University Hospitals Plymouth NHS Trust

Gastroenterology Guidelines

Guideline on the use of Proton Pump Inhibitors (PPIs) in Adults

1. Key messages

- PPIs are highly effective and very safe drugs, however the evidence based around the adverse effects from long-term use of PPIs is increasing.
- Prescribers should only use PPIs for recognised indications at the lowest possible dose and for appropriate durations to minimise PPI overuse and the associated increased risk of harm.
- Older people may be more susceptible to the adverse effects of long-term PPI use
- Clinicians should constantly review PPI indications and should consider stopping if clinically not indicated or agree a stop date with patient after completion of treatment.
- Inform GP on discharge summary to review PPI during community consultations.

2. Background

Proton pump inhibitors (PPIs) are one of the most frequently prescribed drugs worldwide, but a number of studies show that they are often prescribed without an appropriate indication or their use not reviewed at appropriate intervals.
This leads to widespread over prescription, which has financial and potentially adverse clinical consequences. The use of PPIs has been linked to Clostridium difficile infection as well as other infections. In the light of this, the prescription of PPIs should be reserved for patients where there is a clear indication.

3. Recommendations

- All admitted patients should have their PPI use reviewed and a decision should be made as to whether this is still necessary. But the use of PPIs should not be stopped without discovering their indication (patients often do not know these).
- Use the lowest dose possible of PPI to achieve the desired therapeutic goals.
- Please 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.
- If a decision is made to stop PPIs long-term, this must be communicated clearly in the discharge documentation to GPs.

Indication	PPI dose and course length
Barrett's oesophagus	Omeprazole 20 mg BD or 40mg OD and refer to outpatient Gastroenterology for Barret's surveillance.
Patients with known/previous benign oesophageal strictures to prevent recurrence	Omeprazole 20-40mg OD long-term.
Treatment and maintenance of significant gastro-oesphageal reflux disease (GORD)	Omeprazole 20-40mg OD for 4-8 weeks then symptom and dose review. If after 4-8 weeks symptoms re-occur offer PPI at lowest dose possible to prevent symptoms for long-term maintenance. 2nd line agents may be lansoprazole or esomeprazole Esomeprazole should only be initiated by a gastroenterologist.
Oesophagitis	Omeprazole 20-40mg OD depending on severity for 8 weeks. Use esomeprazole 20-40mg OD for endoscopically proven high grade oesophagitis.
Patients with a history of haematemesis and/or melaena	Await endoscopy, if delayed consider omeprazole 40mg OD until endoscopy and alter according to findings.
Duodenal, gastric and non-steroidal anti-inflammatory drug (NSAID) associated ulcers	Omeprazole 40mg OD for 4-6 weeks
NSAID/aspirin/steroid protection for high risk patients*	Omeprazole 20mg OD whilst taking NSAID, stop NSAIDs if possible The use of H2 receptor blocker is not appropriate for this indication.
Duodenal and Gastric ulcer (*H pylori* positive)	Omeprazole 20mg BD for 7 - 10 days (in addition to H pylori eradication) then 40mg OD for 6 weeks total
Zollinger-Ellison Syndrome	Omeprazole 20-120mg OD (above 80mg in 2 divided doses) or lansoprazole 60mg OD adjusted according to response, daily doses of 120mg or more in two divided doses) long term
Prevention of stress ulceration in NBM Intensive Care patients	PPI not indicated. Ranitidine 50mg IV TDS or 150mg PO BD. Discontinue when patient re-starts feeding. See ICU guidelines.
Following endoscopic procedure with intervention which has been used to control non-variceal bleeds or revealed high risk ulcer	72 hour IV Omeprazole infusion then change to oral therapy. This may be high dose (omeprazole or esomeprazole 40mg BD for 11 days in patients with Rockall score 6 or greater, then OD)

Table 1. Recommended Indications and doses for PPIs

***High-risk patients:** Previous peptic ulcer disease; Long-term NSAID, steroids or clopidogrel treatment; Patients aged >65 years on aspirin, NSAIDS, steroids, clopidogrel, prasugrel, ticagrelor

4. Risks / Adverse effects:

1) Clostridium difficile infection:

There is weak evidence supporting an association between PPI use and an increased risk of Clostridium difficile infection. Although a causal link has not yet been proven, as gastric acid is thought to play a principal role in sterilising the stomach contents entering the digestive tract, it is plausible that raising the pH of the stomach with a PPI may increase the load of pathogenic microbes. However, it is possible that these associations are confounded by other CDI risk factors. These include older age, antibiotic treatment, underlying morbidity, hospitalisation, and history of CDI**.**

Prescribers should consider reviewing the need for PPIs in people with CDI or in people at high risk of CDI.

