorphine and therefore their clinical competence in this area could be minimal. The JFG discussed the practicalities of amber vs red, and it was felt that it should remain red to ensure that clinical responsibility for the prescription lies with the specialist. It was noted that posting prescriptions could be an option in between clinic visits.

Action:

1. **NB to inform applicant of decision to remain Red.**

5.4 Denosumab SCP update

The MHRA had issued advice in the Drug Safety Update (Sept 2014) re: Denosumab and minimising the risk of osteonecrosis of the jaw and monitoring for hypocalcaemia. It now recommends:

- Denosumab 60 mg (osteoporosis indication)

Check for ONJ risk factors before starting denosumab 60 mg. A dental examination and appropriate preventive dentistry are now recommended for patients with risk factors.

And,

- Denosumab 60 mg (osteoporosis indication)

Check calcium levels:

- before each dose
- within two weeks after the initial dose in patients with risk factors for hypocalcaemia (e.g., severe renal impairment, creatinine clearance <30 ml/min)
- if suspected symptoms of hypocalcaemia occur.

NB has been in contact with Dr SC to update the existing SCP. There is ongoing discussion regarding the need for a dental examination for patients at risk. An updated SCP should be available for presentation at the November meeting.

Action:

1. **NB to continue to liaise with Dr Clark and finalise updated SCP**

6 Individual Funding Requests

No common themes were discussed. However, it was noted that Paul Freeman (IFR team) will
provide a report 3 times a year for review.

**Action:**

1. **SB/NB** to progress IFR monitoring

7 Chapter review and formulary process

7.1 Chapter 11 (Eye)

NB stated that chapter 11 had now been finalised after specialist and general review of the chapter. No additional comments were received during the general review. Chapter 11 has been reviewed in depth by the Eye Hospital and it is hoped that the chapter is now a fair reflection of the majority of prescribing and should work across the interface.

**Action:**

1. **NB** to upload chapter 11.

8 Items for Discussion

8.1 NDRs for November Meeting

Currently the NDRs for discussion at the October meeting are:

1. Magnesium aspartate for hypomagnesemia.
2. Beclometasone and formoterol (NEXThaler) for asthma.
3. Insulin Degludec (Tresiba) for type 2 diabetes on haemodialysis.
4. Fluticasone and azelastine (Dymista) for moderate to severe seasonal and perennial allergic rhinitis.
5. Tocilizumab – Treatment of Rheumatoid arthritis in accordance with NICE TA 247 however via SC route not IV.

8.2 Duloxetine and Neuropathic pain – NICE Clinical Guideline 173

NB stated that duloxetine is included within the Clinical Guideline…

‘Offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain (except trigeminal neuralgia)”

Within the formulary currently, duloxetine is only mentioned for treatment of diabetic neuropathy. Therefore we should consider including duloxetine within the formulary for neuropathic pain. It was decided to pick this up within chapter review.

8.3 Dexamethasone IV – Change in concentration

NB noted that there is going to be a change with the IV dexamethasone preparation and therefore it will now be 3.8ml/ml and not 4mg/ml.

8.4 Fondaparinux – Removal of UHB only restriction

NB confirmed that the UHB only restriction alongside the fondaparinux entry has been removed and therefore there are no site restrictions.

9 AOB
NB
Interface Pharmacist
16th October 2014
### BNSSG JFG

#### Action Log for 14th October 2014

<table>
<thead>
<tr>
<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
<th>Responsible Officer</th>
<th>Deadline</th>
<th>Date of Update</th>
<th>Update</th>
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<tbody>
<tr>
<td>14.10.14</td>
<td>1</td>
<td>JFG ToR</td>
<td>Review the ToR in relation to the Prescribing leads and quoracy</td>
<td>NB</td>
<td>Nov 14</td>
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<tr>
<td>14.10.14</td>
<td>2.1</td>
<td>Molludab NDR</td>
<td>Inform applicant of decision to remain blue and include on the formulary</td>
<td>NB</td>
<td>Oct 14</td>
<td></td>
<td></td>
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<tr>
<td>14.10.14</td>
<td>3</td>
<td>NICE TAs</td>
<td>Ensure all of the June positive TAs are included on the website</td>
<td>NB</td>
<td>Oct 14</td>
<td></td>
<td></td>
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<tr>
<td>14.10.14</td>
<td>4.1</td>
<td>Ubidecarenone NDR</td>
<td>MP – Ask neurosciences for directorate sign off. If agreed, NB to inform applicant of the decision and include on the formulary</td>
<td>MP/NB</td>
<td>Nov 14</td>
<td></td>
<td>MP – Confirmed Neurosciences directorate approval October 14</td>
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<td>4.2</td>
<td>DuoResp NDR</td>
<td>Inform applicant of the decision, include on the formulary</td>
<td>NB</td>
<td>Nov 14</td>
<td></td>
<td></td>
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<tr>
<td>14.10.14</td>
<td>4.3</td>
<td>Botox NDR</td>
<td>Inform NBT finance team of need to submit to the annual commissioning round</td>
<td>MP</td>
<td>Nov 14</td>
<td></td>
<td>MP Oct 14</td>
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<tr>
<td>14.10.14</td>
<td>4.3</td>
<td>Botox NDR</td>
<td>Link with CCG colleagues to ensure Botox is picked up within annual commissioning round.</td>
<td>SB</td>
<td></td>
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<tr>
<td>14.10.14</td>
<td>4.4</td>
<td>Paliperidone NDR</td>
<td>Inform applicant of decision, include on the formulary TLS Red</td>
<td>NB</td>
<td>Nov 14</td>
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<tr>
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<td>Acamprosate SCP</td>
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<td>5.3</td>
<td>Apomorphine</td>
<td>Inform applicant of decision to remain Red</td>
<td>NB</td>
<td>Nov 14</td>
<td></td>
<td></td>
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<tr>
<td>14.10.14</td>
<td>5.4</td>
<td>Denosumab SCP</td>
<td>Liaise with Dr Clark re updating SCP to include hypocalcaemia and osteonecrosis guidance.</td>
<td>NB</td>
<td>Nov 14</td>
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<tr>
<td>14.10.14</td>
<td>7.1</td>
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<td>NB</td>
<td>Nov 14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.10.14</td>
<td>8.2</td>
<td>Duloxetine and neuropathic pain</td>
<td>Ensure NICE Clinical guidance is considered in chapter 4 review</td>
<td>NB</td>
<td>Nov 14</td>
<td></td>
<td></td>
</tr>
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</table>
### MEETING DATES 2014

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SPCs</th>
<th>Time</th>
<th>Venue</th>
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<tbody>
<tr>
<td>Tuesday 21st January 2014</td>
<td>3rd December 2013</td>
<td>10am to 1pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<tr>
<td>Tuesday 4th March 2014</td>
<td>21st January 2014</td>
<td>1.30 – 4.30pm</td>
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<tr>
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<td>11th March 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<tr>
<td>Tuesday 14th October 2014</td>
<td>2nd September 2014</td>
<td>9am to 12pm</td>
<td>Pharmacy Seminar Room Brunel Building Southmead Hospital</td>
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<tr>
<td>Tuesday 25th November 2014</td>
<td>14th October 2014</td>
<td>9am to 12pm</td>
<td>Boardroom South Plaza</td>
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</table>

**NB.** The times of the morning meetings have changed so that the meetings now start at 9am and finish at 12 midday.
BNSSG Joint Formulary Group
Meeting held on: Tuesday 25\textsuperscript{th} November 2014 9.00am - 12midday
Board Room, South Plaza, NHS Bristol CCG

Minutes

Present:

- Interface Pharmacist, NHS Bristol CCG (Chair)
- Deputy HoMM, NHS Bristol CCG
- HoMM, NHS North Somerset CCG
- Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust
- Public Health Consultant, Bristol City Council (Chair)
- Consultant Renal Physician, and Joint D&TC Chair, North Bristol NHS Trust
- Clinical Effectiveness Research Lead, Bristol City Council
- Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust
- GP, North Somerset

Apologies:

- Deputy Chief Pharmacist Weston General Hospital
- Head of Medicines Management, South Gloucestershire CCG
- GP, Bristol and member of Bristol CCG board
- Joint D&TC Chair, North Bristol NHS Trust
- Chief Pharmacist, AWP
- Director of Pharmacy Weston Area Health NHS Trust
- Formulary Pharmacist, AWP
- GP, Bristol

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest

None

2 Minutes of the meeting of 14\textsuperscript{th} October 2014 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 14\textsuperscript{th} October 2014 had been circulated by NB following the meeting. No comments had been received that needed further discussion.
Matters arising from October 2014 meeting

2.1 Botox for urinary incontinence
The JFG requested an update. The Planned Care steering group in Bristol CCG have been made aware of the current situation regarding Botox and urinary incontinence and it has also been raised with the commissioners that a business case needs to be submitted to the OPP. It has been confirmed that Urology is on their list of priorities. This will therefore go into the annual contracting round. NBT is co-commissioned by South Glos and Bristol. The second letter of intentions should go out in December/January and therefore more progress is expected then. We need to ensure that all three CCGs are aware of this. NBT have also ensured that it is within their commissioning intentions.

Action:
1. NB/SB to ensure the group is kept up to date

2.2 Olodaterol (Striverdi) NDR decision, Sept 2014
NB/VH informed the group that we had received a letter appealing the decision to reject the inclusion of olodaterol for the treatment of COPD in the BNSSG formulary. We have been informed that the SMC are due to reconsider their advice in January 2015 before the next JFG meeting. Therefore we will re-discuss the application on the 20th January in light of the SMC re-submission and decision.

Action:
1. NB to include Olodaterol on the January agenda

3 NICE New Technology Appraisals
Published

3.1 Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma. TA321 TLS Red

Adopted into the BNSSG Joint Formulary - October 2014

Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen TA316 TLS Red
Prasugrel with percutaneous coronary intervention for treating acute coronary syndromes TA317 TLS Amber
Lubiprostone for treating chronic idiopathic constipation TA318 TLS Blue
Ipilimumab for previously untreated advance (unresectable or metastatic) melanoma TA319 TLS Red

4 New Drug Requests (NDRs)

SUMMARY

4.1 Magnesium aspartate – Hypomagnaesaemia.
Agreed for inclusion onto the formulary on the grounds of being a cost effective alternative to the current options on the formulary. TLS green.

4.2 **Fostair Nexthaler (Beclometasone and formoterol)** – Regular treatment of adult asthma where the use of inhaled ICS/LABA is appropriate.

Agreed for inclusion onto the formulary on the grounds of being a cost effective alternative to the current options on the formulary and also a unique inhaler device which would be preferable to some patients. TLS Green.

4.3 **Insulin Degludec** – Patients with type II diabetes on haemodialysis.

Agreed for inclusion onto the formulary for this specific cohort of patients. TLS Red.

4.4 **Dymista (Fluticasone and azelastine)** – Moderate to severe seasonal and perennial allergic rhinitis who are referred to secondary care.

Agreed for inclusion onto the formulary for this specific cohort of patients; there is evidence to show that patients gained better control with Dymista compared to standard treatment and is a useful option prior to desensitisation. TLS Red.

4.5 **Melatonin** – Prophylaxis of delirium in ICU patients.

Agreed for inclusion onto the formulary for the specific cohort of patients in the ICU setting, TLS Red. A protocol will need to be developed to give assurance that clear guidance is given when to prescribe melatonin. The applicant is asked to report back to the group in a year’s time regarding local evidence, outcomes and experience and patient numbers.

**Decision Criteria used by JFG for NDR**

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

**Full Discussion**

4.1 **Magnesium aspartate** – Hypomagnesaemia. *Dr AD, Consultant Medical Biochemist, UH Bristol*

Please see application form for full details. NB presented a brief summary of the application.

The application is for a different magnesium salt to be included onto the formulary for the treatment of hypomagnesaemia in line with proposed updated BNSSG guidelines. We currently have Magnesium hydroxide, Magnesium oxide, Magnesium glycerophosphate as the oral options on the formulary. There are no licensed alternatives. The different products are licensed differently – some are food for special medicinal purposes and some are unlicensed medicines. It is clear from the UKMI document (2013) that there is no clear evidence suggesting one salt is more efficacious than another and that a choice will come down to local availability, patient choice and the cost. The small amount of evidence that does exist suggests that the aspartate salt has better bioavailability compared to glycerophosphate and equivalent to the others. It is also known
that patients generally do not adhere well to taking the glycerophosphate tablets mainly due to the size of the tablet. The aspartate salt is available as a sachet of granules which can be taken either by sprinkling on food or suspended in a drink. Magnesium aspartate is cheaper than glycerophosphate.

Magnesium aspartate is listed within the BNFc however magnesium glycerophosphate is noted within the adult BNF.

Within UHB Mg aspartate is already being used throughout the hospital, however within oncology, the glycerophosphate salt remains the agent of choice though this is probably due to historic use. The gastro team use the oxide.

It is necessary to confirm with NBT what the agent of choice is currently within their trust. The hydroxide preparation was included in the formulary a few years ago as the preferred agent. If NBT agree magnesium hydroxide could be removed from the formulary and replaced with aspartate.

The proposed updated magnesium supplementation guidelines include aspartate, glycerophosphate and oxide but does not include hydroxide. If the decision is to include aspartate then these can be circulated around the BNSSG D&TC committee for e-approval. It was discussed to include some clear indications within the formulary or guidelines to help direct prescribers.

- **Patient safety** – No safety concerns specifically relating to the aspartate salt have been identified.

- **Clinical effectiveness** – There are no national guidelines or studies comparing oral magnesium salts for the treatment or prevention of hypomagnesaemia which evaluated clinical outcomes. There are several small studies which have compared the bioavailability of various magnesium preparations, but these studies did not look at clinical outcomes and were conducted in healthy volunteers.

- **Cost effectiveness or resource impact** – Magnesium aspartate has been identified as being more cost effective at the doses stated within the proposed updated Magnesium supplementation guidelines when compared to the glycerophosphate salt. However it would be more expensive than magnesium hydroxide that is currently first line on the guideline. As discussed already, it is not clear if this is currently being used.

- **Strength of evidence** – No evidence looking at clinical outcomes, only small studies comparing bioavailability in healthy volunteers.

- **Place in therapy relative to available treatments** – It would be a suitable first line option for the treatment of hypomagnesaemia.

- **National guidance and priorities** – No national guidance.

- **Local health priorities** – Not listed as a high priority locally.

- **Equity of access** – Other local formularies include aspartate as an option.

The JFG considered the application and the evidence submitted. The JFG agreed that there was sufficient evidence to include it on the formulary as an option to treat hypomagnesaemia, TLS green. It is cost effective alternative to glycerophosphate and patients may prefer the granules compared to the large glycerophosphate tablets.
Action:

1. **NB** to inform applicant.
2. **MP** to find out which magnesium preparation is in use in NBT
3. **NB** to include on the formulary, TLS green
4. **NB/SB** to circulate updated Mg supplementation guidance around the BNSSG D&TC for e-approval.

4.2 **NEXThaler (Beclometasone and formoterol)** – Regular treatment of adult asthma where the use of inhaled ICS/LABA is appropriate. *JG, Medicines Waste Project Manager, NHS Bristol CCG*

JG attended the meeting to present the application. Please see application form for full details.

This is the first dry powder ICS/LABA combination inhaler licensed for asthma in >18 year olds. This is the same concentration and formulation as the Fostair inhaler which is already on the formulary however this is a standard pressurised metered dose inhaler. It is licensed for those patients who are not adequately controlled at Step 2 but for also those who are stable and therefore switching is possible. It is the only small particle size dry powder combination inhaler.

The device appears to be easier to use and there is no wastage if the dose is primed and not taken as there is an in built dose protector. It is not possible for a double dose to be inhaled if the inhaler is primed more than once without the dose being inhaled. It counts the successful inhalations and therefore can be used by prescribers to check concordance and will also give patients confidence. The NEXThaler requires a much lower inspiratory flow rate compared to other DPIs (35L/min compared to 60 – 90 L/min).

A study found that patients found the NEXThaler device the easiest to open, prepare and to set a dose. They also found that it had the clearest dose counter, was the easiest to use overall and would be the patients’ most likely device of choice for every day use.

In terms of efficacy, NEXThaler has been shown to be non-inferior compared to Fostair. In terms of cost, it is the cheapest ICS/LABA combination inhaler. The inhaler needs to be stored at room temperature.

Currently there is no license for ‘MART’ therapy and it is unsure whether this is likely to happen in the future. We are under the impression that a COPD license is likely to be applied for in the near future.

- **Patient Safety** – No safety concerns over and above the existing Fostair device currently on the formulary.
- **Clinical effectiveness** – Fostair NEXThaler has been shown to be non-inferior to Fostair pMDI. The combination beclometasone and formoterol is included in the current BNSSG Asthma guidelines. The device has been shown to be more acceptable to patients.
- **Cost effectiveness or resource impact** – It is the cheapest ICS/LABA combination inhaler and therefore prescribing the NEXThaler would result in some savings.
- **Strength of evidence** – Non-inferiority studies with the objective of demonstrating comparability of NEXThaler and the pMDI. Relatively small, short term studies.
- **Place in therapy relative to available treatments** – Would be appropriate within our existing Asthma guidelines where Fostair pMDI is currently listed – Step 3. The device is
particularly useful for a lot of patients but not all. It can be used in patients who have a respiratory rate as low as 35L/min.

- **National guidance and priorities** – None relating to the device itself.

- **Local health priorities** – Long term conditions.

- **Equity of access** – Inhalers are very patient specific and therefore no one device will be suitable for all.

The JFG considered the application and information submitted. Fostair pMDI is on the formulary already, the only difference is the device. Non-inferiority has been shown and it appears that the NEXThaler device offers a number of advantages for patients e.g. Patients can’t ‘test’ or waste doses; doses are not wasted or accumulated, which avoids accidental double dosing by the patient; Helps patients to track their intake; and useful to monitor patient adherence with treatment. The JFG agreed for Fostair NEXThaler to be included on the formulary due to its equivalent or lower acquisition cost compared to the other ICS/LABA combination inhalers, TLS green. The BNSSG Asthma guidelines will need to be updated to accommodate this.

**Action:**

1. **NB** to inform applicant

2. **JG** to communicate to prescribers and update the asthma guidelines.

3. **NB** to add to the formulary, TLS Green.

### 4.3 Insulin Degludec – Patients with type II diabetes on haemodialysis. *KM, Lead renal diabetes clinical nurse specialist, NBT.*

The applicant was not available to attend the meeting to present the application. NB presented a brief summary of the application.

Insulin Degludec is a long acting insulin analogue which is available in two different strengths 100units per ml and 200units per ml. The 100units per ml product was agreed for inclusion onto the formulary over a year ago for patients who are unsuitable for insulin pump therapy and is TLS red.

Currently, there are patients with type II diabetes who are on haemodialysis – of the 172 patients that the Richard Bright Dialysis unit treats, 143 of these have type II diabetes although not all are treated with insulin. Currently pre-dialysis Lantus (insulin glargine) is used in a small number of patients who for clinical or social reasons are unable to manage subcutaneous insulin at home. The Lantus is individually prescribed and administered pre dialysis three days per week. The dose varies between 40 unit per dialysis session up to 280 units per session. In addition there are some patients who are on sc insulin bd which is administered by district nurses in their own home and are failing on this regime. These could potentially be switched to Degludec as this is a once a day dosing which would reduce nursing costs.

There was some uncertainty of the exact patient cohort that would be prescribed the deguldec – is this all patients who require pre-dialysis insulin? The directorate need to be happy with the application from a safety aspect as well as an increase in costs. The 200 units per ml is double the strength of the standard insulin although the pen is designed so that the number of units are dialled on the device therefore ensuring that even if the wrong strength pen is selected, the same number of units will be administered. There is an additional cost of £2.03 for every 100units of
Degludec used compared to Lantus. However the number of patients expected to be treated in this manner is very small – up to 5 patients per year.

- **Patient Safety** – Currently on the formulary for those patients in whom an insulin pump is being considered. No additional safety concerns in this cohort of patients and indication.

- **Clinical effectiveness** – The department and Specialists have experience of analogue insulin in this patient cohort although neither Degludec nor Lantus have any good evidence for their use.

- **Cost effectiveness or resource impact** – This is the main impact. An additional £2.03 per 100 units is needed to prescribe Degludec over Lantus. Lantus will require more injections to deliver the same volume. The number of patients is very small and therefore this additional cost is not significant.

- **Strength of evidence** – No RCTs, just based on local experience and local audit.

- **Place in therapy relative to available treatments** – Would only be used in those patients on pre dialysis insulin and therefore only prescribed by the renal unit. This is a significant point as the risk of having two strengths of insulin needs to be considered.

- **National guidance and priorities** – No national policies.

- **Local health priorities** – Not listed.

- **Equity of access** – Would be appropriate for some patients to reduce the number of injections.

The JFG discussed the information and evidence submitted with the application. There appears to be a reasonable rationale for using Degludec in a small number of patients who require large units of insulin pre-dialysis and by using Degludec would reduce the volume of insulin required. There is no evidence to support this use but it is supported by years of local knowledge. This is specialist prescribing and would therefore remain TLS Red. The directorate would need to support the application.

**Action:**

1. **NB** to inform applicant

2. **MP** to discuss with the renal directorate

3. **NB** to include on the formulary, TLS Red.

**4.4 Dymista (Fluticasone and azelastine)** – Moderate to severe seasonal and perennial allergic rhinitis who are referred to secondary care. **Dr MG, Consultant Immunologist, NBT**

No one was available to attend the meeting to present the application however the immunology specialist pharmacist had sent comments prior to the meeting. NB gave a brief summary of the application. Please see application form for full details

This is the first combination steroid and antihistamine nasal spray licensed for the treatment of
moderate to severe seasonal and perennial allergic rhinitis. The applicant has only requested to use it in those patients referred to secondary care and also in those patients prior to desensitisation therapy which would more expensive.

The cost has recently reduced from £18.91 to £14.80. The SMC recently re-considered a submission from the company and accepted it for use in Scotland provided that it was supplied as part of the Patient Access Scheme or a list price that is equivalent or lower.

JB commented that they see some patients in primary care who have severe nasal symptoms for which the usual repertoire of drugs have been used but the patient is still symptomatic in which Dymista may have a benefit.

It is a once a day combination product which will help patient adherence.

There was discussion as to the potential size of the cohort if this were to be included on the formulary. As the application stands, this would only be for a small number of patients seen in secondary care for whom desensitisation would be the next step. However this could be increased and we are currently unaware of the thoughts of the ENT specialists in the region. A further application from these would be required if they wanted to prescribe it in their patients.

- **Patient Safety** – adverse effects in trials include headache, bitter taste, epistaxis and nasal discomfort. As the product contains benzalkonium it may have a drying and irritant effect however other nasal sprays include this and therefore is not unique to Dymista.

- **Clinical effectiveness** – Intranasal antihistamines have been shown to be superior to oral antihistamines for rhinitis but less effective for associated symptoms in the eye, pharynx, lower airways or skin. Trials have investigated the efficacy of Dymista comparing with similar doses of other available formulations of existing nasal sprays or placebo. Trials in patients with moderate to severe rhinitis (involving 3398 patients) showed that Dymista is more effective (in terms of patient-rated nasal symptom scores) than either of the component drugs used alone. Using a combined product is moderately more effective than either of the two component drugs alone.

- **Cost effectiveness or resource impact** – We have recently been informed that the list price has dropped from £18.91 to £14.81 making it a more cost effective option. SMC originally rejected it for use in Scotland due to its high cost but accepted it once a PAS was available. It is still however more expensive than the current pharmacological options of oral/intranasal antihistamine, intranasal steroids and antihistamine eye drops. It would be more cost effective than de-sensitisation which is the following step in the treatment pathway.

- **Strength of evidence** – Large RCTs. No trials have compared azelastine/fluticasone with nasal steroid plus oral antihistamine, the most widely used treatment for rhinitis.

- **Place in therapy relative to available treatments** – Due to its moderate effect on symptoms, and increase in cost, this should not be a first line option. It should only be used in those patients who have moderate to severe symptoms which have not responded to single agent products (antihistamine/steroid) or where these are not tolerated/inappropriate. It should be reserved for patients who otherwise would be offered desensitisation.

- **National guidance and priorities** – None applicable.

- **Local health priorities** – Not listed as a local priority.

- **Equity of access** – SMC have accepted it for use in Scotland. Other local formularies list
as non-formulary and formulary classifications.

The JFG considered the application and evidence submitted. There is evidence to suggest that the combination product is more effective than the single agents alone. Being a combination product it will help to improve adherence. It is however more expensive than the other available agents. Dymista should only be used in those patients who have moderate to severe symptoms who have not experienced relief with the first line options and in those patients in whom de-sensitisation would be considered, TLS amber (no shared care, specialist recommendation).

**Action:**

1. **NB** to inform applicant

2. **NB** to add to the formulary TLS amber (no shared care, specialist recommendation)

### 4.5 Melatonin – For patients at high risk of delirium in intensive care. *Dr MT, Consultant Intensivist, NBT*

The JFG originally discussed the application in July 2014 and the applicant was not able to attend the meeting. The outcome of the discussions at that meeting were:

‘The JFG considered the application and the evidence submitted. It was not possible to fully ascertain exactly which patients would be prescribed melatonin in ICU. There is no evidence to suggest that this is an effective treatment, although there is theoretical potential. The use of melatonin in this cohort appears to be more experimental at this stage. The JFG acknowledged that it was unlikely that a large RCT would be undertaken in this particular cohort, and therefore it may be that local research/audit may be required. At this current time, the JFG was not able to make a definitive decision and therefore the decision will be deferred until next meeting when the information can be obtained and the applicant can attend the meeting.’

Dr MT attended the meeting and explained that they have taken on board the JFG’s initial comments. Currently at NBT, they are using melatonin to reset the sleep-wake cycle with the hope that this will reduce the occurrence of delirium. This is currently one of the main concerns in ICU, and approximately 3 out 4 patients suffer with an element of delirium which will impact on morbidity. Using melatonin would be part of a package of care designed to reduce the risk of delirium, and there is well documented evidence of melatonin and its effects on the sleep wake cycle. Other drugs that are used, e.g. benzodiazepines and ‘Z’ drugs do not promote good sleep whereas as melatonin is endogenous this should not be the case.

The unit are hoping to target those patients who are at highest risk from delirium e.g. Neurotrauma patients, those that have had a prolonged stay on ICU, those with sepsis and the elderly. It would not be a first line choice, and basic interventions such as regulating light and noise would be used first. The melatonin would be complimentary to these measures.

The group asked about when the melatonin is likely to be stopped and it was suggested that a duration of treatment would be 2 weeks, but it should be discontinued when the whole package of care is stopped and this is likely when the patient is discharged to the general wards.

Anecdotally, patients have been given all of the usual interventions to promote the normal sleep wake cycle with no effect and it has only been when melatonin has been introduced that this has worked. There are bits of evidence available, some showing improvement in sleep, some reducing delirium in the elderly but none specifically looking at this particular cohort or indication.

The 2mg dose was questioned. The available research considered 2 or 3mg doses, and the pilot study in Sheffield used 2 or 10mg. The 10mg dose caused somnolence in the daytime and
therefore 2mg has been chosen. Sheffield have melatonin on their formulary for this indication.

The NICE guidance on prevention of delirium in ICU discussed different packages of care available and stated that non-pharmacological interventions were the most evidence based. This would be true for the majority of general ICUs however it is particularly the cohort of patients that NBT treat that would find the most benefit from melatonin. NBT is the regional neurotrauma hospital and therefore the ICU may need additional options that others do not require.

- **Patient safety** – Melatonin is generally accepted as safe and no adverse effects were reported in the studies reviewed in the evidence appraisal. Safety data underpinning the licence indicate that there are no serious adverse effects associated with use of melatonin at its licensed dose. However, the effect of any stage of renal insufficiency on melatonin pharmacokinetics has not been studied and there is no experience of the use of melatonin in patients with liver impairment or in patients with auto-immune disease.

- **Clinical effectiveness** – There is no good quality evidence that compared the effectiveness of melatonin with any other intervention designed to prevent delirium. There is limited evidence for effectiveness of melatonin (or melatonin agonist) in the prevention of delirium but these studies are limited in their generalisability to an ICU population as they have predominantly been conducted in the elderly not within an ICU setting. There is tentative evidence for the effectiveness of melatonin to increase sleep duration in an ICU setting; however significant study limitations make these findings highly uncertain. It is recognised however that the evidence behind some common practice ICU interventions generally lacks e.g. patients are ventilated at an angle of 30° however there is no evidence to base this on.

- **Cost effectiveness or resource impact** – This would not present a significant cost pressure if this were to be included on the formulary – suggested £2,790 per year for approx. 300 patients. There is no data that examines the cost effectiveness of this intervention. Delirium and sleep disturbances are recognised as significant management complications in the ICU setting, and therefore any intervention that improves the management of these could have a significant impact on ICU length of stay.

- **Strength of evidence** – The studies which considered melatonin in the prevention of delirium are limited in their generalisability as they were not conducted in the ICU setting and nearly all carried methodological flaws.

- **Place in therapy relative to available treatments** – There is no other pharmacological treatment that would be used in the prophylaxis of delirium in ICU. Sleep disturbances may be treated with benzodiazepines and zopiclone. Melatonin would be used as a preventative measure along with a bundle of non-pharmacological interventions.

- **National guidance and priorities** – None found that related to melatonin. NICE guidance (2010) for the general prevention of delirium recommends non-pharmacological interventions.

- **Local health priorities** – not listed as a local priority.

- **Equity of access** – It is currently being prescribed in the ICU as non-formulary. Other areas are believed to be using it in this manner, although we have not been able to identify a particular area to discuss this with.

The JFG considered the application and evidence submitted. The lack of evidence to support melatonin in this particular patient cohort and indication was acknowledged. However it is also acknowledged that there is a lack of evidence to support some common ICU interventions and that it is unlikely that a well-designed large RCT will be conducted to
investigate melatonin in this cohort of patients. It has been demonstrated that the cohort of patients being treated at the NBT ICU are different to a general ICU and therefore more unique treatments and interventions maybe required. Delirium can have significant effects on ICU patients, increasing length of stay and morbidity. Melatonin is a relatively safe intervention as part of a package of interventions that may reduce delirium in ICU patients. The JFG have approved the inclusion of melatonin for the prevention of delirium in ICU patients, TLS Red. The JFG have asked for a treatment protocol and to report back the results of the intervention within a year.

Action:

1. NB to inform applicant
2. NB to ask for a treatment protocol
3. NB to add to the formulary TLS red

5 Shared Care Protocols/TLS status

5.1 Denosumab (Review of existing SCP in view of MHRA guidance)

The current SCP had been reviewed and updated by in view of the recent MHRA guidance which now suggests

The MHRA had issued advice in the Drug Safety Update (Sept 2014) re: Denosumab and minimising the risk of osteonecrosis of the jaw and monitoring for hypocalcaemia. It now recommends:

- Denosumab 60 mg (osteoporosis indication)

Check for ONJ risk factors before starting denosumab 60 mg. A dental examination and appropriate preventive dentistry are now recommended for patients with risk factors.

