

## Introduction

- The guideline follows the advice issued from the MHRA for the restricted use of domperidone
- In April 2014, the MHRA revised the licensed indications and doses for domperidone
- It was found that the drug was associated with a small increased risk of potentially life-threatening cardiac side-effects
- A higher risk was observed in patients aged over 60 years, adults taking daily doses in excess of 30mg, and those taking concomitant CYP-3A4 inhibitors or QT-prolonging medicines

## Summary of MHRA recommendations

- The licenced use is now only for the relief of symptoms of nausea and vomiting for the **shortest duration possible**
- **New recommended doses:**

### Adults (and adolescents over 12 years ≥ 35kg)

- 10mg orally up to THREE times a day
- or 30mg twice a day rectally as suppositories (currently only available as unlicensed import)

### Children (under 12 years ≤ 35kg)

- 0.75mg/kg in 24hrs
- (0.25mg/kg up to THREE times a day)

### It should **no longer be used** in patients with:

- severe hepatic impairment
- conditions where cardiac function is, or could be impaired or where there is underlying cardiac disease such as congestive heart failure
- when co-administered with QT-prolonging medicines (e.g. clarithromycin, citalopram or amiodarone – see website at end of document) or potent CYP3A4 inhibitors (e.g. diltiazem or verapamil)

## Formulary Status

	3Ts	BCAP	ICID
Licensed Use	Green	Green	Green
Unlicensed Use	Amber	Amber	Amber

## Prescribing Advice

- For patients requiring doses of domperidone **above the recommended maximum dose or who are at risk of QT prolongation, they should be reviewed for a trial of stopping**, reducing the dose or consider alternatives
- If domperidone treatment is to continue, the risks and benefits should be explained to the patient with documentation of the discussion detailed in the patient's clinical records
- Such patients should be reviewed with cardiac monitoring as described below

## Recommended Cardiac Monitoring

- For patients who are at risk of developing QT prolongation or require treatment above the recommended maximum dose, **an ECG should be performed prior to initiating treatment and at one week** after commencing domperidone therapy
- If there is evidence of significant QT prolongation, therapy should be stopped
- For patients that are continuing existing domperidone treatment, an ECG should be recorded by the patient's clinician or GP at the earliest opportunity
- If there is no evidence of QT prolongation, therapy may be continued if clinically appropriate
- If the patient is to subsequently receive a short course of a treatment that can prolong the QT interval in addition to domperidone, and there is no suitable alternative (e.g. an antibiotic), then either discontinue the anti-emetic if possible, or undertake close ECG monitoring for the period they are receiving treatment
- For treatment with an additional agent that can prolong QT interval that would be used long-term with domperidone, consider alternative option

Clinical use of domperidone for unlicensed indications following MHRA advice now AMBER so should be specialist initiated

- Domperidone is used for a variety of unlicensed and other indications not covered directly by the MHRA's advice
- The following are the main conditions where documentation of **off-licence use of domperidone needs to be recorded in medical notes and patients should be informed:**

## 1. Adults with gastro-oesophageal reflux disease, dyspepsia or gastroparesis

- For patients who do not respond to two months of full-dose proton-pump inhibitor (PPI) or one month of double dose or alternative PPI: trial of an H2 antagonist such as ranitidine. NICE says: Do not offer metoclopramide, domperidone or erythromycin to treat GOR or GORD without seeking specialist advice and taking into account their potential to cause adverse events.<sup>3</sup> If no alternative, try a trial of domperidone (on demand or intermittent therapy).
- A review for all patients receiving long-term domperidone should be undertaken and consideration of a trial withdrawal in conjunction with optimising other treatment options
- For patients with gastroparesis, 'on-demand' domperidone (i.e. up to 10mg three times a day for up to 1 week) continues to be an option with due consideration to the revised contra-indications

## 2. Adults receiving chemo-therapy for the prevention of nausea and vomiting

- Domperidone at a dose of 10mg three times a day should be used as standard for all patients, or those with the contraindications highlighted by the MHRA
- Patients that require high dose domperidone (unlicensed) should be reviewed by a specialist oncologist and records of an informed decision should be documented in the patient's notes after explaining the risks and benefits
- If continued supplies are to be prescribed by the patients GP, a letter of recommendation of the higher dose should be forwarded to the respective GP surgery
- The risk for developing QT-prolongation should be considered with ECG monitoring as described above
- All patients receiving domperidone or any other antiemetic should be prescribed these agents for the shortest time necessary and regularly reviewed for continued clinical need for on-going treatment

## 3. Children with gastro-oesophageal reflux disease

- **seek advice from a paediatrician or medicines management if you are unsure of what to do**

### Congenital heart disease:

- Consider stopping domperidone therapy or discuss with patients/carer and ensure cardiac monitoring
- Consider offering an alternative treatment where appropriate

### Established GORD:

- Consider reducing the dose where appropriate to 0.25mg/kg three times a day at the next convenient review
- Consider routine cardiac monitoring where there are concerns of cardiac instability or concomitant CYP3A4 inhibitors are prescribed

### Newly diagnosed GORD:

- Simple measures should be introduced first such as feeding the infant upright and positioning them upright after feeds, in addition, use of thickeners should be considered when the child is on liquid feeds
- If after at least a two week trial of these first-line measures has occurred, the child is still symptomatic or in more serious cases, consider the benefits and risks of anti-reflux/anti-acid secretion
- If domperidone is to be used, give an initial maximum of 0.25mg/kg three times a day
- Where reflux or nausea is refractory to this then give increased doses to a maximum of 0.4mg/kg (max 20mg) three times a day with cardiac monitoring as described above

## 4. Use in nursing mothers to promote lactation

- If it is considered that the benefits outweigh the risks for the unlicensed use of domperidone as a galactagogue for an individual patient, **the lowest effective dose** (maximum 10mg three times a day) should be used for a **maximum of 1 week**

## 5. Pre-treatment for patients to be commenced on apomorphine for Parkinson's Disease

- Prior to commencing patients on high dose domperidone (20mg three times a day) prior to the emetogenic agent, apomorphine, any risk factors for QT-prolongation (for example, age over 60 years and concomitant drugs) should be reviewed
- The risks and benefits of therapy should be explained to each individual patient and documented in the notes
- **Treatment should not continue for greater than 14 days** without specialist review

## References

1. MHRA safety alert on Domperidone: <http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON418518>
2. Combined list of drugs that prolong QT: <https://www.crediblemeds.org/pdftemp/pdf/CompositeList.pdf>
3. Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. Jan 2015. [www.nice.org.uk/guidance/ng1](http://www.nice.org.uk/guidance/ng1)