2) Fractures:

Studies suggest that PPIs may cause a modest increase in the risk of hip, wrist or spine fracture, especially if used in high doses over durations of more than one year. The increased risk was seen mainly in older people.

The likely mechanism is a decreased absorption of calcium due to increased pH in the small intestine secondary to the PPI.

There is no association between PPIs and osteoporosis.

People who are at risk of osteoporotic fractures and require PPIs should be assessed using the FRAX score and bisphosphonate and calcium replacement should be considered.

3) Acute interstitial nephritis:

In acute interstitial nephritis a first option is to immediately discontinue the PPI, **spontaneous recovery occurs after withdrawal in most case**s. PPIs can often be replaced with lifestyle measures, an antacid and/or alginate treatment, and/or ranitidine (which is very rarely associated with acute interstitial nephritis)

Because PPIs are often co-prescribed with NSAIDs, there is a possibility that the PPI could be overlooked as the causative agent of the acute kidney injury. Any patient presenting with deteriorating renal function who has been prescribed both a PPI and an NSAID should have both medicines reviewed.

PPI should be used with caution in CKD patients.

4) Hypomagnesemia:

There is a low risk of hypomagnesemia with PPI, which most commonly occurs 1 year after PPI treatment. Routinely monitoring serum magnesium levels in all people taking a PPI is not recommended. However, measuring serum magnesium levels should be considered before prescribing PPIs to people who will be taking them on a long-term basis and particularly to people who will also be receiving digoxin, diuretics or other treatments associated with hypomagnesaemia.

In case of hypomagnesemia replace with oral supplementation but if it remains persistent PPI or other causative medications should be discontinued.

5) Vitamin B12 deficiency:

Gastric acid is needed to cleave vitamin B12 from ingested dietary proteins and enable it to be absorbed. Therefore, PPIs, which suppress gastric acid production, may lead to malabsorption of vitamin B12 but currently there is virtually no evidence this is clinically significant.

Routinely monitoring vitamin B12 in all people taking a PPI is not recommended. However vitamin B12 levels can be affected in people at particular risk of vitamin B12 deficiency such as older or malnourished people, taking PPIs for more than one year or people taking other medicines that can affect vitamin B12 levels, such as metformin.

6) Cardiovascular events:

An association has been observed between PPI use and adverse cardiovascular outcomes in people at high cardiovascular risk. Among patients with GORD, taking a PPI was associated with a

16% increased risk of myocardial infarction. This association does not in itself provide proof of causation, and further studies are needed.

Link to NICE interactive flowchart on dyspepsia

https://pathways.nice.org.uk/pathways/dyspepsia-and-gastro-oesophageal-reflux-disease

The take home message is that PPI like any drug should only be given for a solid indication at the appropriate dosage and their use reviewed.

Trust Guidelines	NHS University Hospitals Plymouth NHS Trust

Guidance Title: Guideline on the use of Proton Pump Inhibitors (PPIs) in Adults

Date	Version
December 2019	1.0

Accountabilities	
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Links to other documents

Version History		
V1	Dec 2019	Guideline introduced

Last Approval	Due for Review
December 2019	December 2024

References :

1) National Institute for Health and Care Excellence guidelines for dyspepsia.
2) British National Formulary.
3) Bjornsson E., Abrahamsson H., Simren M. et al. Discontinuation of proton pump inhibitors in patients on long-term therapy: a double-blind, placebo-controlled trial. Aliment Pharmacol Ther 2006;24(6):945-54.
4) BSG dyspepsia guidelines.
5) MHRA drug safety update on PPI related adverse effects.
6) North Bristol NHS Trust guidelines.