And,

- Denosumab 60 mg (osteoporosis indication)

Check calcium levels:

- before each dose
- within two weeks after the initial dose in patients with risk factors for hypocalcaemia (e.g., severe renal impairment, creatinine clearance <30 ml/min)
- if suspected symptoms of hypocalcaemia occur.

NB has been in contact with Dr SC regarding the BNSSG SCP and the SPC changes. The local Rheumatologists feel that the MHRA and SPC recommendations would amount to a significant number of patients who need to be referred to a dentist prior to initiating treatment initiated which would cause significant pressure on local dentists. The company have been contacted to find the actual number of patients who have suffered ONJ.

The data around ONJ is sparse and the Rheumatologists looked at the numbers and translated into approximate risks that may be helpful for the treating GP in discussing with a patient. The following wording was suggested for inclusion…

'Osteonecrosis of the jaw (ONJ) is a rare side effect of treatment to reduce risk of osteoporotic
fracture. The overall risk of a patient developing osteonecrosis of the jaw over a typical 3 year treatment cycle is about 1 in 800. Patients who undergo invasive dental procedures (dental implants, tooth extraction, natural tooth loss, scaling or root planning) during that time have a higher risk of developing ONJ (1 in 350 over 3 years), compared to those who do not (1 in 3400 over 3 years).

Patients should be advised to maintain good oral hygiene under these circumstances and inform their dental practitioner of their treatment. Denosumab should be discontinued if any features of osteonecrosis of the jaw develop and the treating rheumatologist contacted, who will liaise with secondary dental care.’

It was also noted in the responsibility section for secondary care that patients should be ‘considered’ for referral to a dentist prior to initiation.

However, the group were not comfortable that the SCP would not be reflecting the MHRA guidance and suggested that this was included in the SCP i.e. that all patients in the at risk group should be referred to a dentist prior to treatment.

Action:

1. NB/KG to discuss with Dr SC
2. NB to bring back to a future JFG for sign off

Individual Funding Requests

SB has obtained the IFRs for BNSSG CCGs via PF (IFR team). A brief review of this has not identified any common themes that require a NDR application to the JFG.

Action:

1. SB/NB to progress IFR monitoring

Chapter review and formulary process

NB stated that further progress on the chapter review has not been made since the last meeting. When NBs job share is in post it is hoped that this will be progressed as a priority.

Items for Discussion

NDRs for January Meeting

Currently the NDRs for discussion at the January meeting are:

1. Umeclidinium for the maintenance of COPD.
2. Olodaterol (Striverdi) for the maintenance of COPD – APPEAL
3. Tacrolimus mouthwash for patients with erosive autoimmune oral mucosal disease.
4. Tocilizumab – Treatment of Rheumatoid arthritis in accordance with NICE TA 247 however via SC route not IV.

Durophat toothpaste
It has been brought to our attention that some GPs are being asked to prescribe this high fluoride toothpaste under the advice of the Dental Hospital. The JFG consider that whilst it may be appropriate that the toothpaste is prescribed for certain patients the patient’s GP is not the most appropriate clinician to prescribe this and it should be dental prescribing only.

Action:

1. **NB** to clarify on the formulary that Durophat should only be prescribed by dentists.

9 AOB

None

**NB**

Interface Pharmacist

1st December 2014
## BNSSG JFG

### Action Log for 25th November 2014

<table>
<thead>
<tr>
<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
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<td>Confirm current practice in NBT</td>
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<td>SB/NB</td>
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## MEETING DATES 2015

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<td>9am – 12 midday</td>
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<td>13th October</td>
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Minutes

Present:

- Interface Pharmacist, NHS Bristol CCG
- Interface Pharmacist, NHS Bristol CCG
- Deputy HoMM, NHS Bristol CCG
- Deputy HoMM, NHS North Somerset CCG
- Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust
- Pharmacist, North Bristol NHS Trust
- Public Health Consultant, Bristol City Council (Chair)
- Clinical Effectiveness Research Lead, Bristol City Council
- Consultant Neurologist and NBT D&TC representative
- Deputy Chief Pharmacist Weston General Hospital
- Head of Medicines Management, South Gloucestershire CCG
- GP, North Somerset

Apologies:

- GP, Bristol and member of Bristol CCG board
- Joint D&TC Chair, North Bristol NHS Trust
- Chief Pharmacist, AWP
- Director of Pharmacy Weston Area Health NHS Trust
- HoMM, North Somerset CCG
- Principal Pharmacist, University Hospitals Bristol NHS Foundation Trust
- Consultant Renal Physician, and Joint D&TC Chair, North Bristol NHS Trust
- GP, Bristol

1  Welcome, Apologies and Declaration of Interests

Declarations of Interest
None

2  Minutes of the meeting of 25th November 2014 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 25th November 2014 had been
circulated by NB following the meeting. No comments had been received that needed further
discussion. A statement on page 2 of the minutes needs to be corrected relating to the
commissioning of NBT – it currently states that NBT is currently co-commissioned by South
Gloucestershire and Bristol, however it should read that NBT is commissioned by South
Gloucestershire only.

Matters arising from November 2014 meeting

2.1 Botox for urinary incontinence

CD requested further information as to the situation regarding Botox for urinary. SB assured the
group that she had been asked to submit an initiative template to be put forward for prioritisation
in the annual contract round. MP also confirmed that it had been raised within NBT finance and
included within their intentions/ proposal of practice for 2015/2016. South Gloucestershire and
North Somerset CCGs need to ensure that they have also done the same. SB has shared the
form. We expect that by the beginning of the end of Feb/early March that we will know more.

Action:

1. NB/SB to ensure the group is kept up to date
2. MG to ensure it is included in the commissioning intentions for S.Glos
3. DC/JT to ensure that it is included in the commissioning intentions for N.Somerset

3 NICE New Technology Appraisals

Published

3.1 Erythropoiesis-stimulating agents (epoetin and darbepoetin) for treating
anaemia in people with cancer having chemotherapy. TA323 TLS Red

3.2 Nalmefene for reducing alcohol consumption in people with alcohol
dependence. TA325

There has been significant discussion nationally and locally about the use of Nalmefene. We
have been in discussion with public health in Bristol about how we will implement the TA. There
is concern that GPs will not have the clinical confidence to initiate treatment in the right patients
and also not be able to provide the psychological support that is required. We need a
coordinated approach across the 3 CCGs in conjunction with public health. We have been in
contact with Dr Kate Rush regarding the implementation and it is felt within Bristol that treatment
should be through the Bristol Drugs Project, ROADS (Recovery orientated Alcohol & Drugs
service). Their opinion currently is that amber would be the most appropriate listing, enabling the
right patients to be initiated however the GP could take on the prescription later. South Glos and
North Somerset also have drugs projects and therefore we need to involve these. We need to
ensure that we have the infrastructure in place in order to be able to deliver the treatment safely
and effectively. We should be including nalmefene on the formulary by the end of February,
however, NICE have recognised that many CCGs will have issues that will delay the
implementation of the NICE TA. We need to liaise with Dr TW at AWP and also public health. It
was the opinion of the JFG that at this stage that nalmefene should be TLS Red. Further work is
required.

3.3 Imatinib for the adjuvant treatment of gastrointestinal stromal tumours
(review of NICE technology appraisal guidance 196). TA326 TLS Red

3.4 Dabigatran etexilate for the treatment and secondary prevention of deep
vein thrombosis and/or pulmonary embolism. TA327 TLS amber 1 month
for those newly diagnosed patients and TLS blue for those patients already
diagnosed with a DVT/PE. A SCP will need to be developed.

Adopted into the BNSSG Joint Formulary – November and December 2014

Dimethyl fumarate for treating relapsing-remitting multiple sclerosis. TA320 TLS Red

Lenalidomide for treating myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality. TA322 TLS Red

4 New Drug Requests (NDRs)

SUMMARY

4.1 Umeclidinium (Incruse Ellipta) – COPD maintenance.
Agreed for inclusion onto the BNSSG formulary. The formulary includes the other Ellipta devices – Relvar (fluticasone and vilanterol) and also Anoro (Umeclidinium) and therefore with the addition of Incruse this would ensure that all the complement of medication choices for COPD are available in the Ellipta device. The ellipta device has been shown to be a popular device amongst COPD patients. TLS green.

4.2 Olodaterol (Striverdi) – COPD maintenance.
Agreed for inclusion onto the BNSSG formulary. The SMC reviewed the submission and accepted it for use within Scotland. The device is useful for frail, elderly patients as it is relatively easy to use. It is expected that the combination tiotropium and olodaterol will be available in the summer and it is expected that this will be a useful combination. TLS Green.

4.3 Beclometasone and formoterol (Fostair pMDI) – COPD maintenance.
Agreed for inclusion onto the BNSSG formulary. Fostair has been available for a number of years, however in May 2014 a licence extension was granted to include maintenance of COPD. More local experience is required to establish its place in therapy, however it should be acknowledged that it has a lower acquisition cost compared to seretide. TLS Green.

4.4 Tiotropium Respimat – Asthma.
Agreed for inclusion onto the BNSSG formulary. It has been licensed and used for a significant number of years in the treatment of COPD and although not been licensed in asthma. The trials have shown that tiotropium is a useful addition to the asthma medication in those severe patients that aren’t controlled at step 4 of the asthma pathway. Locally it has been prescribed in asthmatic patients off formulary. A clear management plan needs to be included so that GPs can take over the care of patients. TLS amber (specialist recommendation, no SCP).

4.5 Tacrolimus Mouthwash – Patients with erosive autoimmune oral mucosal disease.
Rejected for inclusion onto the BNSSG formulary due to a lack of evidence. It was acknowledged that a lack of evidence was not unexpected, however it was not sufficient to include on the formulary. No clear information could be given as to the procurement/manufacture of the mouthwash. The use of tacrolimus mouthwash should be managed within the trust.

4.6 Cyclogest pessary – Recurrent miscarriage, during infertility treatment, and threatened preterm labour.
Agreed for inclusion onto the BNSSG formulary for during infertility treatment and threatened
preterm labour but delayed decision for recurrent miscarriage. Evidence and national guidance recommends cyclogest pessaries for recurrent miscarriage and during infertility treatment. A large trial is due to report in March in respect of recurrent miscarriage and therefore the JFG agreed to await these results before making a decision. TLS Red.

**Decision Criteria used by JFG for NDR**

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

**Full Discussion**

General discussion with Dr JC

There has been a change in the emphasis of COPD management which is reflected in the GOLD guidelines. Too many COPD patients are being treated with inhaled steroids which we know increases the risk of pneumonia by an annual risk of 6%. 1 in 5 COPD patients should be on an inhaled steroid and actually about 60% of patients are. For this reason, more Long acting bronchodilators should be being used earlier in the treatment pathway. The inhaler device is becoming increasingly more and more important for COPD patients. During 2015, we should be able to restrict the formulary in order to provide guidance and reassurance to GPs. However at this current time, we are still improving local experience in order to develop this pathway.

4.1 Umeclidinium (Incruse Ellipta) – COPD maintenance. **Dr James Calvert, Respiratory Consultant, NBT**

Please see application form for full details. Dr JC and LM (specialist respiratory pharmacist) attended the meeting to present the application.

Incruse is manufactured by GSK, and is delivered via the Ellipta device. Anoro (umeclidinium and vilanterol) and Relvar (Fluticasone and vilanterol) are also delivered by the Ellipta device, both of which are already included on the formulary. It would be beneficial to be able to offer umeclidinium on the formulary so that all the treatment options are available in this device, providing patients with familiarity. Umeclidinium is a long acting antimuscarinic inhaler (LAMA). It is important to be able to provide the least number of inhalations as possible and therefore combination and once daily medications are preferred. This is a once a day preparation. The Ellipta device is popular amongst patients. However, an inspiratory flow rate of at least 40L/min is needed to be able to operate the device; this is the same for all DPIs.

The side effects relate to the antimuscarinic effects such as dry mouth which again is similar to tiotropium.

The evidence has not shown a reduction in exacerbations, but a reduction in symptoms. No head to head trials against another LAMA are available.

The current COPD NICE guidelines are out of date and not due to be updated until 2018. Therefore the most up to date guidelines are the GOLD guidelines.
• **Patient safety** – The studies conducted have shown that umeclidinium to be well tolerated. The CHMP concluded that the overall safety profile of umeclidinium was consistent with that of other LAMAs and the comorbidities commonly present in patients with COPD. However, they also stated that, although umeclidinium belongs to a well-established and known class of molecules, it is a new active substance and safety data from this class may not be necessarily applicable.

• **Clinical effectiveness** – Two well conducted, phase III, randomised controlled studies demonstrated that after 12 and 24 weeks of treatment, umeclidinium significantly improved lung function, with a reported improvement in symptomatic outcomes, compared with placebo in patients with moderate to severe COPD. No head to head trials against other LAMAs are available.

• **Cost effectiveness or resource impact** – Umeclidinium is competitively priced, being equal to glycopyrronium and less than both aclidinium and tiotropium. For this reason, an increase in drug costs is not likely to be seen.

• **Strength of evidence** – Two well conducted phase III randomised controlled studies. The European Medicines Agency (EMA) recommends that lung function parameters alone are insufficient to assess therapeutic effect. Additional evidence of efficacy must be demonstrated via secondary endpoints which should be symptom based. There is no direct comparative evidence of umeclidinium with other LAMAs.

• **Place in therapy relative to available treatments** – Umeclidinium is the fourth LAMA marketed in the UK for treatment of COPD; it is anticipated that it will be used as an alternative to other available LAMAs, tiotropium, aclidinium and glycopyrronium.

• **National guidance and priorities** – COPD itself is a national priority. It is an expensive area of practice.

• **Local health priorities** – Long term conditions.

• **Equity of access** – Patients should be able to have access to this treatment via the Ellipta device as the other devices are included on the formulary and will improve familiarity with the device.

The JFG considered the application and the evidence submitted. The JFG agreed that there was sufficient evidence to include Umeclidinium on the formulary and that the device itself was recognised by patients and clinicians as a relatively easy device to use. Whilst there is a lack of direct comparison data, the indirect treatment comparisons have shown that umeclidinium is as efficacious in COPD patients compared to tiotropium, glycopyrronium and aclidinium. TLS green.

**Action:**

1. **NB** to inform applicant.
2. **NB** to include on the formulary, TLS green

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4.2 **Olopatadine (Striverdi)** – COPD maintenance. Dr JC, Respiratory Consultant, NBT.
Please see application form for full details. Dr JC and LM (specialist respiratory pharmacist) attended the meeting to present the application.

Olodaterol (a long acting beta agonist LABA) is manufactured in the same device as tiotropium, the respimat. The MHRA in November 2010 reported safety concerns regarding tiotropium respimat: the respimat was associated with a non-significant increase in all-cause mortality compared with placebo. However, since this report, a large RCT has demonstrated that the tiotropium via the respimat device is as safe as the handihaler.

The original application was rejected in October 2014: ‘The JFG considered the application and evidence submitted. The JFG was unable to approve the inclusion of olodaterol to the BNSSG formulary due to a lack of comparative efficacy data against other LABAs. There are also no other unique factors supporting olodaterol over existing formulary LABAs.’ The JFG received a letter of appeal following the decision. It was agreed to re-consider the application based on that there would be new information available as the SMC was due to offer new advice. Their advice published in January stated that:

‘ADVICE: following a re-submission Olodaterol (Striverdi® Respimat®) is accepted for use within NHS Scotland. Indication under review: maintenance bronchodilator treatment in patients with chronic obstructive pulmonary disease.

In two 48-week studies there was no significant difference between olodaterol 5 microgram and another long acting beta2 agonist for the primary endpoints of trough forced expiratory volume in 1 second (FEV1) and FEV1 area under curve (0 to 3 hours) at week 24.’

A combination of tiotropium and olodaterol via the respimat is nearing completion for licensing and it is expected to be available during the summer 2015. This inhaler is likely to be an interesting combination for COPD patients and it is potentially more efficacious than Anoro. It would therefore be useful to have olodaterol available on the formulary if LABA monotherapy is required. It is suggested that a LAMA is more effective than a LABA however a LABA would be more appropriate for cardiac patients.

Trials do not suggest that olodaterol is superior to any other LABA, however, it is clear that the device type is a significant factor in choosing therapy in individual patients. As the evidence doesn’t identify one LABA as the most effective, it is also important to consider the cost of the inhalers.

The benefits of the Striverdi respimat is that it is an easy device to use, and does not require a certain level of inspiratory flow to operate. Therefore this would be especially useful for frail, elderly patients. It is also a once a day preparation – as indacaterol is. Formoterol and salmeterol are twice daily preparations.

- **Patient Safety** – Overall, across all treatment groups, the most common on-treatment SAE were COPD exacerbation (5.8%) and pneumonia (1.8%) and these occurred in 4.7% and 1.6% of patients on olodaterol 5 microgram (versus 5.9% and 1.5% of patients on formoterol).

- **Clinical effectiveness** – In two 48-week studies there was no significant difference between olodaterol 5 microgram and another long acting beta2 agonist for the primary endpoints of trough forced expiratory volume in 1 second (FEV1) and FEV1 area under curve (0 to 3 hours) at week 24.

- **Cost effectiveness or resource impact** – Olodaterol (Striverdi) has a lower acquisition cost compared to salmeterol and indacaterol however is more expensive than formoterol.
• **Strength of evidence** – Good quality trials, two of which assessing efficacy versus formoterol.

• **Place in therapy relative to available treatments** – NICE guidance recommends the use of LABA monotherapy as a treatment option for patients with stable COPD who have FEV1 > 50% predicted and who remain breathless or have exacerbations despite use of SABAs as required. In more severe COPD, inhaled corticosteroids, LAMA or both can be added to LABA therapy. When an inhaled corticosteroid is added to a LABA, a combination inhaler is recommended.

• **National guidance and priorities** – As above.

• **Local health priorities** – COPD remains a priority locally.

• **Equity of access** – Most areas have not approved the use of Olodaterol yet. This is mainly due to either that areas have not reviewed the device yet, or that they have not updated their advice since SMC have re-published. The Greater Manchester Medicines Management group approved the use in November 2014.

The JFG considered the application and information submitted. Whilst there is no evidence to suggest that Olodaterol is superior to other LABAs, the device type is an important factor in COPD patients’ therapy. It has been shown to be equivalent to the other LABAs and that LABA monotherapy is indicated in patients with stable COPD who have FEV1 _50% predicted and who remain breathless or have exacerbations despite use of SABAs as required. It is expected that the combination of tiotropium/olodaterol via the respimat device will be a useful device when it becomes available in summer 2015. Olodaterol is also competitively priced. It was therefore agreed for inclusion onto the formulary, TLS Green. The COPD pathway and preferred inhalers will be reviewed during 2015 to improve clarity.

**Action:**

1. **NB** to inform applicant

2. **NB** to add to the formulary, TLS Green.

4.3 **Beclometasone and formoterol (Fostair pMDI)** – COPD maintenance. *Dr JC, Respiratory Consultant, NBT.*

Please see application form for full details. Dr JC and LM (specialist respiratory pharmacist) attended the meeting to present the application.

The Fostair pMDI device contains fine particle beclometasone (more potent than beclometasone in other preparations) and formoterol. It has been licenced and available for prescribing in asthma since 2007. In April 2014, a licence extension was agreed for the treatment of COPD in those with severe disease, with a history of exacerbations who have significant symptoms despite regular therapy with long acting bronchodilators. Evidence has not shown that fostair pMDI is superior to other ICS/LABA combinations, however this will be the only pMDI ICS/LABA combination licensed for COPD. Seretide evohaler is currently used off licence.

From the published data, beclometasone/formoterol appears to work as well in COPD as the 2 commonly used ICS/LABA combinations, its constituent ingredients have been available for many years so their safety profile is known, it costs less than most alternatives and it can be used with a
Following an abbreviated submission the SMC accepted Fostair® 100/6 μg for use within NHS Scotland.

- **Patient Safety** – The studies conducted have not identified that Fostair has significantly more side effects associated with its use.

- **Clinical effectiveness** – From the published data, beclometasone/formoterol appears to work as well in COPD as the 2 commonly used ICS/LABA combinations, its constituent ingredients have been available for many years so their safety profile is known, it costs less than most alternatives and it can be used with a spacer, which many people with COPD need.

- **Cost effectiveness or resource impact** – Apart from Relvar, Fostair pMDI has the lowest acquisition cost and therefore has the potential to reduce drug costs.

- **Strength of evidence** – Two RCTs comparing seretide and symbicort.

- **Place in therapy relative to available treatments** – Is licensed for severe COPD in those who are still exacerbating despite regular long acting bronchodilator therapy.

- **National guidance and priorities** – In people with stable COPD who remain breathless or have exacerbations despite use of short-acting bronchodilators as required, offer the following as maintenance therapy:

  If FEV1 ≥ 50% predicted: either long-acting beta2 agonist (LABA) or long-acting muscarinic antagonist (LAMA) if FEV1 < 50% predicted: either LABA with an inhaled corticosteroid (ICS) in a combination inhaler, or LAMA.

  Offer LAMA in addition to LABA+ICS to people with COPD who remain breathless or have exacerbations despite taking LABA+ICS, irrespective of their FEV1.

- **Local health priorities** – COPD remains a local health priority.

- **Equity of access** – Other areas have included Fostair pMDI on their formularies for COPD.

The JFG discussed the information and evidence submitted with the application. The ICS/LABA combination is an important step in the COPD management pathway. Currently, seretide evohaler is being prescribed off licence. The evidence has shown Fostair to be as beneficial compared to both seretide and symbicort. It is the only licensed pMDI for COPD and useful if a patient requires a spacer device. It was agreed to include on the formulary, TLS green. It is necessary to review those patients on seretide 250 evohaler to see whether it would be appropriate to switch to fostair pMDI.

**Action:**

1. **NB to inform applicant**

2. **NB to include on the formulary, TLS Green.**

**4.4 Tiotropium Respimat** – Asthma. *Dr JC and Dr MP, Respiratory Consultants, NBT.*
Tiotropium has been used off licence in asthmatic patients for a number of years although this has been off licence use. This was on the back on the evidence in 2012 that showed that it was a useful treatment in difficult to control asthmatics. It has taken a while for the licensing to be approved; this is probably due to the company focussing on the data to provide evidence that the tiotropium respimat device was safe. This was subsequent to the MHRA identifying that the respimat could be linked to an increase risk in cardiovascular death, myocardial infarction or stroke. The company conducted further trials to show that the overall incidence of adverse effects were not significantly higher with the use of tiotropium respimat.

Two publications in the New England Journal of Medicine published in 2010 and 2012 showed that tiotropium when added to an inhaled glucocorticoid improved asthmatic symptoms and lung function. Tiotropium also reduced severe exacerbations.

The decision to initiate tiotropium should be taken by the specialists. These patients will be at step 5 of the asthma pathway and therefore will be referred and being treated by secondary care. At this time, the patients’ management will be considered in depth.

- **Patient Safety** – The studies have shown that the overall incidence of adverse effects were not significantly higher with the use of tiotropium respimat.

- **Clinical effectiveness** – Tiotropium Respimat is effective in improving lung function, reduces the risk of exacerbations and was well tolerated in patients with symptomatic asthma inadequately controlled on ICS plus LABA.

- **Cost effectiveness or resource impact** – It is comparable to other asthmatic inhalers at this stage of the asthma pathway.

- **Strength of evidence** – Large RCTs.

- **Place in therapy relative to available treatments** – Will represent an alternative add on therapy at stage 4/5.

- **National guidance and priorities** – None applicable.

- **Local health priorities** – Asthma is a local priority.

- **Equity of access** – Other formularies include tiotropium on their formularies for asthma and some do not.

The JFG considered the application and evidence submitted. The evidence suggests that tiotropium is a useful addition to the management of asthmatics who are not controlled despite ICS and LABA treatment. It has been being used locally for a number of years off license and non-formulary. It was agreed for inclusion onto the formulary, TLS amber (no shared care, specialist recommendation). A clear individualised management plan should be in place to enable the GP to continue the treatment and continually assess the patient.

**Action:**

1. **NB** to inform applicant

2. **NB** to add to the formulary TLS amber (no shared care, specialist recommendation)
4.5 Tacrolimus Mouthwash – Patients with erosive autoimmune oral mucosal disease.

Dr KS, Consultant Oral Medicine and Dermatology, UHBristol

Please see application form for full details. Dr KS was not able to attend the meeting; however Dr LW attended to present the application.

The application was for the approval to use a tacrolimus mouthwash formulation rather than the ointment, or tacrolimus in orabase. There appears to be no good evidence for this in this patient cohort and a number of questions were raised regarding the procurement/manufacturer of the product. It appears that Newcastle pharmacy make the mouthwash although were unwilling to provide details. The tacrolimus in orabase has been in use for a number of years within UHB. The evidence available consists of a paper which includes a series of 8 patients.

Discussion with Dr LW

Dr LW explained that tacrolimus is commonly used in oral medicine and that this mouthwash is manufactured in Newcastle. They commonly use protopic – tacrolimus ointment. They are proposing the mouthwash formulation; there is less evidence, but the evidence that does exist suggests that it works well. The problem with the ointment is that it does not stick well to the oral area and that patients with extensive areas affected would prefer to use the mouthwash. This will be prescribed for patients in whom systemic steroids do not control the disease before oral tacrolimus is prescribed.

The Cochrane review for oral lichen planus (OLP) found no overwhelming evidence for the efficacy of a single treatment, including topical steroids.

There is a lot more data on the efficacy of tacrolimus ointment than tacrolimus mouthwash. The only published data following use of mouthwash comes from a series of 8 patients and 2 separate case reports. These showed that the mouthwash was effective. The concentration of tacrolimus mouthwash is lower compared to the ointment, and there is no systemic absorption. The primary end points were pain at all times, pain at meal times and the extent of the erosive lesions.

Most if not all patients relapse when treatment is stopped, and therefore it should be assumed that it is long term treatment.

The patient would use the mouthwash 4 times a day by holding it in the mouth for 2 minutes before spitting it out. This is similar to how patients use beclometasone as a mouthwash. They would be asking UHB Pharmacy to manufacture this. The costs of this are unknown and would need to be considered.

- **Patient safety** – Topical application appears to be safe with few adverse effects – these predominantly involve burning sensations. However we are not fully aware of the precise details of the formulation so this is difficult to assess. Being a mouthwash, there is the potential for accidental ingestion.

- **Clinical effectiveness** – There are far more data on the efficacy of tacrolimus ointment than the mouthwash. The only published data following use of the mouthwash comes from a series of 8 patients and 2 separate case reports. There is some limited evidence from a number of small studies of variable quality with short follow up to suggest that topical tacrolimus may be effective in controlling the extent of mucosal lesions and the related symptoms of OLP.

- **Cost effectiveness or resource impact** – This is difficult to assess without knowing the cost of the manufacture within the pharmacy department. The applicant suggests a cost of £37.13 in drug costs per year.

- **Strength of evidence** – No good quality data to support the use of tacrolimus
mouthwash. Long term data is lacking.

- **Place in therapy relative to available treatments** – It is suggested that topical tacrolimus would be used if systemic steroids fail to control the lesions. Currently, they are using tacrolimus ointment or tacrolimus in orabase, however as detailed above, there are occasions when a mouthwash would be more appropriate. The ointment and the orabase does not stick particularly well to the lesions and a mouthwash is useful for when there is extensive disease.

- **National guidance and priorities** – There is no evidence from national or professional guidelines.

- **Local health priorities** – Not listed as a local priority.

- **Equity of access** – Tacrolimus mouthwash 0.1% has been found in one formulary and tacrolimus 0.1% in orabase in another formulary.

The JFG considered the application and evidence submitted. It is recognised that the amount of evidence in this area is not expected to be high. The BNSSG formulary does not currently include any topical tacrolimus treatment though there is more evidence for the ointment. The JFG were unable to approve the use of unlicensed tacrolimus mouthwash to be included on the formulary as there was insufficient evidence in this patient cohort. This may be appropriate to follow up through the one-off non-formulary request route within UHB MAG.

**Action:**

1. **NB** to inform applicant
2. **HC/KG** to follow up through UHB MAG

**4.6 Cyclogest pessary** – Recurrent miscarriage, during infertility treatment, and threatened preterm labour. *Dr JC, NBT.*

No one was available to attend the meeting to present the application; however Victoria Wiggins, rotational pharmacist at NBT who completed the critical appraisal attended the meeting to give a brief overview. Please see application form for full details.

We are aware that cyclogest pessaries are currently being use in the three listed indications above within the trust, although non-formulary and unlicensed.

**Recurrent Miscarriage**

There is not a lot of evidence and is not recommended by any National guidelines. In the NICE guideline154 (Ectopic pregnancy and miscarriage: Diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage) a very large multicentre randomised controlled trial of women treated with either progesterone/progestogen or placebo should be conducted to look at the effects on miscarriage. The BNF denotes that Cyclogest is a preparation that is considered to be less suitable for prescribing. We are currently awaiting publication of the PROMISE trial, which is due to be in March of this year. This trial is testing the hypothesis that in women with unexplained recurrent miscarriages, progesterone (400mg pessaries, twice daily), started as soon as possible after a positive pregnancy test (at < 6 weeks gestation) and continued to 12 weeks of gestation, compared to placebo, increases live births beyond 24 completed weeks of pregnancy by at least 10%.
Whilst it appears that cylogest pessaries are used widely, currently there is no evidence to support this. As the PROMISE trial is due to report in March, it appears to be sensible to await these results before the JFG makes a final decision.

**Threatened pre-term labour**

There are no national recommendations, and again it is unlicensed for this use; however there is much stronger evidence and involving large numbers of patients. The studies involved dose ranges between 90 – 200mg per day in women with a cervix of < 20mm. It is current practice at NBT to use 400mg in those women with a cervix length of < 25mm. Therefore the dose would need to be clarified. There are trials and a meta-analysis which provide evidence that it is beneficial in patients at risk of pre-term labour.

**During IVF treatment**

NICE CG 156 (Fertility: Assessment and treatment for people with fertility problems) recommends that women should be offered progesterone for luteal phase support after IVF treatment. The pessaries are use in all major IVF units.

- **Patient safety** – As this treatment is a hormonal, topical formulation, little side effects are to be expected. The SPC (Actavis UK Ltd, 2012) states the following potential undesirable effects: Menstruation may occur earlier than expected, or, more rarely, menstruation may be delayed; Soreness, diarrhoea and flatulence may occur with rectal administration; as with other vaginal and rectal preparations, some leakage of the pessary base may occur.

- **Clinical effectiveness** – We are awaiting the results of the PROMISE trial to assess the efficacy of progesterone in recurrent miscarriage. There is good quality evidence to support the use of progesterone in threatened pre-term labour.

- **Cost effectiveness or resource impact** – 15, 400mg suppositories cost £12.96. It is suggested that 220 patients per year at NBT would be treated for threatened preterm labour and recurrent miscarriage, and all IVF cycles. Cyclogest is currently being used in these patients and therefore I would suggest that an increase in drug costs would not be seen.

- **Strength of evidence** – As above.

- **Place in therapy relative to available treatments** – Used in all patients who experience recurrent miscarriage, and those patients with a cervix length <25mm and in all IVF patients.

