



- **New MHRA warnings on proton pump inhibitors (PPIs)**

<http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/index.htm>

The April issue of the MHRA Safety Update highlights 2 issues relating to long-term PPI use.

- **Recent epidemiological evidence of increased risk of fracture**

There is recent epidemiological evidence of an increased risk of fracture with long-term use of PPIs. Patients at risk of osteoporosis should be treated according to current clinical guidelines to ensure they have an adequate intake of vitamin D and calcium.

- **Reports of hypomagnesaemia**

Prolonged use of proton pump inhibitors (PPIs) has been associated with hypomagnesaemia. Healthcare professionals should consider measuring magnesium levels before starting PPI treatment and repeat measurements periodically during prolonged treatment, especially in those who will take a PPI concomitantly with digoxin or drugs that may cause hypomagnesaemia (eg, diuretics).

The Prescribing Team is currently investigating the availability and the cost of magnesium tests locally.

These issues highlight the importance of review of long-term PPI use to ensure it is appropriate.

- **Cohort study: Losartan is not associated with an increased risk of all-cause mortality compared to candesartan in heart failure patients**

According to a study published in the Journal of the American Medical Association, losartan is not associated with increased mortality in patients with heart failure compared to candesartan.

Researchers conducted the study to assess the hypothesis that losartan use is associated with increased all-cause mortality in heart failure patients as compared with candesartan. The hypothesis was based on results from previous observational studies suggesting that losartan may be associated with increased mortality in patients with heart failure compared with other angiotensin II-receptor blockers (ARBs).

Compared with candesartan, losartan was not associated with increased all-cause mortality (adjusted hazard ratio [HR], 1.10; 0.96-1.25) or cardiovascular mortality (adjusted HR, 1.14; 0.96-1.36).

Compared with high doses of candesartan (16-32 mg), low-dose (12.5 mg) and medium-dose losartan (50 mg) were associated with increased mortality (HR, 2.79; 2.19-3.55 and HR, 1.39; 1.11-1.73, respectively)

The researchers conclude that "Whereas lower doses of losartan were associated with increased mortality risk as compared with higher doses of candesartan, there was a decreasing risk of mortality with increasing losartan dose; and no significantly increased mortality risk was observed when comparing the highest dose of losartan against the highest doses of candesartan. These findings do not support the hypothesis of differential effects of specific ARBs in patients with heart failure."

- **Valsartan "warning" on SystmOne**

It has come to our notice that a notation stating "High Risk" is displayed against valsartan on SystmOne. It also appears as red text, similar to drugs like methotrexate, and so the wording plus the colour is understandably causing concern. On investigation it appears that this warning is in place because the liquid special formulation of valsartan may have different bioavailability to the capsules – however this would only be an issue if the liquid is prescribed. SystmOne are looking to revise / resolve this warning.

- **Amber 1 medicine definition**

The definition of "amber 1" medicines previously stated that specialists must initiate these medicines and only transfer prescribing when the patient was stabilised. This was causing some confusion for prescribers in primary care as the shared care protocols for the "amber 1" medicines leflunomide and DMARDs indicate that the specialist need only recommend the initial dose. The definition has been amended to incorporate this as follows:

AMBER 1: These are medicines that require significant monitoring and the decision to treat with an AMBER medicine should be made by specialists only. Prescribing may be transferred to a GP under a shared care agreement. Therapy should either be initiated and the patient stabilised by the specialist, or the specialist may recommend the initial dose for the GP to prescribe while continuing to monitor the patient closely during the stabilisation phase; this will be specified in the shared care protocol e.g. for leflunomide and all other DMARDs. Amber 1 medicines attract a "near patient testing fee" under the GP Local Enhanced-Service Contract.

This edition is also available on HNN (Health Network Northants)

<http://www.northants.nhs.uk/Display/Dynamic.jsp?topid=14070&lhsid=514&oid=2854¤tid=2854>

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