PAN MERSEY AREA PRESCRIBING COMMITTEE
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NHS Pan Mersey Area Prescribing Committee

DOMPERIDONE: updated indications, dose and contraindications

Domperidone is restricted to short term use in the relief of nausea and vomiting. The maximum recommended dose is 30 milligrams daily for one week. Contraindications include cardiac disorders, hepatic impairment, and concomitant QT prolonging or CYP3A4 inhibiting drugs.

The MHRA warning [1] regarding an increased risk of serious cardiac adverse effects with domperidone has led to updated recommendations on indications, dose and contraindications:

- Domperidone is restricted to use in the relief of nausea and vomiting
- It is no longer recommended for use in, or, for treatment of gastro-oesophageal reflux disorder (GORD) and dyspepsia
- It should be used at the lowest effective dose for the shortest possible time: 10 milligrams three times a day for adults
- The maximum recommended dose is 30 milligrams daily for one week (see below for information for special patient groups)

Contraindications

- People with conditions where cardiac conduction is, or could be, impaired
- People with underlying cardiac diseases such as congestive heart failure
- People receiving other medications known to prolong QT interval e.g. erythromycin, citalopram, amiodarone, haloperidol
- People receiving other medications known to be potent CYP3A4 inhibitors e.g. fluconazole, itraconazole, verapamil, diltiazem
- People with severe hepatic impairment

A Pharmacovigilance Risk Assessment Committee (PRAC) review [1] of published and unpublished clinical and non-clinical data found a small increased risk of serious cardiac adverse reactions relating to domperidone use including QTc prolongation, torsades de pointes, serious ventricular arrhythmia and sudden cardiac death.

A higher risk was observed in patients aged over 60 years; adults taking doses greater than 30 milligrams daily; those on medication which can cause QTc prolongation for example antipsychotics, macrolide antibiotics, amiodarone or citalopram; those on any medication which is a CYP3A4 inhibitor for example macrolide antibiotics, HIV antivirals.

Special Patient Groups

Parkinson's disease patients on long term domperidone for the relief of nausea and vomiting associated with apomorphine or L-dopa, should remain on their usual dose. Seek specialist advice if required, or for new patients.

Patients with gastroparesis whose symptoms persist can be managed with domperidone (providing no contraindications exist). This is an off label indication and prescriber and patient should be made aware of this. For these patients, an antiemetic agent may be used to control any symptomatic nausea and vomiting.

Paediatrics – Domperidone use should be avoided wherever possible. If existing patients are unable to stop domperidone, the recommended dose is:

- adolescents over 12 years and over 35 kg 10 - milligrams up to three times daily
- children under 35 kg - 250 micrograms/kg up to three times daily

End of life / oncology patients - Specialist centres routinely prescribe licensed doses of domperidone. On occasions off-label use of 20 milligrams four times a day or an extended duration of treatment may be necessary is exceptional situations. Prescribing in these situations for oncology patients should be retained by the specialist centre.

Prokinetic Alternatives

There are currently no drugs in the UK licensed as prokinetic agents. Domperidone and metoclopramide have been the most widely prescribed prokinetic agents in the UK. In 2013, the MHRA [2] issued a warning for metoclopramide regarding risks of extrapyramidal side effects.

References

[1] European Medicines Agency, "Domperidone-containing medicines," 25 April 2014. [Online]. Available: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Domperidone-containing_medicines/human_referral_prac_000021.jspandmid=WC0b01ac05805c516f. [Accessed 31 July 2017].

[2] Medicines and Healthcare products Regulatory Agency, "Domperidone: risks of cardiac side effects," 30 may 2014. [Online]. Available: https://www.gov.uk/drug-safety-update/domperidone-risks-of-cardiac-side-effects. [Accessed 24 July 2017].

[3] Medicines and Healthcare products Regulatory Agency, "Metoclopramide: risk of neurological adverse effects," 07 August 2013. [Online]. Available: https://www.gov.uk/drug-safety-update/metoclopramide-risk-of-neurological-adverse-effects. [Accessed 31 July 2017].