- **National guidance and priorities** – There is NICE guidance for the use of progesterone in IVF. No other national guidance could be found, though it is noted that it is part of standard care in most areas.

- **Local health priorities** – Not a local health priority.

- **Equity of access** – Part of standard care in most areas.

The JFG considered the application and evidence submitted. NICE guidance recommends progesterone in IVF therapy and therefore it should be included on the formulary for this indication, TLS Red. There is good evidence supporting the use of progesterone in threatened preterm labour and therefore it should be included on the formulary for this indication, TLS Red. A trial investigating the use of progesterone in recurrent miscarriage is due to be published, and as there aren’t other large RCTs available, the JFG agreed to await until this is published to make a decision for this indication.
**Action:**

1. **NB** to inform applicant

2. **NB** to include on the formulary, TLS Red for threatened preterm labour and IVF.

3. **NBT** to report back to the JFG with the PROMISE results once these are made available.

5  **Shared Care Protocols/TLS status**

5.1 **Eplerenone TLS Change request from amber 1 month to amber specialist recommendation, no shared care**

Eplerenone is currently amber 1 month. The proposal is for it to be amber (specialist recommendation, no SCP). This is to give the community heart failure nurses the confidence to initiate treatment if this has been recommended by a cardiologist. Eplerenone should be initiated in those MI patients who have evidence of heart failure and ejection fraction of <40%. It should be started within 3 – 14 days of an MI. Patients are often discharged prior to eplerenone being started and therefore it can be expected that the GP should initiate, which does not support the amber 1 month category. The application was submitted by the heart failure nurses in the north Somerset clinic. Within the application it is stated that due to its current TLS this drug has to be initiated and supplies made available from secondary care, but this creates a delay in treating patients as many patients need to be seen in a cardiology clinic to enable treatment initiation. GP’s are reluctant to initiate Eplerenone due to its current amber one month status which contributes to delays in patient treatment. The Heart Failure Team in North Somerset is supported by a Cardiologist in a mentorship and clinical team development role but this cardiologist is not clinically responsible for the patients as this is a Nurse lead service, therefore it is often inappropriate for this cardiologist to take prescribing responsibility. Some of the nurses within the Heart failure service are not independent prescribers which mean prescribing responsibility remains with the patients GP.

The JFG felt that eplerenone is appropriate for GP initiation providing the recommendation has come from a specialist. It has been available since 2012, and is an aldosterone antagonist like spironolactone. The JFG acknowledged that potassium levels were required during initiation; however it was felt that these patients would be having blood monitoring post MI and discharge.

It was noted that full communication from secondary care should be included in the discharge letter so that GPs/heart failure nurses know exactly how to prescribe.

**Action:**

1. **NB** to inform applicant

2. **NB** to invite cardiologists to write a brief article regarding eplerenone to include in our newsletters.

3. **NB** to change TLS Status on website

5.2 **Ivabradine TLS Change request from amber 1 month to amber specialist recommendation, no shared care**
This application was similar to the discussion as for eplerenone – see above. Post meeting - However, the NICE TA267 states that ‘Ivabradine should be initiated by a heart failure specialist with access to a multidisciplinary heart failure team. Dose titration and monitoring should be carried out by a heart failure specialist or in primary care by either a GP with a special interest in heart failure or a heart failure specialist nurse.’ For this reason, for the time being, ivabradine should remain amber 3 months.

**Action:**

1. **NB to inform applicant**

### 5.3 Lisdexamfetamine TLS Change request from red to amber 3 months

The JFG approved the inclusion for lisdexamfetamine for ADHD in adults back in June 2014. At this time, we agreed to review the TLS status in December 2014. Dr OB, Consultant psychiatrist and clinical lead of the AWP adult ADHD clinic attended the meeting.

**Discussion with Dr OB**

Currently on the BNSSG Joint formulary, methylphenidate mr is amber 3 months. The experience so far with this has been mainly positive though it is recognised that some GPs cannot support the prescribing in primary care. Lisdexamfetamine itself is similar to methylphenidate mr, though slightly more dopaminergic. It has been prescribed in the US for years, and within the UK for about 2 years. It is longer acting than methylphenidate mr but has a similar efficacy. It is less susceptible to abuse as it requires oral ingestion to be metabolised to dextroamfetamine and L-lysine. The monitoring is the same as required for methylphenidate mr.

Some of these patients are being transferred from the CAMHS team, and some of these patients are new patients.

It is suggested that around 80% of patients are successfully being treated with methylphenidate, 15% on lisdexamfetamine and around 5% atomoxetine. Atomoxetine used to be second line until lisdexamfetamine became available.

The JFG felt that it was appropriate for lisdexamfetamine to be changed to TLS amber 3 months in line with methylphenidate mr.

**Action:**

1. **NB to inform applicant**

2. **NB to coordinate a SCP and bring back to a future meeting.**

### 5.4 Donepezil Preliminary discussion re: Change in status request from amber to green

The JFG had a discussion around the suitability of donepezil being green on the formulary. NICE guidance currently states that ‘Treatment should be under the following conditions: Only specialists in the care of patients with dementia (that is, psychiatrists including those specialising in learning disability, neurologists, and physicians specialising in the care of older people) should initiate treatment. Carers’ views on the patient’s condition at baseline should be sought...’

Currently across BNSSSG there are different models of care. Within Bristol CCG, some GPs are
signed up to the dementia LES which enables GPs to diagnose and initiate treatment. If the GP operates under this LES, they are considered a specialist. Within South Glos, a dementia LES was available up until 13/14. Now, GPs are initiating treatment without this LES i.e. treating it as TLS Green. Within North Somerset, no LES exists.

As the NICE guidance states that treatment should be initiated by a specialist donepezil should remain TLS Amber at this current time.

**Action:**

1. **NB to inform applicant.**

6. **Individual Funding Requests**

No discussion

7. **Chapter review and formulary process**

No discussion during the meeting. However, JC (Interface Pharmacist, Bristol CCG) has now joined the team. She will now be leading on this aspect of the formulary and it is expected that the review of the chapters will commence shortly.

8. **Items for Discussion**

8.1 **NDRs for March Meeting**

Currently the NDRs for discussion at the March meeting are (no paperwork included in the January minutes – just noted for information):

1. **Versatis** for management of pain secondary to rib fractures.
2. **Aclidinium and formoterol (Duaklir)** for the maintenance of COPD
3. **Tocilizumab** – Treatment of Rheumatoid arthritis in accordance with NICE TA 247 however via SC route not IV.
4. **Hylan G-F (Synvisc)** – Osteoarthritis

9. **AOB**

An application for Ultibro (indacaterol and glycopyrronium) was discussed in the December 2013 meeting and approved for inclusion onto the formulary for COPD. It has not been available until now, and therefore hasn’t been included on the formulary. The JFG agreed for the inclusion onto the formulary now that it is available for prescription.

**NB**

**Interface Pharmacist**

**26th January 2015**
## BNSSG JFG
### Action Log for 20th January 2015

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<td>SB/NB/JC</td>
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<td>5.3</td>
<td>5.3</td>
<td>Lisdexamfetamine</td>
<td>Inform applicant, facilitate SCP</td>
<td>NB</td>
<td>March</td>
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</table>
### TLS Change Request

| 5.4 | Donepezil TLS Change | Inform applicant | NB | February |

### MEETING DATES 2015

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SCPs</th>
<th>Time</th>
<th>Venue</th>
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<tbody>
<tr>
<td>Tuesday 20th January</td>
<td>9th December</td>
<td>9am – 12 midday</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
</tr>
<tr>
<td>Tuesday 3rd March</td>
<td>20th January</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room, South Plaza</td>
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<tr>
<td>Tuesday 21st April</td>
<td>10th March</td>
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<td>Tuesday 24th November</td>
<td>13th October</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room, South Plaza</td>
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</tbody>
</table>
BNSSG Joint Formulary Group
Meeting held on: Tuesday 3rd March 2015 1.30pm – 4.30pm
Bevan Room, South Plaza, NHS Bristol CCG

Minutes

Present:

Interface Pharmacist, NHS Bristol CCG
Interface Pharmacist, NHS Bristol CCG
Deputy HoMM, NHS Bristol CCG
Pharmacoeconomics and Interface Pharmacist, North Bristol NHS Trust
Public Health Consultant, Bristol City Council (Chair)
Clinical Effectiveness Research Lead, Bristol City Council
Deputy Chief Pharmacist, Weston General Hospital
HoMM, South Gloucestershire CCG
GP, North Somerset
HoMM, North Somerset CCG
Principal Pharmacist, UH Bristol NHS Foundation Trust
Consultant Renal Physician, and Joint D&TC Chair, North Bristol NHS Trust
Rotational Pharmacist, North Bristol NHS Trust
Head of IFR for BNSSSG

Apologies:

GP, Bristol and member of Bristol CCG board
Joint D&TC Chair, North Bristol NHS Trust
Chief Pharmacist, AWP
Director of Pharmacy Weston Area Health NHS Trust
GP Bristol and member of Bristol CCG board
Director of Pharmacy, NBT
GP, Bristol

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest
None

2 Minutes of the meeting of 20th January 2015 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 20th January 2015 had been
circulated by NB following the meeting. No comments had been received via email that needed further discussion. DC raised the decision regarding the TLS status of tiotropium in asthma. The group has agreed to include it onto the BNSSG formulary, providing there was a clear individualised management plan, with a TLS of amber (specialist recommendation, no SCP). At the time of discussion, it was felt that these patients would be under the care of a specialist and therefore the decision to initiate tiotropium would be made by the specialist, for the GP to continue prescribing. However it was raised that we would not want patients to be referred into secondary care just for the initiation of tiotropium, as we are trying to reduce the number of referrals. DC has had some queries about this decision from practice nurses and GPs who felt that it should be green/blue.

**Action:**
1. **NB to seek the views of the GP members of the group to ascertain their views on the TLS status of tiotropium in asthma and feedback to the group.**

**Matters arising from January 2015 meeting**

2.1 **None**

Nalmefene to be discussed in SCPs and TLS

3 **NICE New Technology Appraisals**

**Published**

3.1 **None in January**

**Adopted into the BNSSG Joint Formulary** – January 2015

Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma. **TA321 TLS Red**

4 **New Drug Requests (NDRs)**

**SUMMARY**

4.1 **Lidocaine 5% patch (Versatis)** – Management of pain secondary to rib fractures.

Agreed for inclusion onto the formulary. Whilst there is not a large evidence base to support this practice, the group appreciated that in the specific cohort that the pain team had identified, i.e. elderly patients with isolated rib fractures, the use of lidocaine patches may provide a more suitable alternative to the current options (NSAIDs, codeine, tramadol and opioids). The amount of analgesia required may decrease and enable patients to take part in breathing exercises which in turn should reduce the number of patients who progress to pneumonia. The JFG approved the inclusion onto the formulary at this time, but have requested the applicant to report back in one year with audit results. At this stage the JFG will review whether it should remain on the formulary. TLS Red, for pain team use only.

4.2 **Aclidinium bromide and Formoterol fumarate (Duaklir Genuair)** – COPD maintenance.

The JFG agreed to defer the decision until the SMC had presented their guidance. There was
discussion around whether the studies provided sufficient evidence that the combination was significantly better than formoterol monotherapy. The BNSSG formulary currently includes the two other LABA/LAMA combination inhalers. The JFG acknowledged that the Genuair device is preferable for some patients and also a twice daily inhaler will be particularly useful for those with night time symptoms. The application will be brought back to the April meeting for discussion with the SMC report.

4.3 Infliximab (Inflectra and Remsima) – Biosimilar.

The JFG agreed that biosimilars can be included on the formulary as they are licensed. This is in accordance with the NICE position statement, January 2015: ‘The Department of Health in England has confirmed that a technology appraisal remit referred to NICE enables NICE to decide to apply the same remit, and the resulting guidance, to relevant licensed biosimilar products which subsequently appear on the market.’ It is acknowledged that biosimilars are not interchangeable and prescription will be required by brand name. The procurement and introduction of biosimilars is outside the remit of the JFG and this will be considered as part of the regional contracting process.

4.4 Methoxsalen (Uvadex) – Photophoresis.

Agreed for inclusion onto the BNSSG formulary for use in the Bristol Apheresis unit to conduct extracorporeal photophoresis. TLS Red.

Decision Criteria used by JFG for NDR

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

Full Discussion

4.1 Lidocaine 5% patch (Versatis) – Management of pain secondary to rib fractures.

Dr JM, Consultant anaesthetist and Pain Consultant, NBT.

Please see application form for full details. Dr JM attended the meeting to present the application.

AT had completed the critical appraisal and presented a summary of the application. Lidocaine patches are only licensed for post herpetic neuralgia; this application is for use in the management of pain due to rib fractures. 2 papers were submitted with the application. One was an observational, retrospective cohort study which suggested that there was a significant reduction in pain reports in patients using lidocaine compared to the control group. However the patient groups were not comparable in terms of the treatment they received, making it difficult to compare. The second was a conference proceeding. This again provided no evidence to suggest benefit. Further literature searching identified a randomised double blind controlled trial which concluded that there was no significant benefit of lidocaine patches to reduce the analgesia in these patients or to decrease length of stay. Therefore based on the evidence, there does not appear to be a benefit of using lidocaine patches.

It is suggested that the reason the RCT did not show a benefit from using lidocaine patches is
that it was poorly designed – patients only used one patch, and if you have multiple fractures you need more than one patch to cover all of the rib fractures. Also rib pain will last for 6 – 8 weeks and will often be worse in the first 72 hours after the fractures.

Discussion with Dr JM

Dr JM has been presented with patients with isolated rib fractures who are treated on medical wards, and therefore not able to be treated using patient controlled analgesia. The only option for these patients is the oral route. Those patients with isolated rib fractures who are often elderly often do not have adequately controlled pain and are not able to conduct the required breathing exercises. This puts them at increased risk of pneumonia. Paracetamol is not sufficient, NSAIDs will often be contraindicated in these patients and codeine and tramadol will not be appropriate. An opioid would be considered too strong. Therefore it is suggested that these patients are the most appropriate for lidocaine patches. The evidence available is acknowledged not to be supportive however there are other areas in the country who have successfully used lidocaine in this manner e.g. Gloucester, Southampton, Tayside, Portsmouth. It is a safe and well tolerated intervention; the only adverse event reported is erythema.

It is unlikely that more than one patch would be used as the patches are relatively large and it is suggested only being used in isolated fractures. It would only be prescribed for 3 days as often after this, the pain settles down. The cost is relatively inexpensive. The numbers of patients suggested in the application (30) is based on the number of referrals to the pain team.

The pain team have developed an evaluation form to collate patient information and results including: how many rib fractures, presence of dementia, pain scores at rest and movement, sedation and doses of analgesia required.

There is no systemic absorption, though the company recommend up to 3 patches at any one time.

- **Patient safety** – The only reported side effect is erythema.
- **Clinical effectiveness** – There appears to be conflicting information regarding the benefit of lidocaine patches post rib fracture. This is mainly due to there being no well-designed large RCTs specifically looking at this patient cohort. The observational studies do suggest a benefit however the limited RCT could not reproduce this.
- **Cost effectiveness or resource impact** – The applicant has suggested a cost of up to £1350 per year for 30 patients. This is significantly less than an ITU stay if a patient progresses to pneumonia requiring ITU admission.
- **Strength of evidence** – Limited observational studies.
- **Place in therapy relative to available treatments** – Lidocaine patches are well tolerated. Lidocaine would be appropriate to try in elderly patients with isolated rib fractures being treated on medical wards. The alternatives (NSAIDs, codeine, tramadol, opioids) may be contraindicated and therefore lidocaine is a safer alternative.
- **National guidance and priorities** – Nothing of note.
- **Local health priorities** – Not listed as a priority.
- **Equity of access** – Other local formularies have reviewed lidocaine for rib fracture and included it on their formularies e.g. Cheltenham & Gloucester, Portsmouth, Tayside and the ABM (Swansea) University Health Board.
The JFG considered the application, the evidence and information submitted. Whilst there is not a large evidence base to support this practice, the group appreciated that in the specific cohort that the pain team has identified i.e. elderly patients with isolated rib fractures, the use of lidocaine patches may provide a more suitable alternative to the current options (NSAIDs, codeine, tramadol and opioids). The amount of analgesia required may decrease and enable patients to take part in breathing exercises which in turn should reduce the number of patients who progress to pneumonia. The JFG approved the inclusion onto the formulary at this time, but have requested the applicant to report back in one year with audit results. At this stage the JFG will review whether it should remain on the formulary. TLS Red, for pain team use only.

Action:

1. **NB** to inform applicant.
2. **NB** to include on the formulary, TLS Red
3. **NB** to change TLS status of lidocaine patches in PHN to blue.

4.2 Aclidinium bromide and Formoterol fumarate (Duaklir Genuair) – COPD maintenance. Dr JC, Respiratory Consultant, NBT and Dr NJ, Respiratory Consultant, UHBristol.

Please see application form for full details. No one was available to present the application.

JC presented the application having completed the critical appraisal. This is the third available LABA/LAMA combination inhaler licensed for COPD maintenance. Anoro (Umeclidinium and vilanterol) was approved for inclusion in Sept 2014 and Ultibro (Indacaterol and Glycopyrronium) was included in January 2015. The evidence appears to be more robust compared to the other combination inhalers although in one of the studies the benefits of Duaklir compared to formoterol monotherapy was unclear - Aclidinium and formoterol monotherapies caused significant improvements in symptoms (both p < 0.005) versus placebo at Week 24, however the differences between both Duaklir doses versus the monotherapies were not statistically significant.

There is good evidence to suggest that patients like the device, which is an important aspect when choosing patients therapy.

The local COPD pathway will be being reviewed in the later stages of 2015 when the preferred choices will be able to be highlighted to provide clarity.

The SMC is due to present their advice in April.

- **Patient Safety** – Duaklir appears to be well tolerated. There was no evidence for additive adverse effects when combining the two drugs.

- **Clinical effectiveness** – The 6 month PIII ACLIFORM/COPD (ACLidinium/FORMoterol fumarate combination for Investigative use in the treatment of moderate to severe COPD) study evaluating fixed dose combinations of aclidinium and formoterol (400/6mcg and 400/12mcg twice a day) delivered by the Genuair® inhaler showed: Both combinations demonstrated statistically significant improvements in the co-primary endpoints of change from baseline in morning predose trough FEV1 vs formoterol 12mcg and in FEV1 at 1 hour post-dose vs aclidinium 400mcg both at week 24. The ALIFORM-COPD trial showed that in terms of lung function the combination was significantly better compared to monotherapy. In terms of COPD symptoms however, the combination was not statistically significantly better than aclidinium or formoterol monotherapy. In addition, the 6-month AUGMENT/COPD trial (n=1,692) compared two formoterol/aclidinium doses with
The first co-primary endpoint was a comparison of aclidinium/formoterol 400/12mcg and 400/6mcg vs aclidinium 400mcg alone in change from baseline in FEV1 at 1 hour post-dose at week 24. Both combination doses achieved statistically significant improvements vs aclidinium. For the secondary co-primary endpoint of morning predose trough FEV1 vs formoterol 12mcg, aclidinium/formoterol 400/12mcg demonstrated a statistically significant improvement, but aclidinium/formoterol 400/6mcg did not.

- **Cost effectiveness or resource impact** – Duaklir is a cost-effective alternative compared to the other LABA/LAMA combination inhalers – equal in cost per 30 days treatment compared to Anoro and slightly cheaper compared to Ultibro.

- **Strength of evidence** – Two good quality, large RCTs. However there are no trials which compare Duaklir with the other available LABA/LAMA combinations and some questions about the beneficial effects in terms of COPD symptoms compared to formoterol monotherapy.

- **Place in therapy relative to available treatments** – NICE guidance currently outlines that use of dual therapy with a LAMA and LABA may be considered if an ICS (as part of combination therapy with a LABA) is declined or not tolerated, however dual bronchodilation with a LABA and LAMA is expected to set a new standard of care in the management of COPD. The intention is to reduce the need/prolong the need to initiate inhaled steroids i.e. it will primarily be used in those patients needed combination bronchodilation prior to introducing steroids. The existing pathway for COPD involving an inhaled steroid in the routine management of COPD is not now the preferred pathway, and a combination LABA/LAMA inhaler would assist in this. Being in one device this should help to improve compliance. The NICE COPD guidelines are due to be updated in 2016.

- **National guidance and priorities** – SMC advice due 13.4.15. The AWMSG will not be reviewing Duaklir. Not on the NICE work plan.

- **Local health priorities** – COPD remains a priority locally.

- **Equity of access** – Most areas have not approved the use of Duaklir yet. This is mainly because they haven’t reviewed the device yet.

The JFG considered the application, the information and evidence submitted. There is evidence that the aclidinium/formoterol combination is effective in COPD in terms of improving lung function, however there is some discussion about the beneficial effects in terms of COPD symptoms when comparing against formoterol monotherapy. There is no data comparing against other LABA/LAMA combination therapy. Patients like the Genuair device. The SMC are due to publish their advice on the 13th April and therefore the JFG agreed to await this publication before making their decision.

**Action:**

1. **NB** to inform applicant

2. **NB** to add to the agenda for final discussion 21st April.

**4.3 Infliximab (Inflectra)** – Biosimilar. JC, Interface Pharmacist, on behalf of BNSSG.

Please see application form for full details. JC presented a brief overview of the application and current situation.
Biosimilars are versions of biologics approved by the EMA as being similar to an approved innovator biologic (reference product) demonstrated through comprehensive analytical and clinical comparability studies. Due to their complexity and potential for subtle differences, biosimilars are not considered bioequivalent and are not generic medicines. To gain approval for use, biosimilar medicines have to demonstrate that they are as safe and as effective as the original reference medicine, and have the same quality. The company does not have to conduct clinical trials in all of the indications in order to be granted a licence. NICE have recently updated their position regarding biosimilars and within this, it states that ‘The Department of Health in England has confirmed that a technology appraisal remit referred to NICE enables NICE to decide to apply the same remit, and the resulting guidance, to relevant licensed biosimilar products which subsequently appear on the market.’

A general discussion took place regarding the role of the JFG and what should be the appropriate steps for reviewing biosimilars and including them on our local formulary. We should be guided as per NICE and that once the biosimilar has been granted a licence it can be included on the formulary once the pricing structure has been agreed. A generic statement should be included on the formulary to reflect the NICE statement. It is outside the remit of the JFG to discuss the procurement arrangements as this is part of the regional contracting arrangements; the Senior Pharmacy Managers will be involved in these.

The JFG agreed at this stage, prescribing should be by brand and that patients should be maintained on the same brand, therefore no intentional/unintentional switching should occur.

There have been two infliximab biosimilars recently licensed – Inflectra and Remsima. These are exactly the same product but marketed differently. At this current time we are unsure of the costs and procurement arrangements specifically for these and it will largely depend on volume across the region. These discussions are outside of the remit of the JFG and the Senior Pharmacy Managers will be involved. Once we have information regarding the costs, and we are assured of cost savings, we will be able to place Inflectra and Remsima on the formulary. It is the general opinion of the specialists that the biosimilars could be used however patients should not be switched but maintained on the brand that they were initiated on. Therefore new patients could be initiated on a biosimilar. The JFG supported this opinion.

The introduction of biosimilars into the local area is complex and requires further discussion outside of the JFG. The JFG have agreed to echo NICE’s statement i.e. that in terms of recommendations a biosimilar product is considered the same way as the reference product. A generic statement about biosimilars will be included on the formulary website. The procurement is to be determined locally by the senior pharmacy managers and once we have agreement Inflectra and Remsima can be included on the formulary.

Action:

1. NB to include a generic statement on the formulary website regarding biosimilars.
2. NB to include Inflectra and Remsima on the formulary once the pricing structure has been identified and agreed locally.

4.4 Methoxsalen (Uvadex) – Photophoresis. Dr JG, Lead Consultant for the Apheresis unit, UH Bristol.

No papers were included with the agenda regarding this application. The Bristol Therapeutic Apheresis Unit has recently moved from NBT to the Bristol Haematology and Oncology Centre. It has come to light that in order to carry out photophoresis, methoxsalen (uvadex) is required. Uvadex is used in conjunction with the photophoresis system and is not injected directly into
patients. Uvadex is classified as a medicinal product. This was being ordered directly from the manufacturer when the service was being delivered within NBT however it is now being asked to be purchased through UHB pharmacy. As it is a medicinal product, it should be reviewed through the JFG. There is no alternative product.

The JFG agreed for retrospective inclusion onto the formulary. There are no other alternatives and is required for the photophoresis. Although it is a medicinal product, it is not injected directly into the patient. TLS Red.

**Action:**

1. **NB to inform applicant**
2. **NB to add to the formulary TLS Red**

5  **Shared Care Protocols/TLS status**

5.1  **Naltrexone for Alcohol (reviewed and updated)**

The SCP had been reviewed and updated. It was requested to try and reduce the amount of information that it contained and to also review it in line with the most recent SPC. It does not need to include all the information that the SPC contains but highlighting most relevant information.

**Action:**

1. **JC to review SCP and liaise with AWP.**

5.2  **Naltrexone for Opiates (reviewed and updated)**

The SCP had been reviewed and updated. It was requested to try and reduce the amount of information that it contained and to also review it in line with the most recent SPC. It does not need to include all the information that the SPC contains but highlighting most relevant information.

**Action:**

1. **JC to review SCP and liaise with AWP.**

5.3  **Lanthanum (reviewed and updated)**

The SCP had been reviewed and updated. A few minor amendments required however the JFG agreed to sign the new version off.

**Action:**

1. **NB to update the website with the new version.**

5.4  **Renagel (reviewed and updated)**
The SCP had been reviewed and updated. A few minor amendments required however the JFG agreed to sign the new version off.

Action:

1. **NB** to update the website with the new version.

5.5 **Nalmefene SCP NEW – DRAFT For discussion**

NICE published the technology appraisal in November 2014, stating that it was an option ‘for people with alcohol dependence who:

• are still drinking more than 7.5 units per day (for men) and more than 5 units per day (for women) 2 weeks after an initial assessment and
• do not have physical withdrawal symptoms and
• do not need to either stop drinking straight away or stop drinking completely.

*Nalmefene should only be taken if the person is also having ongoing support to change their behaviour and to continue to take their treatment, to help them reduce their alcohol intake.*

Since this was published many discussions have taken place within BNSSG and public health as to how we implement this technology appraisal. We included it on the formulary as TLS Red at the end of February whilst ongoing discussions take place. We need to ensure that we have the appropriate infrastructure in order for it to be safely prescribed; specifically the psychosocial support that is required alongside the treatment. A SCP and a treatment pathway have been drafted for discussion. This has been based on the Wessex AHSN document.

Action:

1. **SB/JC/NB** to liaise with BNSSG and public health to further discussions and formalisation of SCP and treatment pathway.

5.6 **Disulfiram – consideration of TLS change from blue to amber**

It has been suggested that disulfiram should be changed from blue on the formulary to amber as it states in the license that it ‘should be initiated only in a hospital or specialised clinic and by physicians experienced in its use.’ The JFG agreed that this should be changed to amber with a SCP after discussion with the specialists.

Action:

1. **NB** to coordinate a SCP and bring back to a future meeting.

6 **Individual Funding Requests**

A brief discussion regarding the IFRs that have been discussed across BNSSG occurred.

7 **Chapter review and formulary process**

JC outlined the review process and that GI, endocrinology and dermatology had been sent out. The hope is that we will be able to narrow the formulary down to some degree. Cardiovascular, CNS and Infections have also been sent out this week. We need to increase the amount of primary care feedback that we receive.
8 Items for Discussion

8.1 NDRs for April Meeting

a. **Hyaluronic acid (Synvisc)** – Osteoarthritis, NBT tbc

b. **Tocilizumab (SC)** – Rheumatoid arthritis, NICE College tbc

c. **Ajmaline** – Diagnostic for Brugada Syndrome.

The JFG discussed this potential application to the JFG. This is an unlicensed medicine that is used in the diagnosis of Brugada syndrome (abnormal ECG and increased risk of sudden cardiac death). It has previously been through UHB MAG and approved for use. Therefore, the JFG were happy to approve its use and include on the formulary. An application is therefore not required at the next meeting.

8.2 New Drug Applications: Medical devices vs medicinal products

No formal discussion.

8.3 Meningitis B for asplenia and splenic Dysfunction

For information – the Department of Health now recommend those without a functioning spleen to have the meningitis B vaccine. This has now been added to the formulary for this indication.

8.4 GP involvement in the BNSSG JFG

We need to increase the amount of GP engagement and involvement in the formulary. We currently have JB who attends regularly and is invaluable but it would be beneficial if we were able to increase our numbers. NB confirmed that there is a GP in Bristol interested in potentially participating in the JFG. She will attend the next meeting.

9 AOB

a. FL: For information, Fosfomycin IV is now licensed, and therefore the formulary needs amending.

b. SB: [NHS E Pregabalin](#) alert regarding the use of generic pregabalin for unlicensed neuropathic pain. We need to ensure that the acute trusts are responding to this alert as well. NBT and UHB confirmed that they currently only stocked Lyrica. NB will add the alert to the formulary.

c. DC: Hyperhidrosis update. NB confirmed that Dr Jonathan Roberts (Consultant in Public Health) was leading on this and has been in contact with Dr Cameron Kennedy last week with timescales. An updated policy should be able to go to the CPRG in June.

d. MP: NOACs. There was a discussion as to whether we maybe able to recommend a particular NOAC over another. It appears that each agent has its nuances and therefore this may not be possible. As NICE recommend them all as an option, we need to have them all on the formulary. This will be picked up during chapter review.

