Domperidone MHRA Safety alert: risk of cardiac side effect – restricted indication, new contraindications, reduced dose and duration of use.

I am writing to you to make you aware of the recent changes which have been made to the marketing authorisation (license) for domperidone (Motilium).

A review of domperidone safety data has been conducted by the MHRA where continued reports of cardiac adverse effects and a small increased risk of serious side effects were confirmed. Furthermore, a higher risk was observed in patients older than 60 years, adults taking daily oral doses of more than 30mg, and those taking QT-prolonging medicines or CYP3A4 inhibitors concomitantly.

The advice below relates to domperidone:

**Indication**
- Domperidone is now restricted to use in the relief of symptoms of nausea and vomiting.
- It should be used at the lowest effective dose for the shortest possible time.

**Contraindications**
- Domperidone is contraindicated in people:
  - with conditions where the cardiac conduction is, or could be, impaired.
  - with underlying cardiac diseases such as congestive heart failure.
  - receiving other medications known to prolong QT or potent CYP3A4 inhibitors.
  - with severe hepatic impairment.
- Patients with these conditions should have their treatment reviewed at their next routine appointment and be switched to an alternative treatment if required.

**Posology**

**Oral formulations**
- For adults and adolescents over 12 years of age and weighing 35kg or more, the recommended maximum dose in 24 hours is 30mg (dose interval: 10mg up to three times a day).
- In children under 12 years of age and weighing less than 35kg, the recommended maximum dose in 24 hours is 0.75mg/kg body weight (dose interval: 0.25mg/kg body weight up to three times a day).

**Suppository formulation**
- Suppositories should only be used in adults and adolescents weighing 35kg or more, the recommended maximum daily dose in 24 hours is 60mg (dose interval: 30mg twice a day)
Duration of treatment

• The maximum treatment duration should not exceed one week.
• Patients currently receiving long-term treatment with domperidone should be reassessed at a routine appointment to advise on treatment continuation, dose change, or cessation.

Regional Drug & Therapeutics Centre Medicines Information department have provided the following abridged general advice which GPs may find useful when actioning this safety alert:

“Domperidone is one of only two prokinetic drugs available on the UK market, along with metoclopramide. However, similar restrictions were placed on metoclopramide last year by the MHRA. UKMi issued a memo in response to those restrictions. The following advice (adapted from that memo) would appear to be the most pragmatic approach:

• All patients receiving long-term domperidone should have their therapy reviewed.
• A trial of withdrawal of domperidone therapy should be tried in all patients, with full patient engagement.
• For GORD or dyspepsia, ensure all other therapeutic and lifestyle options are optimised. Options are limited. If nausea or vomiting is the predominant symptom, an antiemetic agent could be tried. Appropriate guidelines on management should be followed, such as those from NICE CKS:
  o Dyspepsia with proven GORD
  o Dyspepsia of unknown cause
• For gastroparesis, ensure any iatrogenic cause is identified. Assess and correct nutritional state and, in patients with diabetes, check glycaemic control.
  o An antiemetic agent may be used to control any symptomatic nausea and vomiting.”

Erythromycin (unlicensed) can be used as a pro-kinetic agent but this is not supported by local microbiologists and it is not recommended that GPs initiate given the strategies to minimise antibiotic resistance and manage the incidence of C. difficile. Additionally, the clinical data to support its role in gastroparesis is too limited to recommend as an option for GPs at this time.

Please ensure this information is shared with all Prescribers, including locums, in your practice.