North of Tyne Area Prescribing Committee
Proton Pump Inhibitors (PPIs) – Prescribing Guidance

Summary

Evidence suggests that the use of proton pump inhibitors may be associated with *Clostridium difficile*, pneumonia, bone fractures and hypomagnesaemia. In order to limit the occurrence of these adverse effects, the prescribing of PPIs should be limited to the following indications:

- Barrett's oesophagus
- Oesophageal peptic stricture
- GORD / oesophagitis
- Ulcer healing
- *Helicobacter pylori* eradication
- Upper GI bleed (including varices)
- Zollinger-Ellison syndrome
- Short bowel syndromes
- Peptic ulcer disease prophylaxis for patients taking NSAID / aspirin / steroid; limited to high-risk* patients only
- Second-line peptic ulcer disease prophylaxis for patients taking clopidogrel; limited to use of lansoprazole in high-risk* patients only
- Second-line non-ulcer dyspepsia
- Stress ulcer prophylaxis in mechanically ventilated patients

***High-risk patients:**

- Previous peptic ulcer disease
- Long-term NSAID, steroid or clopidogrel treatment
- Patients aged >65 years on aspirin, NSAIDS or steroids
- Patients on long-term concomitant medications that increase risk of bleeding (at any age)

Please see below for further information and prescribing advice.

Background

The use of PPIs is generally associated with few adverse effects, the most common of which are headache, nausea, abdominal pain, constipation and diarrhoea. These are usually mild and self-limiting. However, there is evidence of a variety of other possible adverse effects. PPIs have been implicated in increasing risk of infection including pneumonia and *Clostridium difficile* (*C.difficile).* Increased susceptibility to *C.difficile* may be caused by raised gastric pH due to reduced secretion of acid that would normally act as a defence mechanism to ingested pathogens, a correlation between the degree of acid suppression and risk of *C.difficile* infection (Odds Ratio 1.53, 95%CI 1.12-2.10 with H2 receptor antagonists, OR 1.74, 95%CI 1.39-2.18 with once daily PPI, OR 2.36, 95%CI 1.79-3.11 with more frequent PPI) having been reported. (See: Updated guidance on the management and treatment of *Clostridium difficile* infection. PHE May 2013 PHE gateway number: 2013043.)

There is evidence of an increased risk of bone fracture with long term use of PPIs. Patients at risk of osteoporosis should be treated according to current clinical guidelines to ensure they have an adequate intake of vitamin D and calcium. Prolonged use has been associated with hypomagnesaemia. Consider measuring magnesium levels before and periodically during treatment, especially in those taking digoxin, or drugs that may cause hypomagnesaemia, e.g. diuretics.

Some PPIs may reduce the ability of clopidogrel to inhibit platelet aggregation. Where prescription is indicated to reduce bleeding risk, lansoprazole has less interactive CYP2C19 inhibitory capacity than omeprazole, and may be preferred. There is no evidence of adverse interaction between PPIs and prasugrel or ticagrelor.

Take into account any use of PPIs obtained over-the-counter. Patients are advised not to use non-prescription PPIs for more than 4 weeks without consulting a doctor.

Recommendations

In order to limit the prescribing of PPIs to those patients where the benefit of potent acid suppression outweighs these potential risks, the prescribing of PPIs should be restricted to the indications provided below. Use the lowest dose possible to achieve the desired therapeutic goals. In addition, medications associated with a reduction in lower oesophageal sphincter pressure or delayed gastric emptying should be avoided where possible, as these may exacerbate symptoms.

Prescribing in secondary care

All admitted patients should have their PPI use reviewed and a decision made as to whether this is still necessary. In addition, as there is increasing evidence that acid suppressing medications, in particular PPIs, are a risk factor for *C.difficile*, especially in patients with or at high risk of *C.difficile*, when prescribed antibiotics, the PPI should be assessed and the PPI only continued if there is compelling reason to do so e.g. confirmed active PUD, concomitant NSAID use (excluding low dose aspirin) in those aged >65 years, GORD which requires daily PPI for symptom control, a definite history of a bleeding peptic ulcer. Alternative lower risk gastro/esophageal protection may be used (consult BNF and or/gastroenterology)-see action below. Once the antibiotic course has been completed, the need to re-start PPI should be reviewed in-line with recommended indications. If a decision is made to stop PPIs long-term, this must be communicated clearly in the discharge documentation to GPs.

Recommended Indications

- **Barrett's oesophagus**
  - long-term treatment dose
- **Oesophageal peptic stricture**
  - long-term treatment dose
- **GORD / Oesophagitis**
  - give the lowest dose which controls symptoms and offer referral for fundoplication if chronic with reduced QOL, or not responding
- **Ulcer healing**
  - short-term use
- ***Helicobacter pylori* eradication**
  - short-term use
- **Upper GI bleed (including varices)**
  - acute use
- **Zollinger-Ellison syndrome**
- **Short bowel syndromes**
- **Peptic ulcer disease prophylaxis for patients taking NSAID / aspirin / steroid**
  - For high-risk* patient groups only
  - Double-dose histamine-2 receptor antagonists may be used as an alternative to PPIs in this situation e.g. ranitidine 300mg once or twice daily.
- **Second-line peptic ulcer disease prophylaxis for patients taking clopidogrel**
  - Lansoprazole only
  - For high-risk* patient groups only
  - Second line to double-dose histamine-2 receptor antagonists e.g. ranitidine 300mg once or twice daily.
- **Second-line non-ulcer dyspepsia (i.e. dyspeptic symptoms with normal endoscopic findings)**
  - Initially treat with antacids / histamine-2 receptor antagonists
  - If unsuccessful, maintenance dose PPIs; there is no evidence for escalating to higher doses of PPI and PPIs should be stopped if there is no benefit after a limited trial
  - Efforts should be made to step down treatment soon after symptom control is achieved
- **Stress ulcer prophylaxis in mechanically ventilated patients**
  - PPIs are used for the prevention of stress ulcer in mechanically ventilated patients. These should not routinely be continued at discharge unless the patient meets one of the above criteria

***High-risk patients:**

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- Long-term NSAID, steroid or clopidogrel treatment
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- Patients on long-term concomitant medications that increase risk of bleeding (at any age)

Primary and Secondary Care Action

PPIs should only be initiated for the indications approved above. Patients currently managed with PPIs should be reviewed to identify those for whom PPI therapy is not approved. Treatment options for these patients may include stepping down to a histamine-2 receptor antagonist, symptomatic relief with antacids or PPI withdrawal. Patients taking PPIs for GORD should receive regular reviews to determine if treatment should continue or be stepped-down. In some cases the use of 'when required' PPIs may be appropriate.