**NB**

**Interface Pharmacist**

**11th March 2015**
## Action Log for 20th January 2015

<table>
<thead>
<tr>
<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
<th>Responsible Officer</th>
<th>Deadline</th>
<th>Date of Update</th>
<th>Update</th>
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<tr>
<td>1.</td>
<td></td>
<td>Tiotropium in asthma – TLS Decisions</td>
<td>Seek views of GP members of the group regarding the TLS decision</td>
<td>NB</td>
<td>April</td>
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<td>4.1</td>
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<td>Lidocaine patch in rib fracture</td>
<td>Include on the formulary. Also add back onto work plan to report back in 1 year</td>
<td>NB</td>
<td>April</td>
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<td>4.1</td>
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<td>Lidocaine patch in PHN</td>
<td>Change to TLS blue</td>
<td>NB</td>
<td>April</td>
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<td>4.2</td>
<td></td>
<td>Duaklir NDR</td>
<td>Inform applicant. Add to April agenda</td>
<td>NB</td>
<td>April</td>
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<td>4.3</td>
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<td>Infliximab biosimilar NDR</td>
<td>Add generic statement on the formulary re Biosimilars. Await confirmation from SPMs regarding pricing before adding Inflectra and Remsima onto the formulary</td>
<td>SB/JC/NB</td>
<td>April</td>
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<td>4.4</td>
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<td>Uvadex NDR</td>
<td>Inform applicant and add to the formulary</td>
<td>NB</td>
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<td>5.1</td>
<td></td>
<td>Naltrexone for opiates SCP</td>
<td>Review and edit SCP and liaise with AWP</td>
<td>JC</td>
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<td>Lanthanum SCP</td>
<td>Update SCP on the web</td>
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<td>5.5</td>
<td>Nalmefene SCP</td>
<td>Liaise with BNSSG and public health to finalise SCP and treatment pathway</td>
<td>SB/JC/NB</td>
<td>April</td>
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<td>Liaise with specialist services to produce SCP and change to amber</td>
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**MEETING DATES 2015**

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SCPs</th>
<th>Time</th>
<th>Venue</th>
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<tr>
<td>Tuesday 20th January</td>
<td>9th December</td>
<td>9am – 12 midday</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<tr>
<td>Tuesday 3rd March</td>
<td>20th January</td>
<td>1.30 – 4.30pm</td>
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<td>13th October</td>
<td>1.30 – 4.30pm</td>
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BNSSG Joint Formulary Group
Meeting held on: Tuesday 21st April 2015  9.00am – 12midday
Pharmacy Seminar Room, Brunel Building, Southmead Hospital

Minutes

Present:

Interface Pharmacist, NHS Bristol CCG
Interface Pharmacist, NHS Bristol CCG
Pharmacoeconomics and Interface Pharmacist, NBT
Clinical Effectiveness Research Lead, Bristol City Council
GP, North Somerset
GP Bristol and member of Bristol CCG board
Deputy HoMM, NHS Bristol CCG
Deputy HoMM, NHS South Glos CCG
Deputy HoMM, NHS North Somerset CCG
Medicines Management Pharmacist, North Somerset CCG
Consultant Neurologist, NBT
GP, Bristol
Public Health Registrar, Bristol

Apologies:

Public Health Consultant, Bristol City Council (Chair)
Deputy HoMM, NHS Bristol CCG
Consultant Renal Physician, and Joint D&TC Chair, NBT
Joint D&TC Chair, North Bristol NHS Trust
Director of Pharmacy, Weston General Hospital
Deputy Chief Pharmacist, Weston General Hospital
HoMM, North Somerset CCG
HoMM, South Gloucestershire CCG
Principal Pharmacist, UHBristol NHS Foundation Trust
GP, Bristol

1  Welcome, Apologies and Declaration of Interests

  Declarations of Interest
    None

2  Minutes of the meeting of 3rd March 2015 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 3rd March 2015 had been
circulated by NB following the meeting. No comments had been received via email that needed further discussion.

**Matters arising from March 2015 meeting**

### 2.1 Duaklir (Aclidinium and formoterol) for COPD NDR March 2015

- SMC advice April 2015 (See discussion below)

### 2.2 Tiotropium in asthma

- Review of TLS Decision Jan 15. The TLS decision regarding tiotropium in asthma was raised at the March meeting. Subsequent to this, NB had contacted the GP members of the group to gauge their opinions. It was felt that a TLS of amber (specialist recommendation, no SCP) was appropriate. These patients would likely be under the care of a specialist and therefore an increase in referrals would not occur. A GP could initiate treatment if this is recommended by a specialist. The JFG upheld this decision.

### 3 NICE New Technology Appraisals

**Published**

3.1 Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (including a review of TA140 and TA262). **TA329**

TLS Red

3.2 Sofosbuvir for treating chronic hepatitis C. **TA330**

TLS Red

3.3 Simeprevir in combination with peginterferon alfa and ribavirin for treating genotypes 1 and 4 chronic hepatitis C. **TA331**

TLS Red

3.4 Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment. **TA333**

TLS Red

3.5 Rivaroxaban for preventing adverse outcomes after acute management of acute coronary syndrome. **TA335**

It was agreed for rivaroxaban to be TLS amber (1 month) for this indication. It was noted that it is difficult to read the formulary page for the NOACs, especially with regard to the TLS and the different indications. To attempt to address this, a table will be put together in order to signpost what the TLS is according to indication. The NICE TA was discussed in relation to the TLS and it was felt that for ACS, that secondary care should initiate and supply the first month however a GP could continue the prescribing.

3.6 Empagliflozin in combination therapy for treating type 2 diabetes. **TA 336**

TLS Blue in accordance with the other SGLT2 inhibitors on the BNSSG formulary.

3.7 Rifaximin for preventing episodes of overt hepatic encephalopathy. **TA 337**
Adopted into the BNSSG Joint Formulary – February and March 2015

Erythropoiesis-stimulating agents (epoetin and darbepoetin) for treating anaemia in people with cancer having chemotherapy (including review of TA142) TA323 TLS Red

Nalmefene for reducing alcohol consumption in people with alcohol TA325 TLS Red (Awaiting SCP development and approval)

Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of NICE technology appraisal guidance 196) TA326 TLS Red

4 New Drug Requests (NDRs)

SUMMARY

4.1 Sterculia (Normacol Plus) – Middle aged to elderly patients with slow transit constipation in whom Fybogel is too “weak” and movicol too “strong”.

Agreed for inclusion onto the formulary. Whilst there is not a large evidence base to support Normacol, it is recognised that this is true for laxatives in general. TLS Blue.

4.2 Aclidinium bromide and Formoterol fumarate (Duaklir Genuair) – COPD maintenance.

Agreed for inclusion onto the formulary alongside the other two available LABA/LAMA combination inhalers. The SMC report was reviewed. The JFG acknowledged that the Genuair device is preferable for some patients and also a twice daily inhaler will be particularly useful for those with night time symptoms.

Decision Criteria used by JFG for NDR

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

Full Discussion

4.1 Sterculia (Normacol Plus) – Middle aged to elderly patients with slow transit constipation in whom Fybogel is too “weak” and movicol too “strong”. Mr GP, Consultant Surgeon, WAHT.

Please see application form for full details. No one was available to present the application.

The application proposed the inclusion of Normacol plus in the formulary for patients where fybogel has been ineffective, but movicol is considered too strong. Weston currently use
Normacol plus even though it is currently non-formulary. Normacol plus contains sterculia, a bulk forming laxative and frangula, which is a stimulant. It was acknowledged that there is a lack of high-quality evidence to support a particular laxative over another.

The NICE Clinical Knowledge Summary (CKS) states that bulk forming laxatives should be first line and then if the stools remain hard, add in a stimulant. It is felt that senna maybe too strong for some people and that Normacol plus would be an interim measure. There are other formularies that include normacol plus.

- **Patient safety** – No issues.

- **Clinical effectiveness** – No specific trials looking at the effectiveness of normacol plus for chronic constipation, though this is the same for the other laxatives on the formulary – it is acknowledged that the evidence base for laxatives is weak.

- **Cost effectiveness or resource impact** – The costs are comparable to the other available formulary laxatives.

- **Strength of evidence** – See above.

- **Place in therapy relative to available treatments** – With a lack of good evidence to support treatment, the recommended approach to treatment of constipation is based largely on expert opinion. The NICE CKS supports this approach in terms of a bulk forming laxative as first line and then to add a stimulant if the stools remain hard.

- **National guidance and priorities** – Nothing of note.

- **Local health priorities** – Not listed as a priority.

- **Equity of access** – Other local formularies have Normacol plus included on the formulary. Weston General already use Normacol plus.

The JFG considered the application, the evidence and information submitted. Whilst there is not a large evidence base to support laxatives in general, the JFG was in agreement to include this laxative based on the NICE CKS and stepwise approach to the management of constipation. TLS Blue.

**Action:**

1. **NB** to inform applicant.
2. **NB** to include on the formulary, TLS Blue

### 4.2 Aclidinium bromide and Formoterol fumarate (Duaklir Genuair) – COPD maintenance

Dr JC, Respiratory Consultant, NBT and Dr NJ, Respiratory Consultant, UH Bristol. RE-discussion with SMC advice.

Please see application form for full details.

The JFG re-discussed this application with the SMC advice. The application was initially discussed during the March meeting, and there were some concerns regarding the evidence around efficacy compared to formoterol monotherapy.

This is the third available LABA/LAMA combination inhaler licensed for COPD maintenance.
Anoro (Umeclidinium and vilanterol) was approved for inclusion in Sept 2014 and Ultibro (Indacaterol and Glycopyrronium) was included in January 2015.

The SMC stated that in two 24-week comparator and placebo controlled phase III studies, treatment with Aclidinium/formoterol combination resulted in statistically significant improvements in FEV1% predicted pre-dose (versus a LABA) and post dose (versus a LAMA).

There is good evidence to suggest that patients like the device, which is an important aspect when choosing patients therapy.

The local COPD pathway will be being reviewed in the later stages of 2015 when the preferred choices will be able to be highlighted to provide clarity.

- **Patient Safety** – Duaklir appears to be well tolerated. There was no evidence for additive adverse effects when combining the two drugs.

- **Clinical effectiveness** – The 6 month PIII ACLIFORM/COPD (AC Lidinium/FORMoterol fumarate combination for Investigative use in the treatment of moderate to severe COPD) study evaluating fixed dose combinations of aclidinium and formoterol (400/6mcg and 400/12mcg twice a day) delivered by the Genuair® inhaler showed: Both combinations demonstrated statistically significant improvements in the co-primary endpoints of change from baseline in morning predose trough FEV1 vs formoterol 12mcg and in FEV1 at 1 hour post-dose vs aclidinium 400mcg both at week 24. The ALIFORM-COPD trial showed that in terms of lung function the combination was significantly better compared to monotherapy. In terms of COPD symptoms however, the combination was not statistically significantly better than aclidinium or formoterol monotherapy. In addition, the 6-month AUGMENT/COPD trial (n=1,692) compared two formoterol aclidinium doses with monotherapy. The first co-primary endpoint was a comparison of aclidinium/formoterol 400/12mcg and 400/6mcg vs aclidinium 400mcg alone in change from baseline in FEV1 at 1 hour post-dose at week 24. Both combination doses achieved statistically significant improvements vs aclidinium. For the secondary co-primary endpoint of morning predose trough FEV1 vs formoterol 12mcg, aclidinium/formoterol 400/12mcg demonstrated a statistically significant improvement, but aclidinium/formoterol 400/6mcg did not.

- **Cost effectiveness or resource impact** – Duaklir is a cost-effective alternative compared to the other LABA/LAMA combination inhalers – equal in cost per 30 days treatment compared to Anoro and slightly cheaper compared to Ultibro.

- **Strength of evidence** – Two good quality, large RCTs. However there are no trials which compare Duaklir with the other available LABA/LAMA combinations and some questions about the beneficial effects in terms of COPD symptoms compared to formoterol monotherapy.

- **Place in therapy relative to available treatments** – NICE guidance currently outlines that use of dual therapy with a LAMA and LABA may be considered if an ICS (as part of combination therapy with a LABA) is declined or not tolerated, however dual bronchodilation with a LABA and LAMA is expected to set a new standard of care in the management of COPD. The intention is to reduce the need/prolong the need to initiate inhaled steroids i.e. it will primarily be used in those patients needed combination bronchodilation prior to introducing steroids. The existing pathway for COPD involving an inhaled steroid in the routine management of COPD is not now the preferred pathway, and a combination LABA/LAMA inhaler would assist in this. Being in one device this should help to improve compliance. The NICE COPD guidelines are due to be updated in 2016.

- **National guidance and priorities** – SMC advice due 13.4.15. The AWMSG will not be reviewing Duaklir. Not on the NICE work plan.
• **Local health priorities** – COPD remains a priority locally.

• **Equity of access** – Most areas have not approved the use of Duaklir yet. This is mainly because they haven’t reviewed the device yet.

The JFG considered the application, the information and evidence submitted. There is evidence that the aclidinium/formoterol combination is effective in COPD in terms of improving lung function and patients like the Genuair device. The SMC have approved it for use in Scotland. The BNSSG COPD pathway will be looked at during the later stages of this year. The JFG approved it for inclusion onto the formulary.

**Action:**

1. **NB** to inform applicant

2. **NB** to add to website, TLS Blue.

5 **Shared Care Protocols/TLS status**

5.1 **Rifaximin** – Change in status request from red to amber

NICE have recently appraised and published the NICE Technology appraisal for Rifaximin – it should be an option for patients for preventing hepatic encephalopathy. Rifaximin is currently on the BNSSG formulary, TLS Red, and therefore currently the specialist retains the prescribing for patients. NBT have submitted a TLS change in status to allow the prescribing to be transferred to the GP. A SCP had been previously developed and was included in the papers for information. These patients will be those with end stage liver failure and the numbers being prescribed would be small – the numbers would not expect to increase if it were to change to amber. The patients would need review with a specialist at no longer than every 6 months. It was agreed for the TLS to change to amber 3 months once the SCP has been reviewed and agreed across BNSSG.

**Action:**

1. **NB/JC** to liaise with NBT/UHB/Weston to review SCP.

5.2 **Nalmefene** – New SCP

The SCP has been developed based on the Wessex treatment pathway. JC has liaised with public health in Bristol and also across BNSSG to bring together the different ways of working in order to produce a BNSSG SCP for nalmefene to change to TLS amber. The funding arrangements are different across BNSSG. The pyscrosocial support was discussed and JC has confirmed that within Bristol, monthly appointments could be supported to enable the GP to prescribe nalmefene alongside. It is not known if this can work in NS or SG. The group support nalmefene being amber; however the SCP needs some further work with regards to outlining the communication between the specialist and GP. The SCP will be developed and sent around for e-approval after the meeting.

**Action:**
1. **JC** to review SCP and to send around for e-approval.

5.3 **Fosfomycin** – Change in status request from red to amber

Fosfomycin is an orally active, bactericidal, broad spectrum antibiotic which is unlicensed in the UK. It is increasingly recommended by micro due to the rise of ESBL UTIs. It was licensed for UTI treatment in the UK some years ago but was not a commercial success and the UK licence lapsed. It is currently on our formulary TLS Red. This causes problems in the community both with regards to prescribing and obtaining the prescription. It is suggested that this becomes amber (specialist recommendation, no SCP) to enable a GP to prescribe it for a patient after Micro have recommended it. There can be delays in obtaining supplies from community pharmacies as it is unlicensed. The JFG discussed the possibility of enquiring whether it can be added to the specialist medicine LES that some community pharmacies are signed up to so that patients can be directed to particular pharmacies to obtain stocks. The JFG agreed for the TLS change to amber and will investigate the LES with NHS England.

**Action:**

1. **NB** to alter the TLS to amber (specialist recommendation, no SCP).
2. **NB** to investigate the LES with NHS England.

5.4 **Pivmecillinam** – change in status request from blue ‘on recommendation of a clinical microbiologist’ to blue without restrictions

Pivmecillinam is now recommended in NHS Public Health England antibiotic guidelines for the treatment of UTIs where resistance caused by ESBL producing bacteria is a possibility. This is especially in patients with a high risk of resistance and poor renal function where nitrofurantoin is contraindicated. Therefore by removing the ‘on recommendation by a microbiologist’ it would enable GPs to prescribe following sensitivity results. The JFG agreed this change.

**Action:**

1. **NB** to alter the formulary website.

5.5 **Rheumatology SCPs** – Updated SCPs

The SCPs had been extensively reviewed over 2 years ago and these all now needed review. There have been minor changes which were discussed at the JFG. It was raised that the contact details need to be ensured that they are correct on the SCPs – this is really important for the GPs. This should be part of the process of reviewing the SCPs. Also, the neutrophil count was raised – the SCP states that if the neutrophils are less than 1.8 you should contact rheumatology. However in practice, when a patient has a neutrophil count of 1.5 and a GP raises this with rheumatology they have been advised to carry on the prescription. The SCP should reflect practice. **NB** to follow this up and make amendments as necessary. The JFG agreed to the updated SCPs.

**Action:**

1. **NB** to upload new SCPs on the website once neutrophils have been clarified.
5.6 **Stalevo** – TLS Change request from amber 3 months to amber (no SCP, specialist recommendation)

These Parkinson’s medications have been available for a number of years and GPs are familiar with the use of them. The TLS of these has been previously been discussed at JFG and it was felt that a TLS of green or blue would not be appropriate. In reality, it should be possible for a GP to phone the specialists up who can recommend the initiation of these medications by the GP. Currently, a patient would have to wait for an outpatient appointment to be able to initiate treatment. The JFG agreed for the TLS to be changed to amber (specialist recommendation, no SCP).

It was also discussed about having clear lines of communication and that it would be beneficial to have email addresses for the specialists and to have formal arrangements for formal advice and guidance from the specialists without necessarily referring for an out-patient appointment. It was suggested that this should be raised at the planned steering group for discussion via Andy Newton.

**Action:**

1. **NB** to amend the website to reflect TLS change
2. **NB** to raise with Planned Steering Group.

5.7 **Entacapone** – TLS Change request from amber 3 months to amber (no SCP, specialist recommendation)

As above.

**Action:**

1. **NB** to amend the website to reflect TLS change
2. **NB** to raise with Planned Steering Group.

5.8 **Rasagiline** - TLS Change request from amber 3 months to amber (no SCP, specialist recommendation)

As above.

**Action:**

1. **NB** to amend the website to reflect TLS change
2. **NB** to raise with Planned Steering Group.

6 **Individual Funding Requests**

No discussion.
7 Chapter review and formulary process

JC outlined the current situation with reviewing the formulary chapters. There have been various meetings so far to discuss the comments from the specialist consultation.

Comments from the meetings so far:

Endocrine chapter:

- Degludec prescribing appears to be increasing in community. This is TLS Red on the formulary currently. It was requested that within each CCG actual usage should be looked into.
- Sulphonylureas: Glimepiride – this could be removed. Currently investigating usage and opinion.
- Pioglitazone – It appears that this may feature in the NICE guidelines on type II diabetes due to be published in August of this year. This should remain on the formulary but changed to blue.
- HRT – the intention is to try and review and formalise choices.
- Testosterone products – the intention is to review and formalise choices.

Skin chapter

- Emollients – these have never been properly considered across BNSSG to gain a consensus. There are lots of different variations of ‘formularies of emollients’ and therefore we will attempt to draw together to publish a consensus on the BNSSG formulary. Prescribing advice is also required.
- Bath and Shower products – remove from the formulary due to lack of evidence and slip risk.
- SCPs – to gain agreement for skin SCPs (e.g. azathioprine) across BNSSG.
- Wound care formulary – there is now a Pan Avon wound care formulary, and individual trusts will pick from list for in house choices. The formulary was a large procurement exercise. A link to this formulary will be included within the formulary. The practice managers need to be aware of this to improve engagement.

Other chapters that are currently out for discussion are the infections, CNS and GI chapters.

8 Items for Discussion

8.1 NDRs for June Meeting (no papers, for information only)

a. **Tocilizumab** - For adult patients with moderate/severe, active, rheumatoid arthritis who cannot take methotrexate, UHB

b. **Abatacept (SC)** - For adult patients with moderate/severe, active, rheumatoid arthritis, in combination with methotrexate, UHB

c. **Rituximab in combination with Lefluonimde** - adult patients with severe, active, rheumatoid arthritis who cannot take methotrexate and who have had inadequate response or intolerance to other DMARDs and one or more anti-TNF therapies, UHB

- **Simbrinza (Brinzolamide & Brimonidine)** - Glaucoma or ocular hypertension when
monotherapy provides insufficient control.

8.2 Overactive bladder drugs review

Dr LJD, a public health registrar has conducted a literature review of the overactive bladder drugs on behalf of BNSSG. It is known that a significant amount of money is spent on these drugs, and yet they are generally not well tolerated and have limited efficacy. L-JD presented her report. NICE have published a clinical guideline in 2013 on overactive bladder and these were assessed a robust and complete, with nothing significant to challenge the findings. It would therefore seem appropriate to adopt the NICE recommendations supported by the development of a treatment pathway to be used across BNSSG and across the interface. One set of guidelines found there was no consistent evidence that one antimuscarinic drug is superior to an alternative antimuscarinic drug for cure or improvement of urinary incontinence, or in Quality of Life outcomes (EAU, 2014). These guidelines are produced by an expert group and are updated annually. The report concluded that the formulary should consider including:

First line treatment for overactive bladder should be:

- **tolterodine (IR) (NICE)** (reduced risk of dry mouth compared to oxybutynin (Cochrane)) [NEW NICE guideline] or

Alternatives to include

- **oxybutynin (IR)(NICE)** [guideline NEW] or
- **darifenacin** (once daily preparation) [new addition to NICE 2013]

Specific indications

- Offer a **transdermal OAB** drug to women unable to tolerate oral medication. [new 2013]
- **Oxybutinin** should not be given IR to frail older women (new to NICE 2013).
- **Fesoterodine** (IR) (based on RCT evidence, 2013)
- **Solifenacin** may be offered as for patients unable to tolerate tolterodine or oxybutynin
- Extending use of **Mirabegron** might be considered in the context of secondary care, although this would need to be in consultation with the clinical team.

In terms of cost, solifenacin is the most expensive option available and in terms of prescribing patterns solifenacin is prescribed more than any other medication and is increasing. This does not appear to follow the current formulary choices (i.e. solifenacin to be considered only if tolterodine or oxybutynin are not tolerated). The evidence does not support solifenacin to be promoted more than other antimuscarinic drugs.

A set of prescribing guidelines for OAB were identified in North Somerset. It has been suggested to develop these to be used across BNSSG to help in the management of OAB across the interface and to support evidence based prescribing.

**Action:**

1. **NB** to send report to acute trusts for dissemination.

2. **NB** to coordinate the development of a treatment pathway/prescribing guidelines to support OAB treatment.
8.3 Linaclotide prescribing review

NB presented a report on the current prescribing trends for linaclotide across BNSSG. The BNSSG JFG agreed for linaclotide to be included on the BNSSG joint formulary in April 2014. It was agreed that the prescribing should be analysed after 6 months to ascertain the prescribing trends after its introduction onto the formulary to ensure that they are within an expected range. After analysis of the prescribing it can be concluded that linaclotide is not being prescribed within BNSSG in significant volumes and well within the predicted number. It was agreed therefore that linaclotide can remain on the formulary and for it to remain TLS amber.

9 AOB

None.

NB
Interface Pharmacist
29th April 2015
# Action Log for 21\(^{st}\) April 2015

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<th>Minute No.</th>
<th>Subject</th>
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<th>Responsible Officer</th>
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<td>NICE TAs</td>
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<td>5.1</td>
<td>Rifaximin – Change in status request from red to amber</td>
<td>Coordinate a review of the draft SCP and bring back to JFG for agreement</td>
<td>NB</td>
<td>May</td>
<td>21.4.15</td>
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<td>21.4.15</td>
<td>5.2</td>
<td>Nalmefene SCP</td>
<td>Develop SCP and send around the group for e-approval</td>
<td>JC</td>
<td>May</td>
<td>21.4.15</td>
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<td>21.4.15</td>
<td>5.3</td>
<td>Fosfomycin – Change in status request from red to amber</td>
<td>Change tls to amber (specialist recommendation, no SCP) and liaise with NHS England regarding specialist medicine LES</td>
<td>NB</td>
<td>May</td>
<td>21.4.15</td>
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<tr>
<td>21.4.15</td>
<td>5.4</td>
<td>Pivmecillinam – change in status request from blue to green</td>
<td>Remove restrictions for pivmecillinam</td>
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<td>May</td>
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<td>5.5</td>
<td>Rheumatology</td>
<td>Liaise with Rheumatology re: neutrophils.</td>
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<td>Tuesday 3rd March</td>
<td>20th January</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room, South Plaza</td>
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<td>Tuesday 21st April</td>
<td>10th March</td>
<td>9am – 12 midday</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<td>Tuesday 2nd June</td>
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<td>Tuesday 24th November</td>
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BNSSG Joint Formulary Group
Meeting held on: Tuesday 2\textsuperscript{nd} June 2015  1.30pm – 12midday
Bevan Room, South Plaza, NHS Bristol CCG

Minutes

Present:

- Interface Pharmacist, NHS Bristol CCG
- Interface Pharmacist, NHS Bristol CCG
- Pharmacoeconomics and Interface Pharmacist, NBT
- Clinical Effectiveness Research Lead, Bristol City Council
- GP Bristol and member of Bristol CCG board
- Public Health Consultant, Bristol City Council (Chair)
- Deputy HoMM, NHS Bristol CCG
- Deputy Chief Pharmacist, Weston General Hospital
- HoMM, North Somerset CCG
- HoMM, South Gloucestershire CCG
- Principal Pharmacist, UHBristol NHS Foundation Trust
- Head of IFR for BNSSSG
- Rotational Pharmacist, NBT (for part of the meeting)

Apologies:

- Consultant Renal Physician, and Joint D&T Chair, NBT
- Joint D&T Chair, North Bristol NHS Trust
- Director of Pharmacy, Weston General Hospital
- GP, Bristol
- GP, North Somerset
- Consultant Neurologist, NBT

1  Welcome, Apologies and Declaration of Interests

Declarations of Interest

None

The meeting was not quorate. In accordance with the ToR of this group, the Chair of the group determined that the meeting should continue and the Formulary Pharmacist will secure endorsement of any decisions via email.

2  Minutes of the meeting of 21\textsuperscript{st} April 2015 and Matters arising
The minutes from the Joint Formulary Group (JFG) meeting on the 21st April 2015 had been circulated by NB following the meeting. No comments had been received via email that needed further discussion.

Matters arising from 21st April 2015 meeting

2.1 Nalmefene
- A SCP for Nalmefene has been developed and agreed for Bristol use only at this stage. There are differences across the three CCGs in terms of how alcohol dependency services are delivered. For this reason, it has not been possible currently to agree a SCP that works across BNSSG. Nalmefene has therefore been altered to amber for patients in Bristol (with a SCP) and it remains Red in North Somerset and South Glos whilst further development and agreement is obtained.

2.2 Wound Care Formulary
- The Pan Avon formulary was developed and agreed at the end of 2014, and each organisation has used this list to develop their own formularies. Each organisation’s formulary should be available on the website.

Action:
1. NB to locate an e-copy of each organisation’s formulary and to include on the formulary website.

3 NICE New Technology Appraisals

Published

3.1 Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia TA343
TLS Red

3.2 Ofatumumab in combination with chlorambucil or bendamustine for untreated chronic lymphocytic leukaemia TA344
TLS Red

Adopted into the BNSSG Joint Formulary – April & May 2015
- Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (including a review of TA140 and TA262). TA329 TLS Red
- Simeprevir in combination with peginterferon alfa and ribavirin for treating genotypes 1 and 4 chronic hepatitis C. TA331 TLS Red
- Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment. TA333 TLS Red

4 New Drug Requests (NDRs)

SUMMARY
4.1 **Simbrinza (Brinzolamide & Brimonidine)** - Glaucoma or ocular hypertension when monotherapy provides insufficient control.

More information required. The JFG recognised that the combination product would lead to a reduction in the number of eye drops required and ultimately the exposure to preservative. However, there does not appear to be any evidence to show that these are issues and that a combination product would benefit. A number of combination products for glaucoma are on the formulary. Information on current prescribing and potential generic availability of brinzolamide to the next JFG meeting, where a final decision can be made.

4.2 **Tocilizumab** - For adult patients with moderate/severe, active, rheumatoid arthritis who cannot take methotrexate.

Agreed for inclusion onto the formulary. Since the NICE TA 247 for tocilizumab with methotrexate was published, there has been more evidence and has since been licensed as monotherapy. The SMC have approved it for use within Scotland as monotherapy and the British Society of Rheumatology have also included it in their recommendations. The UHB Rheumatology biologic pathway clearly defines where it fits in. TLS Red.

4.3 **Abatacept (SC)** - For adult patients with moderate/severe, active, rheumatoid arthritis, in combination with methotrexate.

Agreed for inclusion onto the formulary. The SC preparation is licensed in the same way that the IV preparation is. IV abatacept has been approved for RA by NICE, and the SC would be used in the same way as IV. When calculating costs, the SC preparation currently works out more cost effective than IV. TLS Red.

4.4 **Rituximab in combination with Lefluonimde** - For adult patients with severe, active, rheumatoid arthritis who cannot take methotrexate and who have had inadequate response or intolerance to other DMARDs and one or more anti-TNF therapies.

Agreed for inclusion onto the formulary. There is a cohort of patients who are unable to tolerate methotrexate, but can tolerate leflunomide. For these patients, in whom the first and second line therapies are ineffective, rituximab with leflunomide is a suitable option, and there is good trial evidence to support this. TLS Red.

**Decision Criteria used by JFG for NDR**

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

**Full Discussion**

4.1 **Simbrinza (Brinzolamide & Brimonidine)** - Glaucoma or ocular hypertension when monotherapy provides insufficient control. *Mr PS, Consultant Optometrist, UHBristol.*

Please see application form for full details. Mr PS attended the meeting to present the application.
The application is to include a combination eye drop, for the treatment of glaucoma or ocular hypertension. This is the only combination eye drop which does not contain a beta blocker. The drops contain a fixed dose combination of brinzolamide 1%, a carbonic anhydrase inhibitor, and brimonidine 0.2%, an alpha 2 agonist (sympathomimetic) drug. The NICE evidence summary states that ‘Combination therapies are preferred to aid compliance and decrease preservative exposure. For patients currently requiring triple therapy, but in whom beta blockers should be avoided, three bottles of eye drops are required. The European Glaucoma Society recommends that the prescribing of more than two bottles for simultaneous use should be avoided.’

In 2 randomised controlled trials in people with glaucoma, brinzolamide/brimonidine combination eye drops were statistically significantly superior to either constituent drug administered alone as monotherapy in reducing intraocular pressure at 3 months. The combination eye drops were non-inferior to brinzolamide plus brimonidine administered concomitantly. Most reported adverse events were mild to moderate and localised, but these were higher in number with the combination eye drops compared with the individual constituent drugs.

There are no published studies comparing brinzolamide/brimonidine combination eye drops with other drug treatments for managing glaucoma and ocular hypertension. Brinzolamide/brimonidine may be an alternative treatment option for some people, for whom prostaglandin analogues and beta-blockers are unsuitable.

These are not titratable and therefore suitable for being prescribed as a combination product. The studies have shown that patients are equally tolerable to both agents.

Discussion with Mr PS

Both brinzolamide and brimonidine alone and in combination are already in use at the eye hospital. This is the first fixed combination without a beta blocker; being a combination product helps with compliance and also minimises the side effects from the amount of preservative. This would be used as 3rd or 4th line in the management of glaucoma, with prostaglandin analogues as first line, and carbonic anhydrase inhibitors and beta blockers as second line. There is a clear and firmly defined pathway for the treatment of glaucoma, based on the NICE guidelines (CG85), and patients are followed up at fixed intervals. A patient is seen in clinic after 2 months when medications are changed. Other combination drops all include a beta blocker, which are included on the formulary. Treatment with a beta blocker is not always required and indicated and therefore a combination of brinzolamide and brimonidine offers an alternative combination eye drop. When compared to prescribing the individual monotherapies, fixed combination therapies offer a simple and convenient dosing regimen. However there does not appear to be any evidence to show that compliance is a problem, and that a combination product helps. Simbrinza is also relatively cost-neutral.

Of the 14,000 patient at the eye hospital, two thirds will be on treatment, and most of these will be on prostaglandin analogues. A proportion (estimate 50% of those on treatment) receives dual therapy and a smaller proportion (estimate 20% of those on treatment) receives triple therapy.

