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

Following a review of Domperidone safety data by the MHRA which showed continued reports of cardiac side effects and a small increased risk of serious side effects. 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 following advice relates to domperidone:
(Ref: https://www.cas.dh.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=102155)

Licensed Indication

- Domperidone is now restricted to use in the relief of symptoms 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 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 which I have attached for your records. 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:
    - Dyspepsia with proven GORD
    - 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.
    - Short-term low-dose erythromycin (250-500mg tds for up to four weeks) may also be an option (unlicensed), although consultation with local microbiologists is advised.
    - An antiemetic agent may be used to control any symptomatic nausea and vomiting.
- Chronic cough due to non-acid reflux may be managed with domperidone. Use a one month trial, continued dependent on risk/benefit. Withdrawal of therapy should be considered when remission has been established.