Domperidone Guidance

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The recent recommendation from both the European Medicines Agency and the MHRA restricting the use of domperidone to short-term use in the relief of symptoms of nausea and vomiting has necessitated review of its use in other clinical conditions (MHRA). (The advice below does not relate to the use of domperidone in the management of chemotherapy induced nausea or Parkinson’s disease).

Domperidone and metoclopramide have been the most widely prescribed prokinetic agents in the UK. Metoclopramide has also recently had restrictions placed on its use due to extrapyramidal adverse effects. It should only be used for short-term use (up to 5 days) and should no longer be used in chronic conditions such as gastroparesis, dyspepsia and GORD, nor as an adjunct in surgical and radiological procedures. As a consequence, there are now no drugs on the UK market licensed as prokinetic agents. The three commonest conditions for which prokinetics have been traditionally prescribed are PPI-refractory gastro-oesophageal reflux disease (GORD), oesophageal dysmotility and gastroparesis.

(i) **PPI-refractory GORD**
Those patients who fail to respond to standard dose of PPI (e.g. omeprazole 20 mg once daily) should have the dose increased to twice daily. If the reflux symptoms are still not adequately controlled, the patient should be referred to Gastroenterology for further management.

(ii) **Oesophageal dysmotility**
The management of patients with symptomatic oesophageal dysmotility can be particularly challenging, and the choice of treatment is determined by the type of dysmotility disorder. Patients should be referred to Gastroenterology for further management.

(iii) **Gastroparesis**
Initial management should include identification of any iatrogenic causes (opioid analgesics, anticholinergic agents, and some diabetic medications including exenatide can all delay gastric emptying). Treatment with low-dose erythromycin* (250-500mg three times daily for up to four weeks) is an option, although long-term effectiveness is limited by declining benefit with repeated doses. An anti-emetic may be required for the symptomatic treatment of nausea and vomiting. Patients with persistent symptoms will need specialist Gastroenterology input.

*NB: Macrolide resistance is a much more significant problem in Staphylococci and Streptococci than penicillin resistance, so macrolide use should be restricted and as short term as possible.

NEW MHRA warning - Combination use of medicines from different classes of renin-angiotensin system

Combination use of medicines from different classes of renin-angiotensin system blocking agents is associated with an increased risk of hyperkalaemia, hypotension, and impaired renal function. New warnings have been agreed following an EU-wide review. In particular, prescribers are advised that people with diabetic nephropathy should not be given an ACE-inhibitor with an angiotensin-receptor blocker as they are already prone to developing hyperkalaemia. Combining aliskiren (non-formulary) with an ACE-inhibitor or angiotensin-receptor blocker is contraindicated in people with kidney impairment or diabetes. For further details see the MHRA drug safety update:

The graph below shows the proportion of high strength steroid inhalers (including combinations), as defined in the BTS/SIGN guidelines, as a percentage of the total prescribing of steroid inhalers* for the CHPs in Grampian. This is one of the National Therapeutic Indicators. This indicator comes from concern that inhaled steroids may be being used at too high a dose in some patients and that patients with well controlled asthma are not having inhaled steroid doses stepped down and, particularly for patients with COPD, inhaled steroids are prescribed outwith guideline recommendations. GP practices should have received practice level graphs indicating where they are in relation to other practices in Grampian. Over 40% of patients in Grampian are receiving high dose inhaled steroids, this increases in the over 40 year olds to around 50% of patients. The NHS Scotland Respiratory prescribing strategy has recently been issued and is designed to promote appropriate, evidence-based, cost-effective prescribing of treatment for asthma and COPD. It sets out the principles and provides advice on the use of steroid inhalers in both asthma and COPD.

*High strength inhaled steroids are those that deliver beclometasone and budesonide >800 micrograms; fluticasone>400 micrograms per day when used as recommended by manufacturers. The number of dispensed prescriptions (items) is used to measure the frequency of prescribing. The number of items of high strength steroid inhalers is divided by total inhaler items.

**Two new inhalers for COPD added to Grampian Joint Formulary**

Both Fostair® and Relvar® Ellipta® have been included on the Grampian Joint Formulary (GJF) for the treatment of severe COPD. Treatment with either inhaler may be initiated in either hospital or primary care.

**Fostair® 100/6 inhalation solution** (beclometasone dipropionate 100microgram and formoterol fumarate dihydrate 6microgram metered dose inhaler) is included for the treatment of patients with severe COPD (FEV$_1$ <50% predicted normal) and a history of repeated exacerbations (>2 per year), who have significant symptoms despite regular therapy with long-acting bronchodilators. Evidence suggests that Fostair® is of equivalent efficacy to Seretide® 500 and Symbicort® 400/12 which are currently in the GJF for this indication. Fostair® is a pressurised metered dose inhaler (pMDI) and offers a licensed pMDI alternative to the established dry powder inhalers for this indication. Fostair® should be used in patients who prefer pMDI treatment after appropriate inhaler assessment. The 100microgram dose of beclometasone in Fostair® is not bioequivalent to a 100microgram dose of beclometasone in several other inhaler formulations. The dose for COPD is two puffs twice a day ideally given via a spacer. It is a well known device with no storage or shelf life issues and is the first pMDI licensed for COPD. Seretide® 250 pMDI is commonly used for this indication but is unlicensed and considerably more expensive than Fostair®. For COPD patients with FEV$_1$ <50% predicted and a history of recurrent exacerbations who prefer a pMDI after appropriate assessment the Respiratory MCN would strongly encourage the use of Fostair® rather than the Seretide® 250 pMDI.

**Relvar® Ellipta® 92micrograms/22micrograms** inhalation powder (fluticasone furoate 92micrograms/vilanterol 22micrograms inhalation powder) is included for restricted use in patients with severe COPD (FEV$_1$ <50% predicted normal) and a history of repeated (>2 per year) exacerbations despite regular therapy with long-acting bronchodilators. (NB: Relvar® Ellipta® is licensed for use in patients with an FEV$_1$ <70%, but the use in COPD patients with an FEV$_1$ of 50% to <70% was not recommended by the SMC). Only the lower strength combination product (92microgram/22microgram) is included in the GJF for COPD. The higher dose product (184/22) is only licensed for asthma and the Grampian Respiratory MCN does not support Relvar® Ellipta® for use in asthma. Relvar® Ellipta® requires a once daily administration and may therefore be beneficial in some patients with poor compliance taking the current twice daily preparations. Once the foil pack is opened and the desiccant removed, the product has a relatively short in-use shelf life of 6 weeks. Ellipta® is the device name and may appear in the description of other inhalers.

Both Fostair® and Relvar® Ellipta® cost less than the relevant alternatives Symbicort® 400/12 and Seretide® 500. [Costs for 30 days treatment excluding VAT - £29.32, £27.80, £38.00 and £40.92 respectively].