Reducing the amount of eye drops helps in the reduction of preservative exposure. It is suggested that preservatives used in large quantities or over a long period of time may damage the eye. However, the JFG were not presented with any evidence to support this and so were unable to quantify how much benefit would be gained by reducing the number of bottles from 2 to 1.

The NICE clinical guideline on glaucoma (CG 85, April 2009) states that ‘Combination products may not always provide the same efficacy as proper use of the individual components.’

The applicant has suggested that the only patients that would be prescribed Simbrinza would be
either; (1) where compliance with multiple drops is judged clinically as likely to be poor; &/or (2) where use of a greater total of drops per eye is likely to lead to promote ocular surface disease (and resulting subsequent additional care requirements) due to introduction of greater amounts of preservative into the conjunctival sac.

The JFG discussed the potential for lack of treatment compliance if patients administer multiple eye drops too quickly, and thus a reduction of absorption. This combination product would help eliminate this.

- **Patient safety** – Across the studies involving Simbrinza, there were few serious adverse events. Ocular adverse effects with the combination appear to be marginally additive compared with the constituent drugs. There is no safety data for use of the combination eye drops beyond 6 months, but longer term data are available for brinzolamide and brimonidine monotherapies. These show that adverse effects are usually transient and do not usually lead to treatment discontinuation. Serious adverse effects are either uncommon or rare.

- **Clinical effectiveness** – In a superiority study in people with glaucoma (n=560), at 3 months the mean change from baseline in diurnal intraocular pressure was statistically significantly lower in the group treated with brinzolamide/brimonidine combination eye drops compared with the groups treated with brinzolamide and brimonidine monotherapy (both p<0.0001). In a non-inferiority study in people with glaucoma (n=890), at 3 months brinzolamide/brimonidine was non-inferior to brinzolamide plus brimonidine administered concomitantly for mean change from baseline in diurnal intraocular pressure.

- **Cost effectiveness or resource impact** – Brinzolamide/brimonidine combination eye drops cost the same as the constituent products combined (£9.23 per 5 ml: 28-day treatment). Both patents have expired for brinzolamide and brimonidine individual constituents. A generic brimonidine eye drop is available however as yet there is no generic brinzolamide eye drop available. If a generic brinzolamide eye drop does become available, then the combination product will be more expensive.

- **Strength of evidence** – There are no published data comparing brinzolamide/brimonidine combination eye drops with other drug treatments used for managing glaucoma and ocular hypertension. The 2 studies were phase III studies that evaluated the efficacy and safety of brinzolamide/brimonidine combination eye drops using twice daily administration. One study was a superiority study, which compared brinzolamide/brimonidine eye drops with the individual constituent monotherapies, and the other was a non-inferiority study, which compared the combination with the 2 constituents used concomitantly. Both studies were double-blind randomised controlled trials in people with chronic open angle glaucoma or ocular hypertension, who were treated for 6 months. Participants were already using 2 or more intraocular pressure lowering medications or did not have sufficient improvement with monotherapy.

- **Place in therapy relative to available treatments** – The applicant suggested that this combination was already in use by the eye hospital, as 3rd or 4th line therapy. The treatment is currently being prescribed as single agent drops. The combination drops would only be used in patients in whom compliance is identified as an issue &/or where use of a greater total of drops per eye is likely to lead to promote ocular surface disease (and resulting subsequent additional care requirements) due to introduction of greater amounts of preservative into the conjunctival sac.

- **National guidance and priorities** – NICE guidance on glaucoma (CG85), NICE evidence summary on Simbrinza. SMC have accepted it for use within Scotland. The European Glaucoma Society recommends that the prescribing of more than two bottles for
simultaneous use should be avoided

- **Local health priorities** – Not stated as a local health priority.

- **Equity of access** – Other local formularies have included Simbrinza – e.g. Lincoln, Nottingham, Gloucester, Warrington, Leeds, Colchester, Pan Mersey. It is currently Non-formulary in York and Scarborough. The other combination eye drops are included on the BNSSG formulary in order to aid compliance.

The JFG considered the application, the evidence and information submitted. The evidence suggests that this combination is of benefit for some patients – patients are currently receiving this therapy but prescribed as two separate bottles. The JFG were unable to identify evidence to suggest that compliance and exposure to preservative were of significant issue and that a combination product would help reduce these, however it was recognised that the other combination products are available on the formulary. It was agreed to delay the decision until the next meeting when data on current prescribing and the potential time frame for generic versions of brinzolamide to be available can be presented.

**Action:**

1. **NB** to acquire prescribing figures of current combination products and time frame for generic brinzolamide for July meeting.

2. **NB** to add to July meeting agenda

**General Discussion re: Rheumatology applications**

The three rheumatology applications were identified during the presentation of the UHB Rheumatology Biologic pathway to the BNSSG NICE college. During the presentation, it was identified that there were three arms of the pathway that were currently using biologics that were not NICE approved, and not on the BNSSG formulary. The NBT and Weston pathways are currently being worked upon.

**4.2 Tocilizumab** - For adult patients with moderate/severe, active, rheumatoid arthritis who cannot take methotrexate. *Dr RP Consultant Rheumatologist, UHBristol.*

Please see application form for full details. Dr RP attended the meeting to present the application.

This application is to include tocilizumab (IV) for monotherapy in RA. The only three biologics that are licensed and NICE approved as monotherapy are Etanercept, Adalimumab and Certolizumab. Tocilizumab is licensed for monotherapy but not NICE’ed. NICE have approved IV tocilizumab use in TA 247 though this is only with methotrexate. Since the publication of the NICE TA, there has been more evidence which lead to it being licensed as monotherapy. There are a number of patients who can’t tolerate methotrexate. It has been approved by the SMC as monotherapy. All Wales have not approved IV tocilizumab monotherapy as they reflect NICE guidance. The British Society of Rheumatology has ‘approved’ its use.

The evidence clearly shows in the ADECTA trial that tocilizumab monotherapy was more beneficial in terms of disease activity compared to adalimumab monotherapy. Also the ACT-RAY study has shown that the addition of methotrexate to tocilizumab does not appear to offer clinical advantages in terms of disease remission.

A review of the NICE TAs for Rheumatoid arthritis involving adalimumab, etanercept, infliximab,
certolizumab pegol, golimumab, abatacept and tocilizumab is due to be published in October 2015 (review [ID537]). This may include the use of tocilizumab monotherapy.

If the patient did not have access to this treatment, they would be continued on a NICE approved biologic however their disease control would likely be sub-optimal. The number of patients is likely to be low – less than 10 per year at UHB. It has been suggested that the numbers at NBT are also likely to be less than 10. We are unaware of figures for Weston, but again, it is not likely to be high.

The costs presented suggest that the costs of IV tocilizumab IV is slightly more expensive than IV abatacept.

Dr RP was asked about SC tocilizumab. This could have the potential for cost savings and be more convenient to the patient. Dr RP was in agreement in looking at using SC tocilizumab monotherapy. A NDR for the SC preparation will be brought to the next meeting.

- **Patient safety** – In the ADACTA study, similar proportions of patients experienced at least one adverse event (AE): tocilizumab 82%, and adalimumab 83%. Serious AEs were reported in 12% tocilizumab patients and 10% adalimumab patients, and serious infections accounted for 3% in each group.

- **Clinical effectiveness** – Tocilizumab monotherapy has been shown to be more efficacious in terms of RA disease activity compared to adalimumab monotherapy. The ACT-RAY study also showed that the addition of methotrexate to tocilizumab did not offer any clinical advantage.

- **Cost effectiveness or resource impact** – The costs presented show that IV tocilizumab is slightly more expensive than the other treatments, though comparable to abatacept IV.

- **Strength of evidence** – The evidence is from a phase IV, and two phase III studies of tocilizumab as monotherapy: ADACTA, AMBITION and a 24-week interim analysis of an ongoing two-year study, ACT-RAY. The trials were heavily sponsored by Roche. However they were well designed trials. The ADACTA study excluded patients who had previously been treated with biologic therapy and so does not generalize to patients who would be treated in such a biologic sequence.

- **Place in therapy relative to available treatments** – As per the UHB biologic pathway. Awaiting NBT and Weston pathways.

- **National guidance and priorities** – SMC have approved monotherapy use. The British Society of Rheumatology have recommended the use of

- **Local health priorities** – High, to improve QoL of patients with RA.

- **Equity of access** – Other local formularies have approved tocilizumab monotherapy use e.g. Worcestershire, Leicestershire, Telford and Wrekin. If a patient was able to tolerate methotrexate, they would be eligible for treatment with tocilizumab under NICE TA247.

The JFG considered the application, the evidence and information submitted. For patients that can’t tolerate methotrexate, tocilizumab monotherapy is a further treatment option. There is good evidence to suggest that tocilizumab monotherapy is more effective than adalimumab monotherapy. The JFG approved tocilizumab monotherapy for inclusion onto the BNSSG formulary, TLS Red.
Action:

1. **NB** to inform applicant.

2. **NB** to include on the formulary, TLS Red

3. Trusts to report activity through the NICE college, and database to be kept for audit purposes for individual indications.

4.3 Abatacept (SC) - For adult patients with moderate/ severe, active, rheumatoid arthritis, in combination with methotrexate. Dr RP, Consultant Rheumatologist, UHBristol.

Please see application form for full details. Dr RP attended the meeting to present the application.

This application is for the use of SC abatacept in place of IV which is NICE approved (NICE TA 195 and 280). Subcut abatacept is licensed in the same way as IV. The group were provided evidence that a direct head-to-head randomized Phase IIIB study had compared both formulations in terms of clinical efficacy where non-inferiority was demonstrated. Also, there is evidence that showed that abatacept is equally as efficacious as SC adalimumab. The NICE technology appraisals 195 and 280 recommending abatacept only considered the intravenous infusion preparation, and only use in combination with methotrexate. NICE will not re-consider this particular TA since the indications for SC are the same as the IV, and therefore NICE would consider them to be equally efficacious. However, a review of the NICE TAs for Rheumatoid arthritis involving adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, abatacept and tocilizumab is due to be published in October 2015 (review [ID537]). This may include the use of SC abatacept. SMC have approved the use of SC abatacept.

There are a number of advantages to using the SC route – potential for a reduction in drug costs, and it offers a more convenient treatment for the patient, who can self-administer, bringing care close to the home for the patient, and reducing the burden on hospital based services.

The figures presented suggest that there are cost savings to be made if patients were able to have SC abatacept in place of the IV infusion. This is due to savings made on cost of treatment is provided by Homecare agencies and thus saving VAT and also a reduction in activity costs, as patients won’t need the number of out-patient attendances.

There is a patient access scheme in operation for abatacept when used in the NHS which applies to both the IV and SC preparations.

- **Patient safety** – The ACQUIRE study compared IV and SC abatacept which showed that the side effect profile of SC was consistent with IV abatacept.

- **Clinical effectiveness** – The ACQUIRE study compared IV and SC abatacept and concluded that the SC formulation was non-inferior in terms of efficacy.

- **Cost effectiveness or resource impact** – The use of SC will reduce drug costs if supplied via Homecare (saves VAT costs). Also activity costs will be reduced as the patient will not require monthly visits to out patients for IV infusion.

- **Strength of evidence** – The trials were of sound methodological quality.

- **Place in therapy relative to available treatments** – To be used in place of IV abatacept in those patients who can administer at home.
• **National guidance and priorities** – Not approved by NICE as it wasn’t licensed at the time of the TA. May be included in the review later this year. SMC have approved its use.

• **Local health priorities** – Would reduce out-patient visits, and therefore pressure on these services, however beds would still be filled.

• **Equity of access** – Other formularies include SC route e.g. Portsmouth, Northampton, Midlands and Lancashire.

The JFG considered the application, the evidence and information submitted. SC abatacept is licensed in the same way as IV and has shown clinical equivalence. The SC route has a number of advantages to the patient and to the local health economy. Therefore it has been approved for inclusion onto the formulary, TLS Red.

**Action:**

1. **NB** to inform applicant.
2. **NB** to include on the formulary, TLS Red.
3. **Trusts** to report activity through the NICE college, and database to be kept for audit purposes for individual indications.

**4.4 Rituximab in combination with Leflunomide** - For adult patients with severe, active, rheumatoid arthritis who cannot take methotrexate and who have had inadequate response or intolerance to other DMARDs and one or more anti-TNF therapies. **Dr RP, Consultant Rheumatologist, UH Bristol.**

Please see application form for full details. Dr RP attended the meeting to present the application.

This application is for the inclusion of rituximab for the treatment of RA, using leflunomide as the anchor medication in place of methotrexate, due to intolerance.

Rituximab was approved by NICE in 2010 (NICE TA195) for the second line treatment of RA post anti-TNF therapy, in combination with methotrexate. There is a cohort of patients who can’t tolerate methotrexate and therefore leflunomide is a suitable alternative, and is recommended by the European League against rheumatism. The evidence for off-license use of rituximab in combination with a non-methotrexate DMARD is limited and characterised by a few small studies of low methodological quality and short follow up. The evidence demonstrates equivalent efficacy with rituximab plus methotrexate although potentially a less favourable safety profile. It is a costly therapy although one of the least costly biologics.

The literature found shows that using leflunomide in place of methotrexate is common practice both nationally and internationally.

It has been suggested that the numbers at NBT are also likely to be less than 10. We are unaware of figures for Weston, but again, it is not likely to be high.

Rituximab is only licensed for RA in combination with methotrexate and therefore this would be an off-label use.

• **Patient safety** – Despite their different modes of action, methotrexate and leflunomide have similar side-effect profiles. The most common adverse events reported with both these agents include gastrointestinal upset, hepatotoxicity, alopecia, and infection.
Though original studies have shown similar incidence and severity of these side-effects, post-marketing studies have shown more toxicity with leflunomide.

- **Clinical effectiveness** – There are no RCTs comparing rituximab plus methotrexate with rituximab plus leflunomide. Pseudo-comparative data comes from both small and large observational studies comparing predominantly disease activity outcomes in cohorts of patients who have received either rituximab plus methotrexate or rituximab plus leflunomide. Most of these studies find no difference in outcomes between the two regimens implying equivalence. There is very limited, tentative evidence that rituximab plus leflunomide may in fact be superior to rituximab plus methotrexate; however, differences in patients’ characteristics, dose regimens and methodological limitations of the studies may explain the findings.

- **Cost effectiveness or resource impact** – Little cost increase using leflunomide compared to methotrexate.

- **Strength of evidence** – Evidence is limited and characterised by a few small studies of low methodological quality and short follow-up. There are no RCTs comparing rituximab plus methotrexate with rituximab plus leflunomide.

- **Place in therapy relative to available treatments** – To be used third line in sero positive patients (there is some evidence to suggest that these patients respond better to rituximab). If a patient can tolerate methotrexate they would continue with this, however if they can't tolerate it, leflunomide would be prescribed instead.

- **National guidance and priorities** – NICE guidance does not advise for this particular patient cohort,

- **Local health priorities** – High, to improve QoL in patients with long term conditions.

- **Equity of access** – Difficult to assess local formularies, as often the detail is not included in terms of combination use. It appears that this is common practice however.

The JFG considered the application, the evidence and information submitted. Using leflunomide with rituximab appears to be common practice in patients who can't tolerate methotrexate. Whilst the evidence is not of high quality, it appears that using leflunomide instead of methotrexate is equally efficacious. The JFG approved the inclusion of rituximab in combination with leflunomide to be used as per NICE guidance in place of methotrexate. TLS Red.

**Action:**

1. **NB** to inform applicant.
2. **NB** to include on the formulary, TLS Red.
3. **Trusts** to report activity through the NICE college, and database to be kept for audit purposes for individual indications.

5 **Shared Care Protocols/TLS status**

- No SCPs to discuss
6 Individual Funding Requests

NM commented that he was undertaking a piece of work looking at the pathway for overactive bladder treatment.

Action:
1. **SB/NB/JC** to liaise with NM.

7 Chapter review and formulary process

JC updated the group with the progress of reviewing the chapters. More chapters are in the process of consultation. It is important that we engage as many people with this process as possible. There been various meetings so far to discuss the comments from the specialist consultation.

8 Items for Discussion

8.1 NDRs for July Meeting (no papers, for information only)

a. **Palonsetron** - For patients at high risk of chemotherapy induced nausea and vomiting, NBT

b. **Sodium oxybate** - Narcolepsy and cataplexy, NBT

c. **Tocilizumab** - SC for the treatment of RA in accordance with NICE TA 247 but via SC not IV, NBT/UHB/Weston.

8.2 Medicinal devices vs Medicinal products for formulary review

NB raised the issue of certain medical devices and their relationship with the BNSSG Joint Formulary. We are often contacted for advice from primary care about certain devices which are prescribeable on the NHS. Historically, the formulary has not looked at devices, only medicinal products, however there is clearly a need for guidance on some devices e.g. therabite. Currently these are being recommended, and yet, there has been no assessment of clinical efficacy and cost. It was decided that if the device is for a medicinal purpose then the JFG would consider it. We will have to be pragmatic in terms of which we consider.

9 AOB

None.

NB
Interface Pharmacist
15th June 2015
### BNSSG JFG

#### Action Log for 2nd June 2015

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<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
<th>Responsible Officer</th>
<th>Deadline</th>
<th>Date of Update</th>
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<td>02.06.15</td>
<td>2.2</td>
<td>Wound care formulary</td>
<td>Ensure that all of the individual trust’s wound care formularies are on the BNSSG JF website – each organisation to feedback to NB</td>
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<td>NICE TAs</td>
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<td>Slimbrinza NDR</td>
<td>Bring back to the next meeting with epact data and information on generic availability.</td>
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<td>4.4</td>
<td>Rituximab plus leflunomide NDR</td>
<td>Include on the formulary</td>
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<td>02.06.15</td>
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<td>Overactive bladder</td>
<td>Liaise with NM</td>
<td>SB/NB/JC</td>
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#### MEETING DATES 2015

<table>
<thead>
<tr>
<th>Date</th>
<th>Cut off for NDRs and SCPs</th>
<th>Time</th>
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<tbody>
<tr>
<td>Tuesday 20th January</td>
<td>9th December</td>
<td>9am – 12 midday</td>
<td>Pharmacy Seminar Room Southmead Hospital</td>
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<tr>
<td>Tuesday 3rd March</td>
<td>20th January</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room, South Plaza</td>
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<td>10th March</td>
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<td>2nd June</td>
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<td>Tuesday 24th November</td>
<td>13th October</td>
<td>1.30 – 4.30pm</td>
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BNSSG Joint Formulary Group
Meeting held on: Tuesday 14th July 2015  9am -12midday
Pharmacy Seminar Room, Southmead Hospital, Brunel Building

Minutes

Present:

Interface Pharmacist, NHS Bristol CCG
Interface Pharmacist, NHS Bristol CCG
Pharmacoeconomics and Interface Pharmacist, NBT
Clinical Effectiveness Research Lead, Bristol City Council
GP Bristol and member of Bristol CCG board
Public Health Consultant, Bristol City Council (Chair) (until 10.30am)
Deputy HoMM, NHS Bristol CCG
Consultant Neurologist, NBT
GP, North Somerset
Principal Pharmacist, UHBristol NHS Foundation Trust
Deputy HoMM, NHS North Somerset CCG
Deputy HoMM, NHS South Gloucestershire CCG
GP, North Somerset

Apologies:

Consultant Renal Physician, and Joint D&TC Chair, NBT
Joint D&TC Chair, North Bristol NHS Trust
Director of Pharmacy, Weston General Hospital
GP, Bristol
Head of IFR for BNSSSG
HoMM, North Somerset CCG
HoMM, South Gloucestershire CCG
Deputy Chief Pharmacist, Weston General Hospital

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest
None

The meeting quorate.

2 Minutes of the meeting of 2nd June 2015 and Matters arising
The minutes from the Joint Formulary Group (JFG) meeting on the 2nd June 2015 had been circulated by NB following the meeting. No comments had been received via email that needed further discussion.

Matters arising from 2nd June 2015 meeting

2.1 Wound Care Formulary

- NB reported back to the JFG that there was now a new section on the JF website for Wound care to host each organisation’s version of the Pan Avon Wound Care Formulary. Currently the Bristol CCG, UHB, South Glos CCG and Weston Hospital’s formulary have been uploaded. We are awaiting a minor amendment of the North Somerset version and then this will be added.

Action:
1. MP to locate an e-copy of NBT’s wound care formulary to send to NB.
2. NB to add line on website to make it clear which formulary applies to which organisation.

2.2 Simbrinza New Drug Application

- Discussed in the New Drug Request section below.

3 NICE New Technology Appraisals

Published

3.1 Omalizumab for previously treated chronic spontaneous urticaria. TA339.
   TLS Red

3.2 Ustekinumab for treating active psoriatic arthritis (rapid review of technology appraisal guidance 313) TA340
   TLS Red

3.3 Apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism TA341
   - Already included on the formulary; SCP to be discussed below.

3.4 Vedolizumab for treating moderately to severely active ulcerative colitis TA342
   TLS Red

3.5 Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia TA343
   TLS Red

3.6 Ofatumumab in combination with chlorambucil or bendamustine for untreated chronic lymphocytic leukaemia TA344
   TLS Red

Adopted into the BNSSG Joint Formulary – June 2015

- Rivaroxaban for preventing adverse outcomes after acute management of acute
coronary syndrome. TA335 TLS amber – SCP to be discussed later
• Empagliflozin in combination therapy for treating type 2 diabetes. TA336 TLS blue

4 New Drug Requests (NDRs)

SUMMARY

4.1 Palonsetron - For adults for the prevention of acute nausea and vomiting associated with highly emetogenic cancer chemotherapy.

Agreed for inclusion on the formulary. The evidence suggests that palonsetron is more effective than the older 5HT3 antagonists. It is significantly more expensive, however the cohort suggested in the application is a small and refined cohort. The JFG agreed for the inclusion of palonsetron on the formulary for young adults who are being treated for Hodgkin’s lymphoma, TLS Red. UHB and Weston to consider their current needs for introducing it in this cohort within their trust.

4.2 Tocilizumab (SC) – For adults with moderate to severe rheumatoid arthritis who have responded inadequately or intolerant to DMARDs or TNF antagonists. In accordance with NICE TA 247.

Agreed for inclusion onto the formulary. The ability to use SC tocilizumab has a number of benefits – patients will be able to administer their own injections at home, which is more convenient than a monthly hospital day case attendance and will also bring about cost savings to the local health economy with the removal of VAT on the drug costs using homecare, and also activity costs will be minimised. TLS Red. This decision is only applicable to the use of tocilizumab in RA.

4.3 Simbrinza (Brinzolamide & Brimonidine) - Glaucoma or ocular hypertension when monotherapy provides insufficient control

Agreed for inclusion onto the formulary. Simbrinza is a combination eye drop which contains brinzolamide and brimonidine – a combination which is already prescribed as the separate constituents. It is cost neutral compared to the separate constituents and a generic brinzolamide does not appear to be imminently available. The combination product would help compliance, especially if the patient is on triple therapy. TLS blue.

Decision Criteria used by JFG for NDR

• Patient safety
• Clinical effectiveness
• Cost effectiveness or resource impact
• Strength of evidence
• Place in therapy relative to available treatments
• National guidance and priorities
• Local health priorities
• Equity of access

Full Discussion

4.1 Palonsetron - For adults for the prevention of acute nausea and vomiting associated with
The application was for the inclusion of oral and intravenous palonsetron, a second generation 5HT₃ antagonist. It has high binding affinity and selectivity for the 5HT₃ receptor, and an elimination half-life of about 40 hours. It is licensed for the prevention of chemotherapy induced nausea and vomiting (CINV) in patients receiving moderately emetogenic chemotherapy (MEC), and in patients receiving highly emetogenic chemotherapy (HEC) it is licensed for the prevention of CINV in the acute phase (0-24 hours after administration of chemotherapy).

It is a different generation and different mode of action compared to the standard care currently given i.e. ondansetron and granisetron. There have been a number of RCTs involving palonsetron and standard practice. 5 meta analyses have been identified, and 4 of these are of good methodological quality. The results indicate that palonsetron is beneficial in MEC and HEC but of particular benefit in MEC regimes and delayed CINV as opposed to acute sickness. Therefore it will be important to identify the particular cohort of patients. It is significantly more expensive than standard care, and it is not excluded from the tariff therefore will require directorate approval. At this current time, we are unaware of the UHB and Weston opinion for the use of palonsetron.

A search of formularies found that there is a 50:50 split in terms of those that include it and those that don't, although some areas have not considered it for inclusion.

Discussion with Dr SO

There is a very specific cohort of patients that are vulnerable to the emetic effect of chemotherapy and experience prolonged vomiting after treatment and typically these are young adults with Hodgkin’s Lymphoma. This isn’t a large cohort of patients, however the current chemotherapy regime for these patients (Doxorubicin, Bleomycin, Vincristine and Dacarbazine (ABVD)) is particularly demanding for patients. Patients are required to attend the unit on days 1 and 15 for the whole day, for 6 cycles, and the major issue is the delayed and anticipatory vomiting, which can be extremely distressing for the patient. The number of patients is about 5 – 6 per year. Conventional anti emetics work well but for a short duration of action. The knowledge and memory of the vomiting impacts on future cycles and can cause anticipatory vomiting.

Palonsetron has been used a lot in the private sector with good results. It has an excellent safety profile, and does not affect the QT interval as the first generation 5HT₃ antagonists do.

The application is for both the IV and oral preparation but in reality, the IV preparation is more likely to be used as it will form part of the standard package of treatment for these patients, and used only once per cycle. The use would be written into the protocol for Hodgkin lymphoma treatment.

All chemotherapy would be given in secondary care, and therefore it should be given a TLS of red.

The medical director has approved the use of palonsetron in SMH if the JFG approve the application.

• **Patient safety** – In contrast to the first generation 5HT₃ antagonists, QTc prolongation has not been described with palonsetron. The BNF lists the main adverse events associated with its use as diarrhoea, constipation, headache and dizziness.

• **Clinical effectiveness** – Efficacy of palonsetron has been evaluated in numerous RCTs
comparing outcomes with older 5HT₃ receptor antagonists. Some trials have focused purely on prophylaxis for particular HEC or MEC regimes; others have focussed on impact of addition of corticosteroids to the regimes or have used palonsetron at different doses; others have considered particular diseases. A total of 5 systematic reviews and meta-analyses/pooled analysis data were found. All demonstrate that palonsetron provides superior prophylaxis of CINV compared to older 5HT₃ receptor antagonists. The best evidence for this effect appears to be during the delayed phase with use of MEC. Evidence for efficacy of palonsetron in the acute phase or with HEC is slightly more conflicting.

- **Cost effectiveness or resource impact** – Palonsetron costs £55.89 per chemotherapy cycle. It is difficult to compare with alternatives due to the different regimes used however it is significantly more expensive than generic ondansetron – 10, 8mg tablets currently cost £3.71.

- **Strength of evidence** – 5 systematic reviews and meta-analyses/pooled data, 4 of which were of good methodological quality. They consisted of different inclusions and exclusion criteria, with varying different end points.

- **Place in therapy relative to available treatments** – The evidence seems to suggest superior efficacy compared to the alternative first generation 5HT₃ antagonists, however conflicting evidence to suggest in which cohorts it would be of most benefit. It will represent a significant cost pressure to the trusts (it is in-tariff). The applicant suggests that the cohort of patients that would benefit by using palonsetron are the young adults being treated for Hodgkin’s lymphoma, and would significantly help reduce the risk of anticipatory nausea and vomiting.

- **National guidance and priorities** – NICE have not reviewed palonsetron. SMC have approved both the IV and the oral preparation for use in Scotland. The IV preparation is accepted for the prevention of nausea and vomiting associated with HEC and MEC and the oral preparation is accepted for the prevention of nausea and vomiting associated with MEC. Palonsetron is included in a number of national guidelines.

- **Local health priorities** – Not stated as a local health priority. Use of palonsetron may improve patient functional status and quality of life post chemotherapy and may reduce hospital visits and administration for post chemotherapy.

- **Equity of access** – Other local formularies have included palonsetron about half of those formularies identified included it. However some formularies have not considered it.

The JFG considered the application, the evidence and information submitted. The evidence suggests that palonsetron is more effective than the older 5HT₃ antagonists. It is significantly more expensive, however the cohort suggested in the application is a small and refined cohort. The JFG agreed for the inclusion of palonsetron on the formulary for young adults who are being treated for Hodgkin’s lymphoma, TLS Red. UHB and Weston to consider their current needs for introducing it in this cohort within their trust.

**Action:**

1. **NB** to inform applicant.
2. **KG/Weston** to inquire within UHB and Weston if it is required within their trusts.
3. **NB** to include on the formulary website.
4.2 **Tocilizumab (SC)** – For adults with moderate to severe rheumatoid arthritis who have responded inadequately or intolerant to DMARDs or TNF antagonists. In accordance with NICE TA 247. SB, on behalf of the NICE college and NBT/UHB/Weston, Deputy Head of Medicines Management, Bristol CCG.

Please see application form for full details.

This application is to include the sub cutaneous preparation of tocilizumab in the same way that the intravenous preparation is included i.e. as per TA 247 and also as monotherapy as per agreed at the JFG June 2015. The SC preparation is licensed as the IV i.e. in combination with methotrexate for the treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to previous therapy with one or more disease-modifying anti-rheumatic drugs or TNF antagonists. Current NICE guidance on the use of tocilizumab (TA 247) relates only to the use of the IV infusion and provides no guidance specific to the use of tocilizumab SC which was not available at the time of the publication. NICE have confirmed that they will not be publishing a new TA specifically looking at the prefilled syringe since the indications for its use remain the same; they have confirmed that commissioners may choose the SC preparation over the IV preparation. However a review of the NICE TAs for RA involving adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, abatacept and tocilizumab is due to be published in October 2015 (ID537).

The SMC have approved SC tocilizumab for use in Scotland.

Not all patients will be suitable to use the SC preparation, however SC offers a number of advantages – potential for a reduction in drug costs and hospital attendances, and it offers a more convenient treatment for the patient who can self-administer, bringing care closer to home for the patient and reducing the burden on hospital based services. Therefore it has the potential for savings for the local health economy when drug costs and attendances are taken into account – the ability to use homecare services and therefore save the VAT on the drug costs included.

Current there are about 20 patients in each trust on tocilizumab (10 - 15 in UHB, 10 – 15 Weston and 26 in NBT). The ability to use it as monotherapy and as a SC preparation will have the potential to increase the patient numbers as it could be offered higher up the patient pathway. The current UHB Rheumatology biologic pathway was presented to the BNSSG NICE college in 2014, and the NBT and Weston ones are being worked on currently.

The SUMMACTA trial is the pivotal trial that showed non-inferiority of the SC preparation compared to the IV preparation. It was also comparable in safety outcomes. More reported injection site reactions for the SC preparation were identified in the trial, therefore it will be necessary to monitor patients as all SC preparations.

In terms cost, the cost of the drug is available through a PAS scheme from the company. When all costs are considered, it has the potential of saving the local health economy around £5000 per patient per year. Any gain share agreements agreed are outside of the remit of the JFG.

