DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)
POSITION STATEMENT

Domperidone 'off-licence' use for the following indications:

- **Gastroparesis and other gastric outlet physiological impairment**
- **Babies and children (normally prescribed by specialists)**
- **Nursing mothers to promote lactation**

Following a European review, the Medicines and Healthcare products Regulatory Agency (MHRA) gave updated advice on domperidone prescribing (MHRA Drug Safety Update April 2014).

Domperidone is associated with a small increased risk of serious cardiac side effects. Its use is restricted to the relief of nausea and vomiting and the dosage and duration of use have been reduced. It should no longer be used for the treatment of bloating and heartburn. Domperidone is now contraindicated in those with underlying cardiac conditions and other risk factors.

The MHRA also recognised that the overall safety profile of domperidone, and in particular its cardiac risk and potential interactions with other medications, should be taken into account if there is a **clinical need** to use it at doses or durations greater than those authorised e.g. to control side effects of Parkinson's disease treatment in some patients.

MHRA December 2019: Domperidone is no longer licensed for use in children younger than 12 years or those weighing less than 35kg (for nausea and vomiting). Results from a placebo-controlled study in children younger than 12 years with acute gastroenteritis did not show any difference in efficacy at relieving nausea and vomiting compared with placebo.

Domperidone is also used outside of its authorised indications in children in the UK for gastrokinetic effects in conditions other than nausea and vomiting. If a specialist physician considers, based on their professional judgement and available evidence of the medical condition, that domperidone use in any condition is justified in a child younger than 12 years, the patient or parent/caregiver should be fully informed of the potential benefits and risks of the different options

Gastroparesis and other gastric outlet physiological impairment

Gastroparesis is a condition whereby the stomach fails to empty despite a normal gastric outlet. This is common in autonomic neuropathy complicating diabetes and after upper GI surgery that disturbs vagal function, including antireflux surgery. This results in chronic vomiting, pain, malnutrition and poor diabetic control.

Domperidone is commonly used as part of management as a prokinetic for this condition [1,2]. Recently both the EMA and MHRA have restricted use to very short periods only (one week), and advised it should no longer be used in patients with certain comorbidities.

Domepridone has advantages over metoclopramide, also used in gastroparesis, as it has no central nervous side effects (excepting pituitary). However, concern has been raised due to potential prolongation of QT_c and rare fatal cardiac dysrhythmias.

Gastroparesis is a difficult condition to manage and alternative drug treatments are also problematic (long term metoclopramide and erythromycin, or repeated BoTox injections to pylorus). The American College of Gastroenterology guidelines[1] confirm the limited evidence base supporting the use of all of these alternatives. Meta-analysis suggests domperidone is efficacious in reducing symptoms[3], and superior to metoclopramide[4].

Derbyshire clinicians managing patients with gastroparesis still consider long-term domperidone an important option for treatment. Prescription will be limited to the following:

- Definite functional outlet delay evidenced by endoscopy and/or transit study
- Avoid in age > 60
- NO significant heart disease, severe hepatic impairment, co-use of CYP3A4 inhibitors* or QTc prolongating drugs** or on pre-treatment ECG
- Under regular review by clinician
- Maximum dose 10mg tds
- Trial of limited courses with drug “holidays”

* e.g. itraconazole, fluconazole, diltiazem, verapamil
**e.g. erythromycin, citalopram, haloperidol, amiodarone

Babies and children[5] (normally prescribed by specialist)

Cardiac arrhythmias in children are rare. In children arrhythmias are more commonly genetic or secondary to congenital heart defects

a. Children with congenital heart disease
   Consider stopping domperidone therapy or discuss with parents/carers and ensure that cardiac monitoring is regularly performed. Consider offering an alternative treatment where appropriate

b. Other children with established reflux or nausea and vomiting
   Take no immediate action in patients already established on domperidone. Consider reducing the dose (where appropriate) to 250microgram/kg three times a day at the next convenient review. Consider routine cardiac monitoring where there are concerns (e.g. cardiovascular instability, concomitant CYP3A4 inhibitors prescribed).

c. Children with newly diagnosed reflux or at risk of nausea and vomiting
   In the majority of cases reflux is self-limiting, not serious and resolves before the child’s second birthday once the child is weaned onto solid food. Simple measures should be introduced first - feeding the infant upright and keeping them upright after feeds, and the use of feed thickeners should be considered first-line where the child is on liquid feeds. These measures should be given a proper trial before considering pharmacological intervention – at least two weeks.

In more serious cases, and after the introduction of thickeners then consider the benefits and risks of medical anti-reflux/anti-acid secretion treatment. If domperidone is to be used (Note- domperidone is no longer licensed for use in children younger than 12 years or those weighing less than 35kg) , give an initial maximum of 250micrograms/kg three times a day. Where reflux or nausea is refractory to this then give increased doses to a maximum of 400micrograms/kg (max 20mg) three times a day and recommend regular cardiac monitoring.

Nursing mothers to promote lactation[6]

There are limited alternative options for the stimulation of lactation, the use of domperidone can be considered provided there is evidence of thorough evaluation for treatable causes such as poor attachment, and when increased frequency of breastfeeding, pumping or hand expression of milk has not been successful.

A maternal dose of 30mg (10mg three times daily) is a commonly accepted dosing regimen. In exceptional circumstances the feeding specialist may recommend a longer duration (never longer than three weeks) at a reduced dose of 10mg twice daily to 10mg daily

Domperidone should not be used if the mother or infant:

- have conditions where the cardiac conduction is, or could be, impaired,
- have underlying cardiac diseases such as congestive heart failure,
- are receiving other medications known to prolong QT interval or potent CYP3A4 inhibitors,
- have severe hepatic impairment

References

1. Hasler WL. Gastroparesis: Pathogenesis, Diagnosis, Management. Nat Rev Gastroenterol Hepatol 2011;8(8):1-16.
2. Camilleri M, et al. American College of Gastroenterology Clinical guideline: management of gastroparesis. Am J Gastroenterol. 2013;108:18-37.
3. Sugumar A, et al. A systematic review of the efficacy of domperidone for the treatment of diabetic gastroparesis. Clin. Gastroenterol. Hepatol. 2008;6:726-733.
4. Sturm A, et al. Prokinetics in patients with gastroparesis: a systematic analysis. Digestion 1999;60:422-427
5. Babies and children – advice taken from position statement- Neonatal and Paediatrics Pharmacists group endorsed by British Society for Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN)
6. Lactation advice taken from UK Drugs in Lactation Advisory Service- UKMI

Document updates	Date updated