

Risk:benefit of Co-proxamol

CSM Pre-hearing

13 October 2004



Consultation; Request for evidence on Risks and Benefits

- ▶ New objective evidence on risks or benefits
- ▶ Special patient groups
- ▶ Impact of local restriction/withdrawal



Objective evidence of risk or benefit

- ▶ No new evidence



Special patient groups for whom risk: benefit may be positive

- ▶ NSAIDs are contraindicated, not tolerated or ineffective
- ▶ Cannot metabolise codeine to morphine due to CYP 450 deficiency
- ▶ Cannot tolerate codeine (GI side effects)

But: no new evidence to support case - views based on clinical experience



Other points arising from public request for information

- ▶ Local initiatives or formulary restrictions produced 20-30% reductions in prescribing
- ▶ Reduced pack size generally not endorsed
- ▶ Other analgesics may not be safer
- ▶ Misidentification of 'at risk' patient groups



Consultation-summary

- ▶ No objective new evidence: Risk/benefit is generally unfavourable
- ▶ Co-proxamol should not remain available
- ▶ Co-proxamol should not be initiated in new patients
- ▶ Withdrawal should be gradual to minimise disruption
- ▶ Supportive of continuing availability:
 - ▶ Current prescribers (rheumatologists, palliative care/pain specialists and some GPs)
- ▶ Patients



MAH Appeal: Safety

(Points 2.1-2.4)

- ▶ "Very safe " at recommended dose
- ▶ 20-25* tablets may have fatal outcome
- ▶ 15-20 tablets with alcohol/CNS depressants
- ▶ Not cardiotoxic at recommended dose
- ▶ Readability testing shows proposed PIL/label warnings will ensure patients clearly understand the risks

* approx 3 days' supply



MAH Appeal: Efficacy

(Points 2.5-2.7)

- ▶ Superiority to paracetamol 650/1000mg alone is unproven
- ▶ No evidence of synergy
- ▶ Efficacy with acute dosing is unproven
- ▶ Not studied in chronic use but strong PK basis supporting premise that repeat doses are more likely to be effective
- ▶ *In-vitro* NMDA antagonism suggests benefit in neuropathic pain
- ▶ 40 years' use - Patient preference



MAH Appeal: Risk/Benefit

(Points 2.8-2.9)

- ▶ Favourable when used at recommended doses
- ▶ All indications and populations
- ▶ Acute and chronic



MAH Appeal: Proposals for safer use

- ▶ Restrict use to second line
- ▶ Introduction of smaller pack size
- ▶ Educational campaign
- ▶ Electronic pharmacy warnings/label for non-electronic dispensing label.

Other points raised

- ▶ Alternative analgesics have their own drawbacks
- ▶ Consequences of revoking MAs for patients and prescribers.



CSM Advice Sought

1) Consultation - any new evidence to inform decision?

2) Company Appeal - whether any points are resolved satisfactorily

- ▶ Points 2.1-2.4 (safety)
- ▶ Points 2.5-2.7 (efficacy)
- ▶ Points 2.8-2.9 (risk:benefit)