- **Patient safety** – In the SUMMACTA study, SC tocilizumab demonstrated a safety profile comparable to IV with the exception of injection site reactions. However the incident rate of reaction (10.1%) was similar to that reported in studies in patients with RA who received other subcutaneous anti-TNF inhibitors.

- **Clinical effectiveness** – In the SUMMACTA study, SC tocilizumab demonstrated an efficacy profile similar to IV tocilizumab.

- **Cost effectiveness or resource impact** – The costs presented show that IV tocilizumab
is slightly more expensive than the other treatments, though comparable to abatacept IV. The use of the SC preparation will realise savings to the local health economy by a reduction in activity costs as patients do not require monthly day case appointments and also VAT savings by using homecare services.

- **Strength of evidence** – The evidence is from a well-designed 2 year randomised active controlled double dummy parallel group, phase III multicentre non-inferiority study of the safety and efficacy of SC vs IV tocilizumab.

- **Place in therapy relative to available treatments** – As per the UHB biologic pathway. Awaiting NBT and Weston pathways. It would be offered where the IV preparation is currently offered. The addition of monotherapy (as per June 2015 JFG decision) and as SC has the potential to alter the local pathways as the choice of agent at the time of initiation was largely governed by whether or not a IV infusion or SC preparation was the preferred route.

- **National guidance and priorities** – SMC have accepted its use.

- **Local health priorities** – High, to improve QoL of patients with RA and bringing patients care closer to home. Additionally reducing hospital attendances therefore reducing burden on overstretched resources.

- **Equity of access** – Other local formularies have approved SC tocilizumab. SC abatacept was approved for use within BNSSG in June 2015.

The JFG considered the application, the evidence and information submitted. The ability to use SC tocilizumab has a number of benefits – patients will be able to administer their own injections at home, which is more convenient than a monthly hospital day case attendance and will also bring about cost savings to the local health economy with the removal of VAT on the drug costs using homecare, and also activity costs will be minimised. The JFG approved SC tocilizumab in combination with methotrexate and as monotherapy for inclusion onto the BNSSG formulary, TLS Red. This decision is only applicable to the use of tocilizumab in RA.

**Action:**

1. **NB** to inform applicant.
2. **NB** to include on the formulary, TLS Red
3. **Trusts** to report activity through the NICE college, and database to be kept for audit purposes for individual indications.

**4.3 Simbrinza (Brinzolamide & Brimonidine)** - Glaucoma or ocular hypertension when monotherapy provides insufficient control. **Mr PS, Consultant Ophthalmologist, UHBristol RE-DISCUSSION**

Follow up discussion after the initial discussion of the NDR at the June 2015 meeting.

At the June 2015 JFG, the application was discussed however a final decision was not able to be reached. Simbrinza is a combination eye drop (brinzolamide and brimonidine) for the treatment of glaucoma and ocular hypertension. The JFG recognised that the combination product would lead to a reduction in the number of eye drops required and ultimately the exposure to preservative. However there does not appear to be any evidence to show that these are currently
issues and that the use of a combination product would benefit. A number of other combination products are on the formulary however they all contain the beta blocker timolol. These would not be appropriate if the patient could not use a beta blocker. The acquisition cost of Simbrinza is similar to the generic brimonidine and branded brinzolamide. If a generic brinzolamide became available, the use of Simbrinza would present a cost pressure, largely in primary care. The JFG requested more information on the potential availability of a generic brinzolamide and also current primary care prescribing trends.

The NICE clinical guideline for glaucoma (CG 85, April 2009) states that ‘combination products may not always provide the same efficacy as proper use of the individual components.’ However it is difficult to assess ‘proper’ use and we do not have a figure for the number of patients who are completely compliant with multiple eye drop administration i.e. leaving time between administering two different eye drops.

The NICE evidence summary for Simbrinza states that ‘combination therapies are preferred to aid compliance and decrease preservative exposure. For patients currently requiring triple therapy, but in whom beta blockers should be avoided, three bottles of eye drops are required. The European Glaucoma Society recommends that the prescribing of more than two bottles for simultaneous use should be avoided.

No information could be obtained to suggest when/if a generic brinzolamide preparation may become available, therefore for the current time, the prescribing costs are as per the application and Simbrinza is cost neutral compared to prescribing the individual components.

Current prescribing trends across BNSSG show that in May 14 – April 15, brinzolamide and brimonidine are in the top 6 eye drops prescribed. The BNSSG spend on glaucoma eye drops in this period was £1,303,698.60. The proportion of prescriptions written for combination eye drops represent 16% of the total number of prescriptions for glaucoma eye drops and account for 22% of the total spend.

The JFG considered the application, the evidence and information submitted. Simbrinza is a combination eye drop which contains brinzolamide and brimonidine – a combination which is already prescribed as the separate constituents. It is cost neutral compared to the separate constituents and a generic brinzolamide does not appear to be imminently available. The combination product would help compliance, especially if the patient is on triple therapy. The JFG agreed for the inclusion on the formulary, TLS blue.

**Action:**

1. **NB** to inform applicant.
2. **NB** to include on the formulary, TLS blue.

5 Shared Care Protocols/TLS status

5.1 **Rifaximin SCP (NEW)**

The JFG agreed for rifaximin to change to amber 3 months at the April 2015 meeting. A SCP was subsequently developed and shared around the trusts. NBT and Weston are happy with the content, but we are awaiting UHB comments. It was stated that that the reason for the application for rifaximin to go amber was so that access to the medicine was easier for the patient. The JFG had a more in depth discussion about access to prescriptions for patients and that this shouldn’t be the reason why drugs are classified as amber, as potentially GPs will be asked to prescribe
medicines for which they have limited clinical experience. The issue of repeat dispensing and access to prescriptions for specialist medicines from the acute trusts requires more work and would be considered outside of the JFG. The reason for moving a medicine from red to amber should be clinically driven and not due to access for patients. In this instance, the issues that GPs had with the rifaximin SCP were more about the monitoring of a patient with hepatic encephalopathy and less with rifaximin itself. It is confirmed in the SCP that patients will be seen at no less than 6 monthly intervals by a specialist. There is no specific monitoring relating to the prescription of rifaximin that wouldn’t be picked up by the specialist review. Some minor amendments are required so that it is clear for the GP that they are not required to take on any additional monitoring. The JFG are approved the SCP after these amendments have been made.

**Action:**

1. **NB/JC** to amend SCP and agree changes with trusts.
2. **NB** to upload onto the formulary and change rifaximin to amber 3 months.
3. **NB** to set up meeting to discuss the delivery of drugs from primary and secondary care and the relationship of the TLS.

**5.2 Hydroxycarbamide SCP updated UHB SCP to include NBT**

This is an update and review of the current SCP to include NBT. The SCP has been reviewed and agreed with the specialists in NBT and UHB. Weston need to review it. The JFG agreed the SCP.

**Action:**

1. **JT** to send SCP for Weston to review and to supply contact details.
2. **NB** to upload onto the formulary.

**5.3 Dabigatran SCP for treatment and prevention of DVT/PE (NEW)**

The SCP has been sent out for comments from the acute trusts. No comments have so far been received. The SCP was based on the current SCP for Rivaroxaban for the treatment and prevention of DVT/PE. It needs to be clear that the 5 days of parenteral therapy is the responsibility of the specialist.

**Action:**

1. **MP/KG/Weston** to send SCP to haematologists for comments.
2. **NB/JC** to coordinate comments and changes to be made.
3. **NB** to upload onto the formulary once agreed via email.

**5.4 Apixaban SCP for treatment and prevention of DVT/PE (NEW)**

As above (dabigatran).
**Action:**

1. **MP/KG/Weston** to send SCP to haematologists for comments.
2. **NB/JC** to coordinate comments and changes to be made.
3. **NB** to upload onto the formulary once agreed via email.

5.5 **Rivaroxaban SCP for ACS (NEW)**

The SCP has been developed following the NICE approval for use in ACS and it was agreed at the JFG in April 15 that for this indication rivaroxaban should be amber 1 month. The SCP has been sent out for comments from the acute trusts. No comments have so far been received. JB commented that there are anxieties about patients being discharged on triple therapy for ACS and there is no guidance about what you should do if the patient bleeds and which drug should be stopped. The acute trusts ACS guidelines should be added to the website as this may provide some information.

**Action:**

1. **MP/KG/Weston** to send SCP to haematologists for comments.
2. **NB/JC** to coordinate comments and changes to be made.
3. **NB** to upload onto the formulary once agreed via email.
4. **NB** to upload trust’s ACS guidelines.

5.6 **Lisdexamfetamine for adult ADHD (NEW)**

The JFG agreed for lisdexamfetamine to change to amber 3 months at the January 2015 JFG. The SCP has been developed with Dr DH at AWP and is based on the current methylphenidate SCP. There was some discussion about the physical monitoring and the JFG felt that it should be the initial prescriber’s responsibility to carry out these baseline tests and therefore the SCP should reflect this. The methylphenidate and depot antipsychotic SCPs to be altered to reflect this too. Some minor amendments required and then the JFG agreed the SCP.

**Action:**

1. **NB** to amend SCP and liaise with AWP.
2. **NB** to upload onto the formulary.
3. **NB** to ascertain whether the specialists are happy with dexamfetamine to be removed from the formulary.

5.7 **Atomoxetine Change in status request – Red to amber**

The JFG agreed for atomoxetine for the treatment of adult ADHD to go to amber 3 months in the same way that methylphenidate mr and lisdexamfetamine are. A SCP will need to be written and agreed.
Action:

1. **NB** to liaise with AWP and bring SCP back to JFG for agreement.

5.8 **Colesevelam Change in status request – Red to amber**

Colesevelam was agreed to be included on the formulary for the treatment of bile acid malabsorption in June 2014. At this time, the applicant (Dr RP, Consultant Gastroenterologist NBT) felt that a TLS of Red would be appropriate. However in time, it may be suitable for GPs to take over the prescribing in stable patients. Colesevelam is relatively straightforward to prescribe – patients will be initiated in secondary care, and will be seen again in clinic to ascertain that it is working. At this stage, if there is clear indication that it is effective, and tolerated by the patient, the prescribing could be taken on by GPs. The JFG agreed for the change in status to amber 3 months and a SCP will be required to be written and agreed.

Action:

1. **NB** to inform applicant and coordinate a SCP across BNSSG.

5.9 **Dymista Change in status request /formulary extension**

Dymista was agreed for inclusion on the formulary in November 2014, for ‘patients referred to immunology with moderate to severe seasonal and perennial allergic rhinitis in those who otherwise could be considering de-sensitisation therapy.’ It was agreed to be amber (specialist recommendation, no SCP) and therefore could be recommended by specialists, but initiated and prescribed by GPs on this recommendation. This application is for Dymista to be recommended by ENT (UHB request) and therefore opening up the cohort. The JFG discussed that the management of rhinitis should be managed in primary care as much as possible, and this is more about where Dymista fits in the pathway – more work is required to enable the JFG to assess.

Action:

1. **NB/JC** to liaise with ENT about the rhinitis pathway and to consider Dymista’s place in therapy.

**General discussion about process of TLS change requests and SCPs.** At times there has been duplication of discussion at different meetings (currently the TLS change in status request is discussed at one meeting, and if agreed, a SCP is discussed at a subsequent meeting), and often not sufficient information on the TLS change application to fully discuss a request. It was felt that a SCP was required at the time of discussing a TLS change so that we had all the information and that only one discussion was required.

6 **Individual Funding Requests**

No information to share.

7 **Chapter review and formulary process**
JC updated the group with the progress of reviewing the chapters. All of the chapters are currently out at different stages of review. Meetings for reviewing the chapters are continuing as we are currently receiving good comments and engagement with the process. The review should be complete by the end of the year.

8 Items for Discussion

8.1 NDRs for September Meeting (no papers, for information only)
   a. Sodium oxybate – narcolepsy and cataplexy (adults) NBT
   b. Synvisc – osteoarthritis NBT TBC.
   c. Glycopyrronium – drooling TBC

8.2 Non-formulary and the TLS

NB raised the issue of how medicines that are non-formulary should be classified in terms of the TLS. Non-formulary medicines are not considered red routinely. There will be instances where deviating from the formulary is necessary and so prescribers need to consider their own clinical competence to decide who the most appropriate clinician is to prescribe. Advice is available from the medicines management teams in the CCGs if GPs require this.

9 AOB

9.1 Botox for urinary incontinence

SB updated the group on the progress with the botox in urinary incontinence application. As the group is aware, the JFG approved the use of botox in urinary incontinence clinically (April 2014), however were not able to fully approve its use based on the financial information and potential cost pressure for the CCGs. This required further approval outside of the JFG.

Bristol CCG transferred the NBT business case in to a QIPP initiative based on the savings shown for the 2015/16 annual planning round and circulated to all CCGs. The initiative was not accepted in to the planning round because the anticipated savings expressed in the business case did not carry an absolute certainty of savings in year and this was agreed by all 3 CCG prescribing leads. SB felt that further work could be done to show realistic savings through NBT finance and commissioning perhaps working on an overall pathway approach with commissioners and Mr MD.

NB
Interface Pharmacist
20th July 2015
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<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
<th>Responsible Officer</th>
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<td>14.07.15</td>
<td>2.1</td>
<td>Wound care formulary</td>
<td>MP to provide NB copy of NBT’s wound care formulary.</td>
<td>MP/NB</td>
<td>September</td>
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<td>14.07.15</td>
<td>3</td>
<td>NICE TAs</td>
<td>Include positive NICE TAs onto the formulary in conjunction with NICE college</td>
<td>NB</td>
<td>90 days post publication</td>
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<tr>
<td>14.07.15</td>
<td>4.1</td>
<td>Palonsetron NDR</td>
<td>Include on the formulary (NBT only). Confirm with UHB and Weston if they require it within their trusts.</td>
<td>NB/JT/KG</td>
<td>August</td>
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<td>4.2</td>
<td>Tocilizumab NDR</td>
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<td>Simbrinza NDR</td>
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<td>14.07.15</td>
<td>5.1</td>
<td>Rifaximin SCP</td>
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<td>NB/JC</td>
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<td>NB/JC</td>
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<td>14.07.15</td>
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<td>Tuesday 20th January</td>
<td>9am – 12 midday</td>
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<td>Tuesday 3rd March</td>
<td>1.30 – 4.30pm</td>
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**Minutes Page 14 of 14**
BNSSG Joint Formulary Group
Meeting held on: Tuesday 13th October 2015 9am -12midday
Pharmacy Seminar Room, Southmead Hospital, Brunel Building

Minutes

Present:

Interface Pharmacist, NHS Bristol CCG
Interface Pharmacist, NHS Bristol CCG
Pharmacoeconomics and Interface Pharmacist, NBT
Public Health Consultant, Bristol City Council (Chair)
Consultant Neurologist, NBT
GP, North Somerset
Deputy HoMM, NHS North Somerset CCG
GP, North Somerset
HoMM, South Gloucestershire CCG
Deputy Chief Pharmacist, Weston General Hospital

Apologies:

Consultant Renal Physician, and Joint D&TC Chair, NBT
Director of Pharmacy, Weston General Hospital
Head of IFR for BNSSSG
HoMM, North Somerset CCG
Clinical Effectiveness Research Lead, Bristol City Council
GP Bristol and member of Bristol CCG board
Deputy HoMM, NHS Bristol CCG
Principal Pharmacist, UHBristol NHS Foundation Trust
Medicines Information Pharmacist, UHBristol NHS Foundation Trust

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest
None

The meeting was not quorate due to their not being any representation from UHB. The minutes will be sent around by email in accordance with the Terms of Reference. Members of the group to email NB if there are any areas of discussion required before the minutes are signed off.

2 Minutes of the meeting of 14th July 2015 and Matters arising
The minutes from the Joint Formulary Group (JFG) meeting on the 14th July 2015 had been circulated by NB following the meeting. No comments had been received via email that needed further discussion. These were agreed as accurate.

Matters arising from 14th July 2015 meeting

2.1 Palonsetron NDR

- NB reported back that following the approval of palonsetron to be included onto the formulary for use at NBT, UH Bristol have considered the application and do not consider that it has a place for use within their trust. Still awaiting information from Weston. It is currently included on the formulary for use within NBT only.

2.2 Action Log

- All actions from last meeting are either completed or in the process of being completed. Of note:
  - Wound care formulary – Await NBT to supply their formulary to include on the formulary website
  - Lisdexamfetamine SCP and atomoxetine change in status request – currently awaiting discussions regarding the monitoring arrangements.
  - Colesvelam change in status request – Dr Parker in Weston currently writing a SCP.

Actions:

1. **MP** to locate an e-copy of NBT’s wound care formulary to send to NB.

3 NICE New Technology Appraisals

Published

3.1 Naloxegol for treating opioid-induced constipation. **TA345**
JFG decision: TLS Blue

3.2 Aflibercept for treating diabetic macular oedema. **TA346**
JFG decision: TLS Red

3.3 Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer. **TA347**
JFG decision: TLS Red

3.4 Dexamethasone intravitreal implant for treating diabetic macular oedema. **TA349**
JFG decision: TLS Red

3.5 Secukinumab for treating moderate to severe plaque psoriasis. **TA350**
JFG decision: TLS Red

3.6 Vedolizumab for treating moderately to severely active Crohn's disease after prior therapy. **TA352**
JFG decision: TLS Red
3.7 Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism TA354
JFG decision: TLS Amber 1 month (see SCP section)

3.8 Edoxaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation TA355
JFG decision: TLS Green

3.9 Pembrolizumab for treating advanced melanoma after disease progression with ipilimumab TA357
JFG decision: TLS Red

Adopted into the BNSSG Joint Formulary – July, August and September 2015

- Omalizumab for previously treated chronic spontaneous urticaria. TA339 TLS Red
- Ustekinumab for treating active psoriatic arthritis (rapid review of technology appraisal guidance 313). TA340 TLS Red
- Vedolizumab for treating moderately to severely active ulcerative colitis. TA342 TLS Red
- Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia. TA343 TLS Red
- Ofatumumab in combination with chlorambucil or bendamustine for untreated chronic lymphocytic leukaemia. TA344 TLS Red

4 New Drug Requests (NDRs)

SUMMARY

4.1 Sodium Oxybate – Narcolepsy with cataplexy (adults).

The evidence base although limited does provide evidence that sodium oxybate can reduce cataplexy attacks and other sleep related effects of narcolepsy with cataplexy. The impact of this on the patients’ quality of life has not been reported. This is a very small number of patients, and in whom treatment options are limited. However this is an expensive treatment option, and the cost effectiveness is therefore limited. The JFG felt that the clinical case for including sodium oxybate on the formulary was satisfactory, however the financial aspects need further investigation; this would prove to be a cost pressure, and there are no cost offsets or savings.

The BNSSG JFG would therefore support a business case to be submitted by NBT to the CCGs.

4.2 Tiotropium & olodaterol (Spiolto) Respimat - COPD.

The use of LABA/LAMA combination inhalers is now well established in the COPD treatment pathway. It is clear that there is no clinical evidence to suggest that one combination inhaler is clinically any better than any other. All inhalers are mechanically different, and will be suitable for different patients. The ability to use the inhaler correctly is paramount to the success of COPD treatment. The JFG approved the inclusion of Spiolto onto the BNSSG formulary, TLS Blue. To follow up with the consultants regarding the potential to remove Ultibro from the formulary.

4.3 Glycopyrronium – Hypersalivation in Motor-neurone disease patients and children and young people with neurological conditions.

There is limited evidence, but the evidence available does suggest that this is a useful treatment option for hypersalivation in MND and NMDisorders. Anecdotally it is effective and well tolerated.
The JFG agreed for the inclusion onto the formulary for those MND patients and NMDisorder patients who have not responded to first line agents or are inappropriate. It was agreed for this to be TLS amber 3 months, and a SCP was also approved.

**4.4 Ulipristal** - for intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age.

Currently there are no approved long-term medical treatment options for the management of patients with symptomatic fibroids. The evidence from the PEARL IV study shows that repeated courses of ulipristal at 5mg and 10mg effectively controls bleeding and pain, reduces fibroid volume and restores quality of life. Ulipristal would be a useful alternative to those patients in whom surgery is not an option, but also may delay or even negate the need for surgical intervention. It is acknowledged that the drug costs may be increased however it is hoped that across the local health economy savings will be made in terms of reduction in secondary care referrals and surgery. The JFG approved the inclusion on the formulary, TLS amber 3 months, where the specialist prescribes the first course, but subsequent courses maybe prescribed by primary care under shared care protocol.

**Decision Criteria used by JFG for NDR**

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
- Equity of access

**Full Discussion**

**4.1 Sodium Oxybate** – Narcolepsy with cataplexy (adults). Dr JH, Locum Consultant Neuropsychiatrist, NBT

Please see application form for full details. Dr JH attended the meeting to present the application.

The application is for the inclusion of sodium oxybate for the treatment of adults with narcolepsy with cataplexy. CCGs commission all adult highly specialist respiratory services, including sleep disorder breathing, and sodium oxybate is PbR excluded.

It is estimated that the prevalence of narcolepsy in adults is 47 in 100,000 however only 20% are diagnosed and of these, 75% have cataplexy alongside the narcolepsy, and therefore it is estimated to be 7.1 per 100,000. Therefore for the population of BNSSG it is estimated that the cohort would be 70 patients.

Sodium oxybate is an orphan drug that has been available since 2006. There are various stimulant drugs licensed for the treatment of narcolepsy, including dexamfetamine and modafinil. However, stimulants do not treat cataplexy effectively. Tricyclics or SSRIs which suppress REM sleep related symptoms are used. Clomipramine is licensed for the adjunctive treatment of cataplexy in patients with narcolepsy. The evidence base for this standard care is relatively weak itself.

The Xyrem Study Group provides most of the evidence base for sodium oxybate. A systematic
review evaluated the efficacy and safety of sodium oxybate on excessive daytime sleep, and cataplexy attacks. Nine randomised RCTs were included, which involved 1,154 patients (771 on sodium oxybate, and 383 on placebo). Sodium oxybate reduced cataplexy attacks along with improvements in subjective nocturnal awakening, daytime sleep attacks, subjective daytime sleepiness and sleep stage shifts. These studies were of short duration up to 8 weeks, however an open label 12 month study demonstrated the long term reduction in cataplexy frequency with sodium oxybate. A further study comparing sodium oxybate with modafanil showed modest improvements with the oxybate group.

It was questioned whether this is something patient driven, and also whether this may progress to becoming first line treatment by default. Other areas have taken various commissioning decisions for this. On the whole, most areas do not commission it on the basis of a lack of robust clinical evidence leading to a cost effective treatment, however, the Pan Mersey Area committee, NHS Crawley, Coastal West Sussex, Dorset (prior approval) all commission treatment.

Discussion with Dr JH

Modafanil treatment is widely used in the treatment of these patients. However, a number of patients have requested treatment with sodium oxybate, and Dr Hicks has submitted an IFR for one particular patient. It is acknowledged that it is an expensive treatment – between £6,000 and £12,000 per year. In the United States, sodium oxybate is widely used, and alongside modafanil. Treatment options are limited in this rare cohort of patients. The current treatment pathway is using modafanil first line (side effects are less compared to the amphetamines), and then amphetamine second line. For the cataplexy, clomipramine is licensed, however it is not generally used and fluoxetine or another SSRI used more frequently. It is suggested that in the UK we undertreat narcolepsy and cataplexy.

Patients lives can be completely dictated to and altered by having narcolpesy with cataplexy with some patients not being able to work because of it.

Dr JH has 3 patients that she would like to offer treatment to, and her colleague also has 3 patients. These patients are within BNSSG however the sleep centre is a tertiary referral centre and therefore not all patients would necessarily be within BNSSG.

The evidence base appears to show that oxybaté is the most effective treatment to reduce the number of cataplexy attacks. In terms of patient outcomes, oxybate will reduce cataplexy attacks, reduce excessive daytime sleepiness and bad night sleep.

There are 9 or 10 sleep centres in the UK, and most offer this treatment e.g. Merseyside, Dorset and more centres are considering it. London have very strict guidelines of when to use it.

The patent expires in 2019 and it was raised as to whether there could be a potential for an increase in acquisition costs after this time.

Dr JH was asked whether she thought that referrals would go up if it was known that sodium oxybate was able to be offered – there is the potential for this, although unlikely to be an issue.

- **Patient safety** – Generally well tolerated. 10 – 20% of patients experience nausea, dizziness and headaches.
- **Clinical effectiveness** – A meta analysis including 9 RCTs reporting data on the effectiveness of oxybate on narcolepsy including symptoms of cataplexy for a total of 1,154 patients demonstrated the effectiveness in treating major clinically significant relevant narcolepsy symptoms and sleep architecture abnormalities.
- **Cost effectiveness or resource impact** – Per patient the average dose would cost around £12,000 per year. This is significantly different to the costs that the applicant has included in the application. It is suggested that we could expect 7 patients across BNSSG
to be prescribed oxybate and therefore the resource impact on drug costs alone could be around £84,000 per year. When reviewing oxybate in 2007 QALY was £65,980 for 6g per day and £49,590 for 9g per day, the SMC suggested that the QALY

- **Strength of evidence** – short term studies, although an open label 12 month study continued to show evidence of benefit. Limited active comparator studies, and none with the only other licensed treatment for narcolepsy with cataplexy clomipramine.

- **Place in therapy relative to available treatments** – limited options currently. This would be third line therapy, behind modafanil and amphetamines.

- **National guidance and priorities** – No information.

- **Local health priorities** – No cure for narcolepsy with cataplexy. Very small number of patients, with limited access to treatments.

- **Equity of access** – Differing commissioning decisions across the UK. NBT is a tertiary referral centre and therefore should have access to specialist treatments.

The JFG considered the application, the evidence and information submitted. The evidence base although limited does provide evidence that sodium oxybate can reduce cataplexy attacks and other sleep related effects of narcolepsy with cataplexy. The impact of this on the patients’ quality of life has not been reported. This is a very small number of patients, and in whom treatment options are limited. However this is an expensive treatment option, and the cost effectiveness is therefore limited. The JFG felt that the clinical case for including sodium oxybate on the formulary was satisfactory, however the financial aspects need further investigation; this would prove to be a cost pressure, and there are no cost offsets or savings. The BNSSG JFG would therefore support a business case to be submitted by NBT to the CCGs.

**Action:**

1. **NB** to inform applicant.

2. **MP** to support Dr JH in the business case to the CCGs.

**4.2 Tiotropium & olodaterol (Spioltto) Respimat - COPD. Dr JC and Dr NJ, Respiratory Consultants, NBT and UHB.**

Please see application form for full details. LM (Respiratory Specialist Pharmacist, NBT) attended the meeting to support the application.

This application is to include the combination inhaler tiotropium & olodaterol (long acting beta agonist and long acting antimuscarinic, LABA/LAMA) on the formulary. Currently there are 3 other LABA/LAMA combination inhalers on the formulary - Anoro (umeclidinium and vilanterol), Duaklir (Aclidinium and formoterol) and Ultibro (indacaterol and glycopyrronium). These are all dry powder inhalers (DPIs) and Spiolto is the first inhaler not delivered via DPI but through the respimat device as a pressurized metered dose inhaler (pMDI). All the LABA/LAMA combinations have been included on the formulary as they all have slightly different modes of administration which suit different patients. However, it was agreed that during the development of the COPD guidelines, the inhalers would be streamlined so that not all of them were included. Current feedback from primary care is that practice nurses and GPs are confused with the different inhalers available and they need some direction as to which to prescribe.

**Discussion with LM**

There is no difference in clinical efficacy between the different LABA/LAMA combinations and they are all priced similarly. The BNSSG COPD guidelines have been written and currently contain the 3 inhalers and it is requested that this is included on the guidelines. All the inhalers are
mechanically different and suit different patients. However it is the feeling of NBT that Ultibro could be removed from the formulary, as well as tiotropium on its own. It is difficult to reach agreement across the trusts though. The pathway would be that Anoro would be first line, but if there are dexterity issues Duaklir would be prescribed. Spiolto is technically more difficult to use, however is useful for those patients with a low inspiratory rate, intolerance to DPIs or a preference to the softmist device. The availability of this device would therefore give patients more choice, allowing therapy to be tailored to the individual.

- **Patient safety** – generally well tolerated. There was a slight increase in reported respiratory infections in the combination inhaler arm compared to the patients on monotherapy.
- **Clinical effectiveness** – Two phase III trials showed similar clinically relevant improvements to those reported in other LABA/LAMA combination trials. The data supports the use of the 2 drugs in combination, showing improvements in respiratory measurements, exercise tolerance and patient quality of life reporting. Tiotropium is an established antimuscarinic, and olodaterol is a less well established LABA.
- **Cost effectiveness or resource impact** – Spiolto costs the same price as Anoro and Duaklir and less than Ultibro. It is significantly cheaper than the separate inhalers used concurrently and therefore may offer cost savings along with helping with patient adherence. Respiratory is a very high cost area.
- **Strength of evidence** - Phase III trials. All of the data for Spiolto is generated by the manufacturer. There is no data comparing spoilto with other combination inhaler. All patients with recent cardiac problems and those with reduced renal function were excluded from the trial.
- **Place in therapy relative to available treatments** – the inhaler device has not seen significant use so far and therefore would require clinician and patient training. It is suggested that this would be third line for patients who have low inspiratory rate, intolerance to DPIs or a preference to the softmist device.
- **National guidance and priorities** – No specific guidance that mentions Spiolto. The NICE COPD guidelines were published in 2010; these do not mention LABA/LAMA combinations. A review in July 2014 concluded that the guidance was not required to be updated and this question will only be asked again in 2016. Guidance from other bodies e.g. GOLD (Global Initiative for Chronic Obstructive Lung Disease) suggests categorisation of patients by exacerbation history and degree of breathlessness. Those with a high degree of breathlessness but low number of exacerbations may be suitable for dual bronchodilator therapy. The recently updated BNSSG COPD guidelines mirror this.
- **Local health priorities** – Long term conditions, to help reduce admissions to hospital. Help reduce or stop inhaled corticosteroids and thus help to reduce admissions to hospital with pneumonia.
- **Equity of access** – Inhaled therapies are central to the treatment of COPD and the effective use of the inhaled therapy is critically dependent upon the nature of the delivery system and the ability of the patient to use the device correctly. Each inhaler on the market have their own individual positive and negative aspects and therefore no one inhaler will be right for all patients.

The JFG considered the application, the evidence and information submitted. The use of LABA/LAMA combination inhalers is now well established in the COPD treatment pathway. It is clear that there is no clinical evidence to suggest that one combination inhaler is clinically any better than any other. All inhalers are mechanically different, and will be suitable for different patients. The ability to use the inhaler correctly is paramount to the success of COPD treatment. The JFG approved the inclusion of Spiolto onto the BNSSG formulary, TLS Blue. To follow up with the consultants regarding the potential to remove Ultibro from the formulary.

*Action:*
1. **NB** to inform applicant.

2. **NB** to include on the formulary, TLS Blue.

3. **JC** to follow up with Trusts to determine if Ultibro can be removed from the formulary.

