North Yorkshire and York
Humber and North Yorkshire
Health and Care Partnership

NHS
Humber and
North Yorkshire
Integrated Care Board (ICB)

FAO: Primary Care colleagues in North Yorkshire and York

Medicines Management Prescribing Focus – April 2023

Review & Deprescribing Advice for Proton Pump Inhibitors (PPIs)

PPIs are among the most frequently prescribed drugs globally. Although they are cost effective when used appropriately, studies have shown they are prescribed without a clear indication in up to 70% of cases.

Adverse effects of PPIs are usually mild and reversible and include the following: abdominal pain, constipation, diarrhoea, dizziness, dry mouth, headache, insomnia, nausea and skin reactions.

However, there is increasing evidence that long-term PPI use is associated with an increased risk of significant adverse effects. Some of these adverse effects are associated with considerable morbidity and mortality. The most widely studied of these is Clostridium difficile infection. Other adverse effects include an increased fracture risk, higher risk of community-aquired pneumonia, acute interstitial nephritis, chronic kidney disease, hypomagnesaemia, vitamin B12 deficiency, cardiovascular events, subacute cutaneous lupus erythematosus and gastric cancer.

In 2017 an observational study of people taking PPIs showed that their all-cause mortality increased the longer they took them. People who received PPIs for between one and two years had a 50% increased risk of death compared with those who took them for less than a month. An increased risk of death was also associated with the lack of a documented gastrointestinal indication for PPI use.

The higher risk of death with PPI use is likely to be mediated by the occurrence of one or more of the adverse events associated with PPI use noted above. Long-term PPI use should be limited to people who have a clear medical indication and in whom the benefits will outweigh any potential risks

The pharmacological management of dyspepsia continues to have significant costs to the NHS. Differences between PPIs in terms of clinical efficacy and safety are minimal. In adults, dispersible tablets should be reserved for patients with swallowing difficulties due to their higher cost. Of note is that Losec 'MUPS' tablets are three times the cost of lansoprazole orodispersible tablets. No PPI is more effective than another at equivalent doses and therefore NICE recommends using the least expensive PPI.

One exception to this is for patients on clopidogrel. Omeprazole and esomeprazole competitively inhibit the CYP2C19 isoenzyme which metabolises clopidogrel to its active metabolite. This reduces the ability of clopidogrel to inhibit platelet aggregation and reduces the beneficial effect. The MHRA advises that concomitant use of clopidogrel with omeprazole or esomeprazole should be discouraged and this interaction is included in the CQC pre-inspection searches. Healthcare professionals should also check whether patients who are taking clopidogrel are also buying 'over-the-counter' omeprazole or esomeprazole.

NICE recommends that people treated with PPIs receive regular reviews and should be encouraged to reduce their use of these medicines where possible (unless there is an underlying condition or comedication that needs continuing treatment). Reviews should be conducted after the initial 4-8 week course of PPI treatment, and at least annually for patients taking PPIs longer-term. This is particularly important for those on higher doses of PPIs.

Rebound hypersecretion (a rise in acid secretion after discontinuing PPI treatment) can occur after courses as short as eight weeks' duration. This can often lead to an increase in GI symptoms, which may be mistaken for disease relapse. Patients should be warned about this possibility when PPIs are deprescribed. The duration of rebound hypersecretion is unknown, but some studies show reflux-like symptoms within two weeks, and for at least four weeks after withdrawal from PPI therapy. To help limit the occurrence of rebound hypersecretion, the dose of PPI could be slowly reduced and an antacid and/or alginate could be prescribed for at least two weeks as cover.

Stopping or reducing therapy may not be appropriate for some people, for example those:

- with Barrett's oesophagus
- with a documented history of bleeding GI ulcers
- with severe oesophagitis or oesophagitis complicated by past strictures, ulcers, or haemorrhage
- co-prescribed a PPI for gastroprotection with an NSAID or other ulcerogenic medicine

Action required:

The MMT requests that practices:

- search for patients prescribed clopidogrel and ensure they are not also on omeprazole or esomeprazole. Such patients should be switched to an alternative PPI or a Histamine H2-receptor antagonist (at the time of writing, both nizatidine and famotidine are available)
- discuss the need for long term therapy with all adult patients prescribed PPIs at each medication review, with a view to tapering the dose or safely deprescribing where possible, as per the attached algorithm
- consider other medications as possible causes of dyspepsia e.g. calcium antagonists, nitrates, theophyllines, bisphosphonates, corticosteroids and NSAIDs
- patient counselling on the long term risks of PPIs should be refreshed at each medication review
- at each review offer simple lifestyle advice, including advice on healthy eating, weight reduction, smoking cessation and avoidance of known precipitants such as fatty foods

Useful resources:

- PrescQIPP Bulletin 267: PPIs - Long term safety and gastroprotection
- NICE CG184: Dosage information on proton pump inhibitors

We would like to take this opportunity to remind all staff involved in making alterations to medication that patients should be informed of any change. Ideally, this should be done face to face, by telephone or by letter. Alternative methods of communication may be considered but must be unambiguous.

Please share the information in this document with all relevant members of staff in the Practice.

For any queries or feedback on this topic please contact us via: hnyicb-ny.rxline@nhs.net

The MMT welcomes ideas and suggestions that you and colleagues may wish to recommend for future prescribing focus editions.

Many thanks,

North Yorkshire and York Medicines Management Team