### 4.3 Glycopyrronium – Hypersalivation in Motor-neurone disease patients and children and young people with neurological conditions. **Dr AM, Consultant Neurologist, NBT**

Please see application form for full details. Dr AM attended the meeting to support the application.

This NDR came out of the chapter review as this appears to be established practice in NBT (and beyond). It is therefore something that has historically been prescribed with benefit although not included on the formulary. There is not much evidence to support its use. This application is specifically for patients with motor neurone disease (MND) and children and young people with neurological conditions. NICE have carried out an evidence review and reported their findings in an evidence summary in 2013. This specifically looked at the use of glycopyrronium for the treatment of hypersalivation. 4 RCTs were considered. Two double-blind, placebo-controlled RCT examined the efficacy and safety of oral glycopyrronium bromide for treating hypersalivation in children and young people with neurological conditions. The two other RCT looked at Parkinson disease patients with associated drooling and the other looked at clozapine-induced hypersalivation in schizophrenic patients. Both trials that involved children and young adults demonstrated a significant clinical improvement in symptoms of drooling after 8 weeks of treatment compared to placebo.

There have also been a number of non-comparative studies that have looked at small population groups in both adults and children. In these studies the numbers have been higher than in the RCT. These studies specifically looked at drooling in patients with neurological impairments. Ages ranged from 2 to 27 years across the studies. Study periods ranged from 5 weeks to 28 months and in one study patients were followed up over a period of 4 years. In all of the non-comparative studies the majority of patients demonstrated a reduction in drooling or cessation of drooling completely.

**Discussion with Dr AM**

This is current practice and is a very useful treatment option in a small number of patients in whom hypersalivation is difficult to treat. They have been using it for 5 or 6 years for the control of saliva in MND patients or other neuromuscular disorder patients. Colleagues are also using it in stroke patients, and within ICU, specifically neuro ICU as it does not cross the blood brain barrier, therefore is used instead of atropine. It would be used 2nd or 3rd line in the pathway. First line, Hyoscine or amitriptyline would be used, and the glycopyrronium would be used if these are ineffective. Glycopyrronium is very effective in those patients who can’t tolerate hyoscine or amitriptyline and in particular the frail elderly patients.

Glycopyrronium is recommended in NICE guidance for non-invasive ventilation in MND. There is reasonably good evidence for clinical efficacy and safety. There are no trials comparing it with other agents and is unlicensed, however all of the agents used in this manner are unlicensed and don’t have any better evidence.

Over the last year, expenditure on glycopyrronium has been around £10K. Personally Dr AM has had no issues with prescribing in patients and has found it to be effective and well tolerated. The major issue is that it is non-formulary and therefore there are constraints around prescribing.
Tablets are used if possible, but the liquid would be required if patients have swallowing difficulties or who have a gastronomy tube (PEG or RIG). Liquid prescribing is kept to a minimum.

In MND patients by the very nature of the disease, treatment will be short term, however in other neuromuscular disease the prescribing of glycopyrronium could be more long term. It is requested that this is amber so that GPs can prescribe it.

Within Bristol CCG over the last 4 months, there have been 66 prescriptions for oral glycopyrronium which has amounted to £18,981.16.

- **Patient safety** – Long term safety data is limited. Most common adverse effects are dry mouth, vomiting, constipation, nasal congestion and flushing.

- **Clinical effectiveness** – There is moderate evidence that oral glycopyrronium bromide (tablets and solution or suspension) reduces hypersalivation (sialorrhoea) or drooling in children and young people with a neurological condition, and adults with Parkinson’s disease, compared with placebo. There is also limited evidence of its efficacy in adults with schizophrenia and clozapine-induced hypersalivation. A number of non-comparative studies specifically looking at drooling in neurological conditions found that the majority of patients demonstrated a reduction in drooling or cessation of drooling completely.

- **Cost effectiveness or resource impact** – No efficacy data comparing the different formulations of glycopyrronium regarding cost. No major RCTs comparing drugs to treat hypersalivation. There is a significant cost associated with unlicensed preparations, and especially if primary care are to take on prescribing. Glycopyrronium is included in the tariff. Currently, it is estimated that there are 15 – 25 patients being prescribed glycopyrronium in this patient cohort within BNSSG. It is estimated that a year’s treatment costs around £2100 per patient but this depends on the dose used.

- **Strength of evidence** – limited good quality long term evidence.

- **Place in therapy relative to available treatments** – no other medication is licensed. This would be used after a trial with hyoscine, and/or amitriptyline.

- **National guidance and priorities** - None

- **Local health priorities** – not listed within local priority

- **Equity of access** – has been being prescribed. Other areas include on the formulary. Limited treatment options available. On the formulary within the palliative care section, TLS blue.

The JFG considered the application, the evidence and information submitted. There is limited evidence, but the evidence available does suggest that this is a useful treatment option for hypersalivation in MND and NMDisorders. Anecdotally it is effective and well tolerated. The JFG agreed for the inclusion onto the formulary for those MND patients and NMDisorder patients who have not responded to first line agents or are inappropriate. It was agreed for this to be TLS amber 3 months, and a SCP was also approved.

**Action:**

1. **NB** to inform applicant.

2. **NB** to include on the formulary, TLS amber 3 months.

**4.4 Ulipristal** - for intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. Ms VM, Consultant Gynaecologist, Weston Area. Also supported by many other clinicians across BNSSG.

Please see application form for full details. Ms VM was unable to attend the meeting; however NB
(interface pharmacist) presented the application.

The application was for the inclusion of ulipristal on the formulary for the medical treatment of uterine fibroids which it has recently been granted a licence extension for.

Ulipristal (Esmya) has been available since February 2012 for the pre-operative treatment of moderate to severe symptoms of fibroids in adult women. The BNSSG JFG approved its inclusion onto the formulary in October 2012. Since then, it has been granted a license for the extended use of Esmya to treat uterine fibroids in adult women of reproductive age. This approval allowed one repeated course of a three-month treatment i.e. a total of 2 3 month courses pre surgical intervention. Subsequently in April of this year it was granted a licence variation to allow use of ulipristal for intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age i.e. medical treatment, and not just pre surgery.

Evidence comes from the clinical development programme Pearl Studies I – IV. PEARL I and II were phase II studies prior to the license. PEARL III looked at two courses pre surgical licence. And PEARL IV was designed to investigate intermittent treatment.

PEARL I – showed that Ulipristal is significantly superior to placebo in reducing excessive uterine bleeding

PEARL II – showed that Ulipristal is non-inferior to leuprorelin in reducing excessive uterine bleeding.

PEARL III – to investigate the clinical efficacy and safety of long term intermittent 3 month administration of Ulipristal 10mg/day.

PEARL IV – to compare and assess the sustained efficacy of two (part I) and four (part II) repeated 12 week courses for the long term management of fibroids.

We are currently awaiting the results of the second part of PEARL IV to be published although they are included in the EPAR report and SPC.

PEARL VI was a phase III, multicenter, randomised, double blind clinical study; the aim was to compare and assess the sustained efficacy of two repeated 12 week treatment courses of daily administration of 5mg and 10mg doses of Ulipristal on uterine bleeding in women with uterine fibroids. The primary end point for both parts of PEARL IV was the percentage of patients in amenorrhoea at the end of both treatment courses 1 and 2 or 1, 2, 3 and 4.

Patients were randomised to treatment with 5mg ulipristal (n = 228), or 10mg ulipristal (n = 223). Each treatment course lasted 12 weeks. Treatment courses were separated by a drug free period until the start of the second menstruation following the end of the previous treatment course. There were 4 treatment courses in total. The clinical study report for Part I presented data after completion of treatment courses 1 and 2 up to visit 8. The final clinical study report (Part II) presented data after completion of all four treatment courses, up to visit 12.

Limitations of the study: Long term treatment has only been studied up to 4 intermittent treatment courses. Additional efficacy data will be available from the ongoing study, a further extension study of PEARL III. This will provide safety and efficacy data of up to 8 treatment courses. The study did not assess treatment related differences in surgical outcomes. This study was not able to be placebo controlled however it has been previously demonstrated that a 3 month course of ulipristal was superior to placebo and non-inferior to a GnRH agonist for the control of heavy menstrual bleeding.
61.9% of patients on the 5mg dose were in amenorrhoea at the end of both treatment course 1 and 2, compared to 72.7% taking the 10mg dose. Menstruation resumed after each treatment course but the magnitude of menstrual bleeding progressively diminished during the off-treatment periods to a median level below the threshold for menorrhagia.

Both doses of ulipristal acetate were effective in shrinking fibroids, more than halving the fibroid volume in more than 50% of patients by the end of the second treatment course. Patients also reported substantial improvements in pain and quality of life during treatment, and these improvements were partly maintained during the off-treatment period. Very few patients (<2%) discontinued the study to undergo surgery.

The proportion of patients with adverse events during the first treatment course was the same (44%) for both treatment groups. Fewer patients reported adverse events during the second treatment course (27% and 30% for the 5- and 10-mg treatment groups, respectively). Headaches and hot flushes were the most frequently reported adverse events, but occurred in ≤10% of patients, and only one event of headache was reported as severe. Overall 21 (<5%) patients discontinued treatment at any time during or after the two treatment courses due to adverse events. There were 18 serious adverse events reported during part I, 9 occurring during treatment and 9 occurring between or after treatment courses.

<table>
<thead>
<tr>
<th>Dose</th>
<th>Goserelin</th>
<th>Triptorelin 3mg</th>
<th>Ulipristal</th>
</tr>
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<tbody>
<tr>
<td>Price per injection/pack of tablets</td>
<td>3 x 3.6mg</td>
<td>3 x 3mg</td>
<td>5mg for 3 months</td>
</tr>
<tr>
<td>65</td>
<td>69</td>
<td>114.13</td>
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</tr>
<tr>
<td>Total drug cost for 3 months</td>
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<td>£207.00</td>
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</tr>
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</table>

The cost of ulipristal drug treatment is more than a GnRH analogue. However, we need to consider how this would fit in the patient pathway as it will change the patient pathway. Dr TP (Primary Care Womens Health Lead NW Locality Bristol CCG, and GPwSI Womens and Sexual Health) who operates community clinics for the North and West locality (i.e. 20 surgeries) has advised that this will reduce the number of referrals into secondary care. Currently clinicians have been using it off licence already but now that it has a license clinicians will consider it more. Fitting a Mirena coil would still be the first line option, however there is a cohort of patients in whom this is not an option, and all other treatment options have failed and surgery is not an option. Usually these patients would be referred into secondary care for potential surgical options, although we now have this as a further option prior to referral. This won’t revolutionize practice, but is a useful option. At a guess, about 1 patient per month in his area i.e. 12 patients per year would fit this option. He also sees it that it would sit as amber 1 month and the GP could initiate further courses, alongside the annual scan and specialist review.

Therefore although drug costs will increase (not significantly), a reduction should be seen in activity in terms of referral to secondary care for fibroids (through the specialist GP clinic), and further OP attendances as the GP can initiate further treatment courses. Also potentially a reduction in surgery: 78% of patients completed the 4 treatment courses suggesting that this was working and so patients didn’t need further intervention. There is no evidence to support the reduction in surgical intervention. Particularly this is a useful intervention for those peri-menopausal patients in whom in may reduce symptoms and overt the need for surgical intervention prior to the menopause.

It is currently Red on the BNSSG formulary as it was felt that the decision to initiate treatment would be taken by a specialist, and that they could provide the full 3 months treatment. With this license extension it was felt that a TLS of amber 3 months would be appropriate. The first 3 month course should be provided by the specialist but then subsequent courses can be initiated and prescribed by primary care.
• **Patient safety** – The proportion of patients with adverse events during the first treatment course was the same (44%) for both treatment groups. Fewer patients reported adverse events during the second treatment course (27% and 30% for the 5- and 10-mg treatment groups, respectively). Headaches and hot flushes were the most frequently reported adverse events, but occurred in ≤10% of patients, and only one event of headache was reported as severe. Overall 21 (<5%) patients discontinued treatment at any time during or after the two treatment courses due to adverse events. There were 18 serious adverse events reported during part I, 9 occurring during treatment and 9 occurring between or after treatment courses.

• **Clinical effectiveness** - 61.9% of patients on the 5mg dose were in amenorrhoea at the end of both treatment course 1 and 2, compared to 72.7% taking the 10mg dose. The efficacy of ulipristal compared to placebo and leuprolelin has already been established.

• **Cost effectiveness or resource impact** – an increase in drug costs will be seen by using this, however the effect on the health economy as a whole should be positive as a reduction in secondary care referrals should be seen along with potentially a reduction in hysterectomy procedures in these patients.

• **Strength of evidence** – Well-designed study, although not placebo controlled. A further extension of PEARL III will provide evidence for up to 8 treatment courses.

• **Place in therapy relative to available treatments** - If we didn't have access to this, patients would have to have surgical intervention, or no other options. It is a unique medical treatment for those patients who can’t have Mirena, or not appropriate for surgery. Particularly useful for peri menopausal women.

• **National guidance and priorities** - none

• **Local health priorities** - Should help to reduce secondary care referrals.

• **Equity of access** – Other areas have included ulipristal on their formularies prior to surgery. It varies across the country in terms of TLS status.

The JFG considered the application, the evidence and information submitted. Currently there are no approved long-term medical treatment options for the management of patients with symptomatic fibroids. The evidence from the PEARL IV study shows that repeated courses of ulipristal at 5mg and 10mg effectively controls bleeding and pain, reduces fibroid volume and restores quality of life. Ulipristal would be a useful alternative to those patients in whom surgery is not an option, but also may delay or even negate the need for surgical intervention. It is acknowledged that the drug costs may be increased however it is hoped that across the local health economy savings will be made in terms of reduction in secondary care referrals and surgery. The JFG approved the inclusion on the formulary, TLS amber 3 months, where the specialist prescribes the first course, but subsequent courses maybe prescribed by primary care under shared care protocol.

**Action:**

1. **NB** to inform applicant.

2. **NB** to include on the formulary, TLS Red until SCP is agreed.

3. **NB** to ensure SCP is included on the agenda for subsequent meeting.

5 **Shared Care Protocols/TLS status**

5.1 **Lisdexamfetamine SCP (NEW)**

The SCP had been discussed at the JFG in July. The JFG felt unable to approve the SCP as it was written as it was felt that the specialist should carry out all required physical monitoring
required prior to initiation. On discussion with AWP, they are not able to carry out e.g. ECGs therefore from their perspective, the GPs will have to undertake. Shire pharmaceuticals (manufacturer of lisdexamfetamine) have been in contact to help address this. Currently we have not moved forward with this, but we will try and progress this further. Some GPs across BNSSG already are prescribing for patients, without a SCP and it is clear that the AWP caseload is over flowing. However the SCP needs to be safe and appropriate to allow GPs to prescribe appropriately.

5.2 Edoxaban for DVT or PE SCP (NEW)

NB commented that a SCP had been produced for edoxaban in the treatment of DVT or PE which has been lifted from the previously SCPs agreed for rivaroxaban, apixaban and dabigatran. This will be sent around electronically for e-approval after the meeting.

5.3 Ranolazine Change in Status request (amber 1 month to amber no SCP)

No paperwork currently submitted, therefore a full discussion could not take place. However it was commented that GPs still feel unfamiliar with this drug and therefore unlikely to agree for it to be changed to amber no SCP.

5.4 Insulin Degludec Change in Status request (red to amber)

There appears to be confusion as to who may prescribe under the category Red. It is felt that if you are considered a specialist in the field e.g. diabetes nurse, they are able to prescribe diabetic red drugs. Therefore the change in status request is not required. It is also considered that with potential changes in the endocrine chapter that the use of degludec may reduce. It is currently only on the formulary for Type I diabetic patients who have failed on insulin glargine and who are not suitable or failed on insulin pump therapy.

6 Individual Funding Requests

NB shared that we have asked for data from IFR regarding applications across BNSSG for the last 6 months. There are no common themes, except Botox for hyperhidrosis, and urinary incontinence.

MG – the RUH are putting through IFRs for sequential use of MABs in RA.

Recent IFR for autologous eye serum. This is classed as a medicine and therefore should be an application to the JFG as there is a cohort.

7 Chapter review and formulary process

JC gave an update on the process. 7 chapters (1, 2, 4, 5, 6, 12 and 13) have been completed and the significant changes were presented at this meeting (see attached paper). The JFG approved the changes to the chapters and therefore these will be uploaded onto the website shortly.

8 Items for Discussion

8.1 NDRs for September Meeting (no papers, for information only)

a. Abasaglar (biosimilar glargine) – for new adult patients
b. **Toujeo** (insulin glarine 300Units per ml)

c. **Apidra – TBC**

d. **Midodrine** - Adult patients with severe orthostatic hypotension due to autonomic dysfunction, which is not managed by corrective factors or other treatment strategies

e. **Olsalazine** - mild active ulcerative colitis and maintenance of remission especially in patients with proximal constipation

f. **Sacubitril & valsartan** – Heart failure

g. **Clopidogrel** – in combination with aspirin post CABG (UHB) Non-formulary and the TLS

9 **AOB**

None

**NB**

Interface Pharmacist

20th October 2015
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<tr>
<th>Date of Meeting</th>
<th>Minute No.</th>
<th>Subject</th>
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<th>Responsible Officer</th>
<th>Deadline</th>
<th>Date of Update</th>
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<td>Palonsetron NDR</td>
<td>Ensure Weston comments on potential usage</td>
<td>NB</td>
<td>October</td>
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<td>NICE TAs</td>
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<td>NB/MP</td>
<td>November</td>
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<td>4.2</td>
<td>Spiolto NDR</td>
<td>Inform applicant, include on the formulary. Liaise with specialists to remove ulitbro</td>
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<td>Ulipristal NDR</td>
<td>Inform applicant, include on the formulary. Liaise with applicant for development of SCP</td>
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<td>5.1</td>
<td>Lisdexamfetamine SCP</td>
<td>Liaise with AWP re physical monitoring</td>
<td>NB</td>
<td>November</td>
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<td></td>
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<td>Edoxaban SCP</td>
<td>Send round SCP for comment. Include on the formulary once e-approved.</td>
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<td>Chapter review</td>
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MEETING DATES 2015-2016

<table>
<thead>
<tr>
<th>Date</th>
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<tr>
<td>Tuesday 24&lt;sup&gt;th&lt;/sup&gt; November</td>
<td>13&lt;sup&gt;th&lt;/sup&gt; October</td>
<td>1.30 – 4.30pm</td>
<td>Bevan Room, South Plaza</td>
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<tr>
<td>Tuesday 12&lt;sup&gt;th&lt;/sup&gt; January</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; December</td>
<td>9am – 12 midday</td>
<td>Pharmacy seminar room, Southmead Hospital</td>
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<tr>
<td>Tuesday 23&lt;sup&gt;rd&lt;/sup&gt; February</td>
<td>12th January</td>
<td>1pm – 4pm</td>
<td>North Somerset TO CONFIRM VENUE</td>
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<tr>
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<td>1st March</td>
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<td>Tuesday 24&lt;sup&gt;th&lt;/sup&gt; May</td>
<td>12 April</td>
<td>1pm – 4pm</td>
<td>Pharmacy seminar room, Southmead Hospital</td>
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<tr>
<td>Tuesday 5&lt;sup&gt;th&lt;/sup&gt; July</td>
<td>24th May</td>
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<td>26th August</td>
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<td>6th September</td>
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<td>18th October</td>
<td>9am – 12 midday</td>
<td>South Plaza, Board Room</td>
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BNSSG Joint Formulary Group
Meeting held on: Tuesday 24th November 2015  1.30pm - 4.30pm
Bevan Room, South Plaza, NHS Bristol CCG

Minutes

Present:

Interface Pharmacist, NHS Bristol CCG
Interface Pharmacist, NHS Bristol CCG
Pharmaco economics and Interface Pharmacist, NBT
Public Health Consultant, Bristol City Council (Chair)
GP, North Somerset
Deputy HoMM, NHS North Somerset CCG
HoMM, South Gloucestershire CCG
Principal Pharmacist, UHBristol NHS Foundation Trust
Deputy Chief Pharmacist, Weston General Hospital
HoMM, Bristol CCG

Apologies:

GP, North Somerset
Consultant Neurologist, NBT
Consultant Renal Physician, and Joint D&TC Chair, NBT
Director of Pharmacy, Weston General Hospital
Head of IFR for BNSSSG
HoMM, North Somerset CCG
Clinical Effectiveness Research Lead, Bristol City Council
GP Bristol and member of Bristol CCG board
Deputy HoMM, NHS Bristol CCG
Medicines Information Pharmacist, UHBristol NHS Foundation Trust

1 Welcome, Apologies and Declaration of Interests

Declarations of Interest
None

The meeting was not quorate due to there being no secondary care Consultant. The minutes will be sent around by email in accordance with the Terms of Reference. Members of the group to email NB if there are any areas of discussion required before the minutes are signed off.

2 Minutes of the meeting of 13th October 2015 and Matters arising

The minutes from the Joint Formulary Group (JFG) meeting on the 13th October 2015 had been
circulated by NB following the meeting. No comments had been received via email that needed further discussion. These were agreed as accurate.

Matters arising from 13th October 2015 meeting

2.1 Action Log

- All actions from last meeting are either completed or in the process of being completed. Of note:
  - Wound care formulary – NBT have supplied their wound care formulary to be uploaded onto the website

3 NICE New Technology Appraisals

Published

3.1 Tolvaptan for treating autosomal dominant polycystic kidney disease. TA358
  JFG decision: TLS Red

3.2 Idelalisib for treating chronic lymphocytic leukaemia. TA359
  JFG decision: TLS Red

Adopted into the BNSSG Joint Formulary – October 2015

- Naloxegol for treating opioid-induced constipation. TA345 TLS Blue
- Afiblercept for treating diabetic macular oedema. TA346 TLS Red
- Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer. TA347 TLS Red
- Dexamethasone intravitreal implant for treating diabetic macular oedema. TA349 TLS Red
- Secukinumab for treating moderate to severe plaque psoriasis. TA350 TLS Red

4 New Drug Requests (NDRs)

SUMMARY

4.1 Biosimilar Insulin Glargine 100 units (Abasaglar®) – Adult patients who are uncontrolled on basal or basal bolus insulin with type 2 diabetes at high risk of hypoglycaemia, and as a basal analogue option for all patients with Type 1 diabetes.

On review of the data on quality, safety and efficacy, the EMA have stated that the risk-benefit balance of Abasaglar® in the treatment of diabetes in adults and adolescents and children over 2 is favourable. The JFG acknowledged that there would be cost savings to be made by prescribing Abasaglar® in place of Lantus® however it should only be prescribed in those insulin naïve patients who meet the requirements for insulin glargine. Patients should not be switched if they are stable on Lantus®. In line with all biosimilars, and insulins, Abasaglar® should be prescribed by brand. The JFG approved the addition of Abasaglar® onto the formulary, TLS blue.

4.2 Insulin Glargine 300 units (Toujeo®) – Adult patients who are uncontrolled on basal or basal bolus insulin with type 2 diabetes at high risk of hypoglycaemia, and uncontrolled on basal bolus insulin with type 1 diabetes.

Toujeo® has been shown to be as effective as Lantus®, and has been particularly developed for those patients with large daily insulin requirements as it is a high strength insulin. It offers a
longer duration of action compared to lantus®. It may offer significant cost savings if it is used in place of Insulin degludec. Training is required amongst nurses and prescribers to ensure that the risk of administration errors are minimised. The JFG approved the addition of Toujeo® onto the formulary, TLS amber (specialist recommendation, no SCP).

4.3 **IDegLira (Xultophy®)** – Adults with type 2 diabetes mellitus in combination with oral glucose-lowering medicinal products when these alone or combined with a GLP-1 receptor agonist or basal insulin do not provide adequate glycaemic control.

The evidence suggests that there may be a small benefit in terms of HbA1c reduction by using IDegLira compared to liragultide alone or degludec alone. Patients in the trials did not have their medications optimised which does not reflect current practice and it is an expensive option. There are other options for the cohort of patients identified e.g. Toujeo® (longer acting), GLP1 agonists once weekly which have lower acquisition costs. In addition, after the meeting, the NICE clinical guideline on type 2 diabetes management was published on 2nd December, and within this it states that there was strong evidence to suggest that degludec was not cost effective. The JFG therefore did not approve the addition of IDegLira onto the formulary.

4.4 **Dulaglutide (Trulicity®)** - in adults with T2D mellitus as monotherapy, or add-on therapy.

The evidence supports efficacy and similarity to other GLP-1s that have already been agreed for the formulary. The improved pricing strategy means that it will not introduce a cost pressure and could result in savings of nursing time and reduction in prescriptions for needles. The improved usability may provide an advantage over alternative GLP-1s. Agreed for inclusion onto the formulary (with GLP-1 restrictions i.e. 6 month review with weight loss and HbA1c improvement expected), TLS green.

4.5 **Midodrine** - Severe orthostatic hypotension due to autonomic dysfunction, Hepatorenal syndrome, Intradialytic hypotension.

There is evidence to show that Midodrine is effective in the management of orthostatic hypotension resulting from autonomic dysfunction. Evidence also exists to show that Midodrine is also effective and well tolerated in intradialytic hypotension and hepatorenal syndrome. It was therefore agreed to include Midodrine on the formulary, amber 3 months for orthostatic hypotension. Prescribing should remain with the specialists if being used for intradialytic hypotension or hepatorenal syndrome, i.e. TLS red. The SCP was agreed.

4.6 **Sacubitril & Valsartan** - Adult patients with chronic heart failure and reduced ejection fraction.

Sacubitril &Valsartan was licensed the day prior the meeting, and therefore the Early Access to Medicines Scheme (providing treatment free of charge prior to licensing) had closed. The JFG recognised that the cohort identified by the applicant were those with most severe heart failure and pragmatically this would be the cohort to initiate treatment in first, however the evidence does not support this group over any of the other classes of heart failure. In view of a lack of a significantly reactive process to manage EAMS within the JFG, the JFG agreed that UHB MAG may manage the 5 patients that you would like to start treatment in prior to NICE publication.

**Decision Criteria used by JFG for NDR**

- Patient safety
- Clinical effectiveness
- Cost effectiveness or resource impact
- Strength of evidence
- Place in therapy relative to available treatments
- National guidance and priorities
- Local health priorities
• Equity of access

Full Discussion

4.1 Biosimilar Insulin Glargine 100 units (Abasaglar®) – Adult patients who are uncontrolled on basal or basal bolus insulin with type 2 diabetes at high risk of hypoglycaemia, and as a basal analogue option for all patients with Type 1 diabetes. VR, Specialist Pharmacist, NBT

Please see application form for full details. VR(Specialist diabetes pharmacist) attended the meeting to present the application.

The application was for the inclusion of a biosimilar insulin glargine 100 units on the formulary which is the first biosimilar insulin. Previously (March 2015) the BNSSG JFG has discussed the issue of biosimilars and their introduction onto the formulary. It was minuted that ‘The JFG agreed that biosimilars can be included on the formulary as they are licensed. This is in accordance with the NICE position statement, January 2015: ‘The Department of Health in England has confirmed that a technology appraisal remit referred to NICE enables NICE to decide to apply the same remit, and the resulting guidance, to relevant licensed biosimilar products which subsequently appear on the market.’ It is acknowledged that biosimilars are not interchangeable and prescription will be required by brand name. Therefore this application was to acknowledge the availability, and to manage the introduction of the medicine into the local population safely and effectively.

There is no clinical efficacy data showing superiority of Abasaglar® compared to Lantus®, and all trials conducted used Lantus® as the comparator. The company completed more research than was required, and the evidence is sufficient to show that Abasaglar® is equivalent to Lantus®.

In line with EMA requirements, the clinical evaluation program for Abasaglar® was undertaken with the aim of demonstrating that Abasaglar® has a highly similar profile compared with Lantus® in terms of: quality; nonclinical characteristics; pharmacokinetics (PK) and pharmacodynamics (PD); clinical efficacy and safety.

Six phase I biopharmaceutical studies demonstrate:
• The pharmacokinetic and pharmacodynamic profiles of Abasaglar® and US-approved and EU-approved Lantus® are similar.
• Across three different doses the relative bioavailability of Abasaglar® and EU-approved Lantus® is similar.
• In patients with type 1 diabetes the duration of action is similar for Abasaglar® and EU-approved Lantus®.

Two phase III studies demonstrate Abasaglar® has equivalent efficacy and safety to Lantus® in patients with type 1 diabetes (ELEMENT-1) and type 2 diabetes (ELEMENT-2). Element-1 demonstrated Abasaglar® was non-inferior to Lantus® for key clinical efficacy variables for patients with type 1 diabetes. ELEMENT-2 demonstrated Abasaglar® was non-inferior to Lantus® for key clinical efficacy variables for patients with type 2 diabetes.

VR has liaised with the local diabetologists and has confirmed that their intentions would be that the Abasaglar® would be used in patients who are insulin naïve where analogues are clinically appropriate. Currently, there is little enthusiasm to switch patients, but potentially they may switch a patient if they are not controlled. Given time, it may be appropriate to switch more patients. The UKMI safety report states that automatic switching from Lantus® cannot be undertaken and would be counter to the MHRA’s recommendation that all biological medicines are prescribed by brand.
It is important that insulins should be prescribed by brand, and this is becoming more and more important from a safety point of view. The Abasaglar® cartridges will not fit any other pens, and therefore this reduces the risk of administration errors. The message still needs to be reinforced that insulin should not be drawn up from pen fills, to reduce errors. NPSA, and Patient Safety First guidance to be uploaded onto the formulary website, including the UKMI safety assessment. It also needs to be clear on the formulary website that this is a biosimilar.

- **Patient safety** – To gain licence approval from the European Commission the manufacturer had to demonstrate that Abasaglar® had similar physiochemical and biological characteristics, similar pharmacodynamics and pharmacokinetics, and a similar safety and efficacy profile to that of the reference product, Lantus®. The JFG discussed the potential administration errors with the introduction of a biosimilar insulin. There is a need for reinforcing prescribing by brand, and also not drawing up from cartridges.

- **Clinical effectiveness** – As above.

- **Cost effectiveness or resource impact** – The yearly cost of Abasaglar® is about 15% lower that Lantus®; £343 per patient per year, compared with £403 per patient per year for Lantus® (assuming 40 units per day for each treatment).

- **Strength of evidence** – As above.

- **Place in therapy relative to available treatments** – Initially to be used in insulin naïve patients where an analogue insulin is clinically appropriate or in patients assessed to need a medication change.

- **National guidance and priorities** – NICE’s biosimilar statement states that NICE guidance on a product also applies to relevant licensed biosimilar products which subsequently appear on the market. The SMC have stated that they no longer routinely assess biosimilar medicines on the basis of a full submission. These products will be considered ‘out of remit’ where the reference product has been accepted by SMC/Health Improvement Scotland (HIS) for the same indication(s) and in the same population or was initially licensed and available prior to 31 January 2002. Insulin glargine is accepted for restricted use in NHS Scotland.

- **Local health priorities** – diabetes is locally a key area to improve care

- **Equity of access** – Should be available to all who would be considered appropriate for glargine.

The JFG considered the application, the evidence and information submitted. On review of the data on quality, safety and efficacy, the EMA have stated that the risk-benefit balance of Abasaglar® in the treatment of diabetes in adults and adolescents and children over 2 is favourable. The JFG acknowledged that there would be cost savings to be made by prescribing Abasaglar® in place of Lantus® however it should only be prescribed in those insulin naïve patients who meet the requirements for insulin glargine. Patients should not be switched if they are stable on Lantus®. In line with all biosimilars, and insulins, Abasalgar® should be prescribed by brand. The JFG approved the addition of Abasaglar onto the formulary, TLS blue.

**Action:**

1. **NB** to inform applicant.

2. **NB** to include on the formulary, TLS blue.

3. **JC** to include the UKMI Insulin safety document on the formulary website.

**4.2 Insulin Glargine 300 units (Toujeo®)** – Adult patients who are uncontrolled on basal or basal bolus insulin with type 2 diabetes at high risk of hypoglycaemia, and uncontrolled on
basal bolus insulin with type 1 diabetes. VR, Specialist Pharmacist, NBT

Please see application form for full details. VR (Specialist diabetes pharmacist) attended the meeting to present the application.

This application is for the introduction of a concentrated form of insulin glargine, Toujeo® 300 units per ml. There are therefore important governance issues that will need to be considered carefully.

NICE have produced a new product evidence summary. Within this, it states that ‘High-strength insulin products such as insulin glargine 300 units/ml (Toujeo®) have been developed for people with large daily insulin requirements to reduce the number and volume of injections. In 1 randomised controlled trial (RCT) in 549 people with type 1 diabetes, Toujeo had similar efficacy to insulin glargine 100 units/ml (Lantus) in terms of HbA1c reduction, but the basal insulin dose used was higher with Toujeo than with Lantus. There was no benefit of Toujeo over Lantus in terms of reduced hypoglycaemic events. The safety profile of Toujeo is largely similar to that of Lantus. Toujeo is not bioequivalent to Lantus and they are not interchangeable without dose adjustment.’

Toujeo® is not bioequivalent to Lantus®; it has been manufactured in a way to provide a flatter and more prolonged (up to 36 hours) profile of insulin concentration and glucose lowering activity compared with Lantus® at the same doses. Lantus® has an average duration of action of about 18 hours.

Switching from once-daily Toujeo® (insulin glargine 300 units/mL) to Lantus® (insulin glargine 100 units/mL) results in an increased risk of hypoglycaemic events, mainly in the first week after the switch. To reduce this risk, patients should reduce their dose by 20%. When switching to or from Toujeo®, close metabolic monitoring is recommended during the transition and in the initial weeks thereafter.

The specialists view its place in therapy more due to its longer duration of action, and can therefore see it potentially being prescribed in those patients in whom insulin degludec may have been considered. Toujeo® is longer acting, and can therefore be used in those patients experiencing hypos, or who are particularly non-compliant. Toujeo® has a lower acquisition cost than degludec, and appears to have similar benefits, although there are no trials comparing the two.

Being a high strength insulin, it is particularly useful for those patients who are on high doses of insulin. It will require reduce the volume and number of injections to be injected. Equally, there are some safety concerns with the introduction of a high strength insulin more widely into the local population. This is a concern, especially given the continuation in administration errors where patients are being given the wrong amount/wrong insulin due to insulin being inappropriately drawn from pen fills, and not vials. Sanofi (manufacturer of Toujeo®) will support the acute trusts/CCGs to put on education sessions e.g. district nurses, community DSNs, hospitals etc. Medicine Safety Offices in each organisation should be aware of this, and to disseminate information. The Toujeo® pens are designed so that only the number of units is visible through the window thereby reducing the potential for administration errors.

- **Patient safety** – The safety profile of Toujeo® is largely similar to that of Lantus®. The most frequent adverse events are nasopharyngitis and upper respiratory tract infection. The most common serious adverse event in people with type 1 diabetes is hypoglycaemia.
- **Clinical effectiveness** – Once-daily Toujeo® was non-inferior to once-daily Lantus in HbA1c reduction from baseline to month 6 (difference between groups 0.04% [0.4 mol/mol], 95% confidence interval [CI] =-0.10 to 0.19% [-1.1 to 2.1 mmol/mol]) in people with type 1 diabetes (1 RCT, n=549). Hypoglycaemia (confirmed or severe, nocturnal, or severe) did not differ between Toujeo® and Lantus® at 6 months in people with type 1
diabetes (1 RCT, n=549).

- **Cost effectiveness or resource impact** – It is estimated that this is likely to be used in 10% of type 1 patients. Only a proportion of type 2s are treated with insulin, and of these, only a small number are likely to use an analogue. Work is being undertaken to ensure that the use of analogues in type 2s is reduced. Toujeo® is cost neutral compared to Lantus® and Levemir, more expensive than Abasaglar®, but significantly less expensive than Degludec, it offers a financial advantage to be able to prescribe this.

- **Strength of evidence** – Edition 4 was open label.

- **Place in therapy relative to available treatments** – Basal insulin supply for adults with type 1 diabetes can be provided by: NPH (isophane) insulin (for example, Insulatard, Humulin I or Insuman Basal) or long-acting insulin analogues: insulin glargine (Lantus®, the biosimilar Abasaglar or high-strength Toujeo®), insulin detemir (Levemir) or insulin degludec (Tresiba). The local specialists expect to initiate Toujeo® in patients in whom compliance is an issue, and in patients who are experiencing nocturnal hypoglycaemic episodes. At this current time, insulin degludec would be considered. As Toujeo® has a longer duration of action, it is likely to replace Degludec.

- **National guidance and priorities** – NICE state that twice daily insulin detemir is the preferred basal insulin therapy. Other basal insulins may be used in certain circumstances. The SMC have accepted Toujeo® within Scotland for restricted use. Its use should be targeted on patients with Type 1 diabetes who are at risk of or experience unacceptable frequency and/or severity of nocturnal hypoglycaemia on attempting to achieve better hypoglycaemic control during treatment with established insulins. It is also acceptable as a once daily insulin therapy for patients who require carer administration of their insulin. In patients with type 2 diabetes it should be restricted to those who suffer from recurrent episodes of hypoglycaemia or require assistance with their insulin injections.

- **Local health priorities** – diabetes is locally a key area to improve care

- **Equity of access** –

The JFG considered the application, the evidence and information submitted. Toujeo® has been shown to be as effective as Lantus®, and has been particularly developed for those patients with large daily insulin requirements as it is a high strength insulin. It offers a longer duration of action compared to lantus®. It may offer significant cost savings if it is used in place of Insulin degludec. Training is required amongst nurses and prescribers to ensure that the risk of administration errors are minimised. The JFG approved the addition of Toujeo® onto the formulary, TLS amber (specialist recommendation, no SCP).

**Action:**

1. **NB** to inform applicant.
2. **NB** to include on the formulary, TLS amber (specialist recommendation, no SCP)
3. **JC/VR** to investigate the potential for removing Degludec from the formulary.

4.3 **DegLira (Xultophy®)** – Adults with type 2 diabetes mellitus in combination with oral glucose-lowering medicinal products when these alone or combined with a GLP-1 receptor agonist or basal insulin do not provide adequate glycaemic control. **Dr SC, Consultant Endocrinologist, UH-Bristol and Dr KJ Consultant Endocrinologist, Weston.**

Please see application form for full details. Dr SC and Dr KJ were unable to attend the meeting; however VR presented the application to the group.

This is an application for the inclusion of a combination of degludec and liraglutide. Insulin
degludec is only on the formulary in BNSSG:

- 100 units per ml: Only for Type I diabetic patients who have failed on insulin glargine and who are not suitable or failed on insulin pump therapy.
- 200 units per ml: Only for Type II diabetic patients requiring pre-dialysis insulin.

It is not currently on the formulary for Type II patients, although there is the feeling that it is being more widely prescribed than the formulary states. The application states that both agents are included on the formulary.

It is a fixed combination and therefore to in order to prescribe 1.2 mg liraglutide this would deliver 42 units of degludec. NICE have stated that a dose of 1.8 mg of liraglutide is not recommended for the treatment of patients with type 2 diabetes.

The application is based on reducing the number of injections i.e. by not having to administer degludec and liraglutide separately, and in addition, Xultophy® is more cost effective than prescribing the two agents together. Also, it is suggested that the combination reduces the risk of hypos, and would be beneficial in the frail elderly patient.

In people who are insulin-naïve, insulin degludec/liraglutide was non-inferior to insulin degludec alone and superior to liraglutide alone for reductions in HbA1c (with a difference of 0.64% compared with liraglutide). In people previously treated with basal insulin, insulin degludec/liraglutide was superior to insulin degludec alone for reducing HbA1c with a difference of 1.1%.

However, over 80% of the patients in the study DUAL I were only taking metformin which does not reflect current practice as patients medication would usually be optimised before initiating insulin.

In terms of other options, human NPH insulin should be used first line in type II diabetic patients, and long acting insulins maybe considered in certain circumstances. **POST MEETING NOTE:**


Within this it states that ‘The GDG reviewed the insulin-based recommendations from NICE guidance CG87 and agreed that the updated evidence supported the use of insulin detemir and insulin glargine as alternatives to NPH insulin under certain circumstances. The GDG agreed that there was strong evidence to indicate that insulin degludec was not cost-effective and therefore was confident that this option should not be recommended.’

- **Patient safety** – The European public assessment (EPAR) report concluded that the safety profile is in general similar to that of the 2 included components. Long-term safety concerns are the same as for the other GLP-1 receptor agonists and long-acting insulin analogues. The most commonly reported adverse reactions listed in the summary of product characteristics (SPC) are hypoglycaemia, decreased appetite, nausea, diarrhoea, vomiting, constipation, dyspepsia, gastritis, abdominal pain, flatulence, gastroesophageal reflux disease, abdominal distension and injection site reactions. Cases of confirmed hypoglycaemia were 32% with insulin degludec/liraglutide, 39% with insulin degludec and 7% with liraglutide.
- **Clinical effectiveness** – Insulin degludec/liraglutide was non-inferior to insulin degludec alone (treatment difference −0.47% points) and superior to liraglutide alone (treatment difference −0.64% points) for change in HbA1c from baseline. Insulin degludec/liraglutide was superior to insulin degludec alone (treatment difference −1.1% points) for change in HbA1c from baseline.
- **Cost effectiveness or resource impact** – Annual cost ranges from £387 for a daily dose of 10 dose-steps (10 units insulin degludec and 0.36 mg liraglutide) to £1987 for a daily dose of 50 dose-steps (50 units insulin degludec and 1.8 mg liraglutide). Would significantly increase drug spend if this is used in place of glargine or detemir.
- **Strength of evidence** – Well-designed trials. The observed differences in HbA1c of around ≥0.5% are generally considered clinically significant. However, the manner in which Xultophy® was added to therapy was not in line with current UK guidance for T2DM in either trial. Over 80% of patients in DUAL I were taking metformin only.
• **Place in therapy relative to available treatments** – The applicant has suggested that this would be an option in preference to the addition of mealtime insulin, or GLP-1 agonist if failing on basal insulin and also as an option in preference to the addition of a second injection (basal insulin) if failing on GLP-1 agonist. However NPH insulin should be used first line.

• **National guidance and priorities** – SMC have approved its use, restricted in Scotland: for use in patients who are uncontrolled on basal insulin analogues (glycosylated haemoglobin [HbA1c] >7.5% [59mmol/mol]) and for whom a GLP-1 receptor agonist is appropriate as an add-on intensification therapy to basal insulin to obtain glucose control.

• **Local health priorities** – diabetes is locally a key area to improve care.

• **Equity of access** – Degludec has not been approved for use in type 2 diabetics within BNSSG.

The JFG considered the application, the evidence and information submitted. The evidence suggests that there may be a small benefit in terms of HbA1c reduction by using IDegLira compared to liraglutide alone or degludec alone. Patients in the trials did not have their medications optimised which does not reflect current practice and it is an expensive option. There are other options for the cohort of patients identified e.g. Toujdeo® (longer acting), GLP1 agonists once weekly which have lower acquisition costs. In addition, after the meeting, the NICE clinical guideline on type 2 diabetes management was published on 2nd December, and within this it states that there was strong evidence to suggest that degludec was not cost effective. The JFG therefore did not approve the addition of IDegLira onto the formulary.

**Action:**

1. **NB** to inform applicant.

4.4 **Dulaglutide (Trulicity®)** - in adults with T2D mellitus as monotherapy, or add-on therapy.  
   Dr KJ, Consultant Endocrinologist, Weston and Mrs JB, DSN for Weston.

Please see application form for full details. Dr KJ and Mrs JB were unable to attend the meeting; however VR presented the application to the group.

This application is for the addition of dulaglutide, a once weekly injectable GLP-1 receptor agonist to the formulary. Currently on the BNSSG formulary, once weekly exenatide is included in accordance with NICE TA248 (since 2012). The other GLP1s Lixisenatide and Liraglutide are also on the formulary, however these are daily injections. Patients have fed back that the administration pen for Bydureon® (once weekly exenatide) is difficult to use which has negatively impacted on the number of patients who are prescribed it. The administration pen has recently been improved however it is still considered not as good as it could be. In terms of cost, it was marketed in the UK at a higher cost compared to Bydureon®. This national price has been reduced now so that it is cost neutral compared to exenatide.

The pen itself is relatively easy to use, and is considered better compared to Bydureon®. In addition, it offers an advantage over other GLP-1s in renal impairment as can be used down to eGFR 30 ml/min/1.73m².

In terms of the GLP1-s as a group, we would have all four agents on the formulary if this were to be accepted. Bydureon® has a NICE TA, and therefore we need to keep this on the formulary. Lixisenatide appears to be better to control post prandial hypos, and liraglutide has a benefit for those patients in whom basal hyperglycaemia is a particular problem. VR is undertaking an exercise to gather data from companies in specific patient groups so that as a formulary group we can potentially make a decision as to which GLP-1 we would put as first line, or in specific cohorts. Twice daily exenatide is not particularly highly prescribed due to a high incidence of sickness.
Therefore this could be removed from the formulary.

- **Patient safety** – According to the summary of product characteristics, the most common adverse events (1 in 10 people or more) are hypoglycaemia, particularly in combination with a sulfonylurea or insulin, and gastrointestinal disorders. According to the European public assessment report (EPAR) possible long-term safety concerns of pancreatitis and pancreatic and thyroid cancers are consistent with other GLP-1 receptor agonists.

- **Clinical effectiveness** - Dulaglutide 1.5 mg or 0.75 mg once weekly was superior to placebo (treatment difference −11.5 mmol/mol [1.05% points] and −9.2 mmol/mol [0.84% points], respectively) and to exenatide twice daily (treatment difference −5.7 mmol/mol [0.52% points] and −3.4 mmol/mol [0.31% points], respectively) for change in HbA1c from baseline (1 RCT, n=978, 26 weeks). Dulaglutide 1.5 mg or 0.75 mg once weekly was superior to sitagliptin once daily (treatment difference −7.8 mmol/mol [0.71% points] and 5.1 mmol/mol [−0.47% points] respectively) for change in HbA1c from baseline (1 RCT, n=1098, 52 weeks). Dulaglutide 1.5 mg once weekly was non-inferior to liraglumide 1.8 mg once daily (treatment difference −0.66 mmol/mol [0.06% points]) for change in HbA1c from baseline (1 RCT, n=599, 26 weeks).

- **Cost effectiveness or resource impact** – The price has now been reduced so that it is now comparable to Bydureon, and liraglutide.

- **Strength of evidence** – Well-designed studies. There are no comparative data with other weekly dose GLP-1 receptor agonists. As with other GLP-1s there are limited data from RCT relating to important patient orientated outcomes.

- **Place in therapy relative to available treatments** – As the price has now dropped, the administration device is easy to use, and its once weekly administration is likely to be attractive to a cohort of patients. It would be offered in accordance with NICE clinical guideline

- **National guidance and priorities** - NICE clinical guideline (NG28) for the management of T2D states that GLP-1 RA therapy should be considered if triple therapy with metformin and 2 other oral drugs is not effective, not tolerated, or contraindicated and the person has:
  - a body mass index (BMI) ≥35.0 kg/m² in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with obesity, or
  - a BMI <35.0 kg/m² and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.

- **Local health priorities** - diabetes is locally a key area to improve care.

- **Equity of access** –

The JFG considered the application, the evidence and information submitted. The evidence supports efficacy and similarity to other GLP-1s that have already been agreed for the formulary. The improved pricing strategy means that it will not introduce a cost pressure and could result in savings of nursing time and reduction in prescriptions for needles. The improved usability may provide an advantage over alternative GLP-1s. Agreed for inclusion onto the formulary (with GLP-1 restrictions i.e. 6 month review with weight loss and HbA1c improvement expected), TLS green.

**Action:**

1. **NB** to inform applicant.

2. **NB** to include on the formulary, TLS green.

3. **NB** to include the American Diabetes Association (ADA) diabetes guidance on the formulary (widely used in the UK)
4. **VR to gauge opinion as to whether Byetta® can be removed from the formulary.**

In addition, two other points were raised in relation to diabetes and the formulary.

4.4a **Alogliptin.** An application was discussed by the JFG back in April 2014. At the time, it was decided not to include on the formulary due to a lack of significant evidence suggesting non-inferiority/superiority over the other gliptins currently available and on the formulary. It was noted at the time that it had a lower acquisition cost but any cost savings would be very small as a switch would not have been undertaken in those patients currently stable on another gliptin. Dr PS at Weston would like to conduct research in to whether patients remain stable when switched from another gliptin to alogliptin. This would give evidence to support a full switch of patients across BNSSG on gliptins to alogliptin which would offer significant savings across primary care. The project would only be conducted by Dr PS, and patients would be monitored over 6 months. It was felt that this was not something that the JFG could agree to as it was outside the remit of the JFG. This proposal should be taken to the local D&TC.

**Action:**

1. **NB to forward proposal to JT and FL for discussion at Weston D&TC**

4.4b **Diabetes formulary.** VR has produced a re-formatted diabetes formulary in anticipation of current applications and this has been sent around the local specialists for agreement. All items included are those that are formulary. Apidra (short acting human insulin) is currently not on the formulary, but included on this version. A NDR needs to be completed for this to be included. The formulary was agreed for publication when the chapter review is complete.

4.5 **Midodrine - Severe orthostatic hypotension due to autonomic dysfunction, Hepatorenal syndrome, Intradialytic hypotension. GC, RB, SP, Pharmacists UHB and NBT.**

Please see application form for full details. This application was for the inclusion of Midodrine onto the formulary, for the treatment of orthostatic hypotension, hepatorenal syndrome and intradialytic hypotension. It has been in use for many years in these cohorts however a licensed product has not been available. Midodrine has recently been licensed in the UK for the treatment of orthostatic hypotension due to autonomic dysfunction and therefore this application is supporting current local practice. Current practice for orthostatic hypotension is still fludrocortisone first line, although this use remains off label. If this fails or isn’t tolerated Midodrine will be initiated. There are no licensed alternatives to treat orthostatic hypotension.

NICE have produced an evidence summary for Midodrine in the treatment of orthostatic hypotension. Two RCTs found that Midodrine significantly increased standing blood pressure 1 hour post dose compared with placebo in people with symptomatic orthostatic hypotension due to autonomic dysfunction. There was also limited evidence that Midodrine improved some symptoms of orthostatic hypotension such as syncope and low energy levels. Results for other symptoms such as light headedness and dizziness are less supportive and the studies did not assess quality of life, falls or ability to carry out daily activities.

It is not licensed for hepatorenal syndrome, or intradialytic hypotension, however it is used in both these cohorts. Midodrine is used in combination with octreotide and albumin in hepatorenal syndrome in non-intensive care settings where terlipressin plus albumin is not available. There is evidence to support its use. UpToDate’s article on hepatorenal syndrome recommends the use of midodrine (with octreotide plus albumin where terlipressin is not available) based on a number of studies.

One non-randomised study compared 13 consecutive patients with type 1 hepatorenal syndrome; 8 patients were treated with IV dopamine and 5 with oral midodrine (75 to 12.5mg TDS) plus SC
octreotide. All received daily IV albumin. All of the midodrine patients showed increases in mean arterial pressure, renal plasma flow, GFR and urine volume; for all patients treated with dopamine there were no changes in any of these parameters. In terms of survival 3 out of 5 patients treated with midodrine survived to discharge compared to only 1 out of 8 patients treated with dopamine. Adverse effects of midodrine were minimal; tingling, goose bumps, and diarrhoea were observed.

A retrospective study compared 60 patients who received midodrine (up to 15mg TDS), octreotide and albumin with 21 patients who received albumin alone. Therapy with midodrine and octreotide was associated with significantly lower mortality (43 versus 71 percent) and a significantly higher proportion of patients who had resolution of hepatorenal syndrome (40 versus 10 percent).

Studies in end stage renal failure patients suffering from dialysis associated hypotension suggest that this drug effectively improves haemodynamic stability during haemodialysis, significantly increasing blood pressure and reducing hypotensive symptoms. Midodrine is effective with chronic administration and appears to be very safe in this population, despite the presence of significant comorbidity. Finally, efficient removal of both prodrug and desglymidodrine with haemodialysis avoids the concerns of hypertension or other adverse effects in the interdialytic period.

Once a patient with orthostatic hypotension has been stabilised it is envisaged that a GP could take on the prescribing. A proposed SCP has been written and is suggested to be included as amber if Midodrine is approved for inclusion.

- **Patient safety** – According to the summary of product characteristics, the most common adverse effects of midodrine are piloerection, pruritus of the scalp and dysuria, occurring in more than 1 in 10 people. Adverse effects occurring in between 1 in 10 and 1 in 100 people include paraesthesia, headache, nausea, dyspepsia, stomatitis, pruritus, rash, chills, flushing, urinary retention and supine hypertension.

- **Clinical effectiveness** - 2 RCTs found that midodrine 10 mg 3 times daily increased standing blood pressure statistically significantly more than placebo, 1 hour after the dose was taken. Improvements in patient- and investigator-rated symptoms were seen with midodrine compared with placebo in both RCTs. However, the symptom measurement scales were not reported to have been validated. Three systematic reviews and meta-analyses have considered midodrine for orthostatic hypotension. They included studies in various types of orthostatic hypotension, although the results are largely driven by the 2 RCTs in orthostatic hypotension due to autonomic dysfunction that are the focus of this evidence summary. Overall, the systematic reviews and meta-analyses concluded that the quality of the evidence supporting the use of midodrine in orthostatic hypotension is limited by the lack of robust clinical data.

- **Cost effectiveness or resource impact** – Midodrine 5 mg (Bramox) costs £75.05 per 100 tablets excluding VAT (MIMS, August 2015). Therefore, 28 days' supply at a maintenance dosage of 10 mg 3 times daily costs £126.08 excluding VAT. The cost of the licensed product is lower than that of unlicensed products used in 2014 (NHS prescription cost analysis for England 2014).

- **Strength of evidence** – The main limitation is the focus on disease orientate outcomes; no published evidence is available for outcomes such as quality of life, falls or ability to carry out daily activities.

- **Place in therapy relative to available treatments** - The manufacturer of Bramox, Brancaster Pharma Limited, considers that up to around 3500 people in the UK may be eligible for midodrine treatment under the terms of the marketing authorisation. It would be used second line in the treatment of orthostatic hypotension, with fludrocortisone used as first line. It is not licensed for the treatment of hepatorenal syndrome or intradialytic hypotension. However due to the comorbid state of the haemodialysis population it is often difficult to differentiate between orthostatic hypotension and intradialytic hypotension.

- **National guidance and priorities** – SMC have approved it use in orthostatic hypotension. NICE have produced an evidence summary, critically appraising the evidence.

- **Local health priorities** – Not listed as a health priority.

- **Equity of access** – Has been in use for a number of years in this cohort of patients,
although as an unlicensed medicine.

The JFG considered the application, the evidence and information submitted. There is evidence to show that Midodrine is effective in the management of orthostatic hypotension resulting from autonomic dysfunction. Evidence also exists to show that Midodrine is also effective and well tolerated in intradialytic hypotension and hepatorenal syndrome. It was therefore agreed to include Midodrine on the formulary, amber 3 months for orthostatic hypotension. Prescribing should remain with the specialists if being used for intradialytic hypotension or hepatorenal syndrome, i.e. TLS red. The SCP was agreed.

**Action:**

1. **NB** to inform applicant.

2. **NB** to include on the formulary, TLS amber for orthostatic hypotension and red for intradialytic hypotension and hepatorenal syndrome.

4.6 **Sacubitril & Valsartan** - Adult patients with chronic heart failure and reduced ejection fraction. **Dr AN, Consultant Cardiologist, UHBristol.**

Please see application form for full details. Dr AN was unable to attend the meeting.

The application was for the inclusion of a first in class combination medication for the treatment of heart failure. The application was originally being brought to the JFG as it was being offered to clinicians under Early Access to Medicines Scheme (EAMS). This was the first time that an ‘in tariff’ medicine was offered under this scheme. Patients could be initiated on this medication prior to licensing under the EAMS scheme, and treatment would be provided free of charge until NICE reports (due June 2016). The JFG were under the impression that licensing was not going to be until December, however the licence was granted the day before our meeting. Unfortunately the opportunity for patients being initiated under EAMS has been missed. This has highlighted that we need a more robust process to be in place to be more reactive to EAMS and this process will be taken forward at the next JFG meeting for agreement – the ToR need to be amended so that we can accept more concise applications (i.e. not a new drug application) and respond in a timely way. With the support of the acute trusts, we hope that this situation does not happen again.

We are therefore now in the position where the medication is licensed and available and UHB would like to use this in a small cohort of patients prior to NICE. Nothing is included within the ToR that states whether we look at medications prior to NICE publication.

Sacubitril+valsartan is a first-in-class angiotensin receptor and neprilysin inhibitor. Valsartan is an angiotensin receptor blocker that competes with angiotensin II for binding to the AT1 receptor. Sacubitril is a prodrug that inhibits neprilysin, an enzyme responsible for the breakdown of several vasoactive peptides. Their combined action reduces vasoconstriction and sodium retention, helping improve some of the underlying causes of chronic heart failure (CHF). The MHRA have stated that there is currently an unmet need in the treatment of HF and that those patients who are considered well controlled still have a mortality rate of 7%. The introduction of this new class of agent has a plausible biological action, which has not been exploited before.

Sacubitril+valsartan has been involved in a major phase III trial, PARADIGM HF involving over 8000 patients across many international centres. Patients had a range severity however the majority (over 70%) have NYHA class II HF. The study showed that the use of sacubitril/valsartan reduced the risk of CV death/hospitalisation by 20% compared to ramipril, with a NNT of 21 over 27 months.

The group agreed that whilst the trial data was good there were some reservations that it was not representative of clinical practice locally, and whether it could be extrapolated to the use of
Ramipril locally. Enalapril was chosen as the comparator, as this is the ACE inhibitor with the most evidence in heart failure, and the FDA directed the company to use this as the comparator. The doses of enalapril in PARADIGM have been questioned – the licensed dose is up to 40mg in heart failure, however only 20mg was used in the trial. In the SOLV-D and CONSENSUS trials (enalapril in heart failure) the average dose that patients tolerated was 18mg. ARBs have not been shown to be superior to ACEIs and as such are reserved for individuals who cannot tolerate an ACEi. An ARB was required to be paired with sacubitril as there is a risk of angioedema when an ACEi is used with sacubitril.

To come to an agreement now that this is licensed, whilst the JFG recognised that the cohort identified by the applicant were those with most severe heart failure, the evidence does not support this group over any of the other classes of heart failure. This however would be the most pragmatic cohort to initiate treatment with. The JFG agreed that UHB MAG may manage the 5 patients that you would like to start treatment in prior to NICE publication.

POST MEETING NOTE: Those present at MAG saw no reason for it to go on the formulary until the NICE TA but it was agreed that if UHB wanted to use it in the interim in the cohort requested in the application there was no objection and prescribing would remain with the specialists.

Action:

1. NB to inform applicant.
2. NB to update ToR to include information on EAMS, free stock and decisions prior to NICE.

5 Shared Care Protocols/TLS status

5.1 Denosumab SCP (updated)

The SCP had been updated post the MHRA updated information regarding calcium levels, and the need to be vigilant about osteonecrosis of the jaw. In addition, the SCP has now been updated so that medication may be reviewed after 5 years of treatment, instead of 3 years. A minor amendment is required regarding the need to check vitamin D levels. The JFG agreed the SCP.

5.2 Ulipristal (new SCP) and treatment pathway

Ulipristal for the intermittent treatment of fibroids was agreed at the October meeting. The SCP and treatment pathway has been developed to support GPs taking over the prescribing. This has been developed with Weston, however needs to be shared with NBT and UHB specialists. Once agreement has been sought with these trusts, the SCP can be uploaded onto the website.

5.3 Colesevelam (new SCP)

The SCP was presented at the meeting. It has been written by Weston to support GPs prescribing for bile acid malabsorption, which was agreed to be included on the formulary over a year ago. This needs to be shared amongst the group, and sent around to all the specialists for agreement.

6 Individual Funding Requests (Lisa Collard arrived to update the JFG)

LC updated the group with issues raised from the BNSSG IFR panel.

1. Tamoxifen and gynaecomastia – requests for surgery for gynaecomastia. However where
does tamoxifen fit in the treatment pathway? Is tamoxifen locally commissioned? A NDR would need to come to the JFG to support this.

2. Autologus eye serum – coming to the IFR panel, but is a cohort of patients. There was a discussion as to whether this is considered a medicine/medical device and whether this is something that should come to the JFG. To continue to investigate.

3. Armour thyroid – there continues to be recommendations coming from secondary care for this. Currently this is not on the formulary and therefore should not be routinely being prescribed. To investigate within the local trusts.

7 Chapter review and formulary process

JC gave an update on the process. 7 chapters (7, 8, 9, 10, 14, 15 and 16) have been completed and the significant changes were presented at this meeting (see attached paper). The JFG approved the changes to the chapters and therefore these will be uploaded onto the website shortly.

The last step of making the chapters live has been complicated by the changes that have been made to the BNF and we are trying to reflect these within our formulary website.

We are still on track to complete the review of the chapters by the end of the year. Feedback is as always very welcome.

8 Items for Discussion

8.1 NDRs for January Meeting (no papers, for information only)
   b. Magnesium – nebulisation for severe asthma
   c. Olsalazine – ulcerative colitis
   d. Peppermint enemas – relief of abdominal colic and distension particularly in IBD.
   e. Infliximab – steroid refractory immune mediated colitis due to ipilimumab
   f. Cangrelor – with aspirin in patients with coronary artery disease undergoing PCI
   g. Levonorgestrel intrauterine device – women needing LARC or women with heavy menstrual bleeding

9 AOB

FL – Identified a UKMI risk assessment tool for new drugs coming to the market. This is a long document of statements to be considered however the JFG agreed that this is a useful tool that could be included within our processes. FL to share with the group.

NB
Interface Pharmacist
25th November 2015
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<th>Minute No.</th>
<th>Subject</th>
<th>Action Required</th>
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**MEETING DATES 2016**

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