Guidance to Review Proton Pump Inhibitors (PPIs) prescribing

Background and RISKS associated with PPIs

- PPIs are one of the most frequently prescribed drugs (17% of the Sunderland population), but are often prescribed without an appropriate indication and continued indefinitely without review.

- **Long term use of PPIs** has been linked to **serious adverse effects** such as:
  - *Clostridium difficile* infection
  - Increased risk of bone fractures
  - Increased mortality in older patients
  - Acute interstitial nephritis
  - Hypomagnesaemia
  - Vitamin B12 deficiency
  - Rebound acid hypersecretion syndrome
  - Community acquired pneumonia
  - Hyponatraemia

- PPIs should be initiated only where **clearly indicated** and for the **shortest duration** that is appropriate, in order to minimise adverse effects.

Indications for long term PPI use:

Indications where the benefits of long term PPI use outweigh the risks:

- Barrett's Oesophagus
- Oesophageal stricture dilation
- Severe oesophagitis complicated by past strictures, ulcers or haemorrhage
- Previous GI bleeding, perforation or haemorrhage
- Zollinger-Ellison Syndrome
- Gastroprotection for NSAIDs used at high doses, long-term, or in high risk patients*

*High risk patients:[1]

- Aged >65 years.
- History of GI bleeding, gastroduodenal ulcer or perforation.
- Concomitant use of medication known to increase risk of upper GI adverse events, e.g. antiplatelets, anticoagulants, corticosteroids, SSRIs.
- Serious comorbidity, e.g. CVD, hepatic or renal impairment, diabetes, or hypertension.
- Heavy smoking or excessive alcohol consumption.
- Previous adverse reaction to NSAIDs.

These lists are not exhaustive, e.g. PPI's may be indicated in some patients taking DAPT (see NICE CKS on antiplatelet treatment[2]). The presence of multiple risk factors may warrant a PPI; apply clinical judgement to assess GI risk on an individual basis and review regularly. Always review PPI therapy when a medication with GI risks is stopped.

Review long term PPIs (see PrescQIPP algorithm[3] in Appendix A)**:**

- Offer an **annual review** to people taking a PPI on repeat. Consider:
  - **Step-down to the lowest effective dose**: Options include reducing the daily PPI dose, giving doses on alternate days or using PPIs 'as required'.
  - **Stop-PPI**: Gradual dose reduction of PPI treatment can help prevent rebound acid hypersecretion. Alternate day therapy for 1-2 weeks before discontinuation is another option.
- Patients should be counselled on managing **rebound acid hypersecretion** when reducing PPI use, as well as non-pharmacological interventions and lifestyle advice for dyspepsia
- Occasional symptoms and rebound acid can be managed by:
  - **Antacid and/or alginate therapy** either prescribed or purchased over-the-counter.
  - H_2-Receptor antagonist (H2RA) such as ranitidine either 'as required' or daily
  - A short course or 'as required' PPI
- Document the decision in the patient's notes.
- Avoid long term, frequent dose, continuous antacid therapy in functional dyspepsia (it only relieves symptoms in the short term rather than preventing them).

A trial published in 2006 showed that discontinuation of PPIs was successful in 27% of long term PPI users. However GORD patients had more difficulty discontinuing PPIs than non-GORD patients.[4]

PPIs and *Clostridium difficile* infection

- Evidence suggests that PPI use is associated with an increased risk of *Clostridium difficile* infection, so stop or review PPIs in patients with or at high risk of *Clostridium difficile* infection.[5]
- **Risk factors** for *Clostridium difficile* infection include advanced age, antibiotic use (most commonly the broad spectrum antibiotics: clindamycin, cephalosporins, quinolones and co-amoxiclav), underlying morbidity, inflammatory bowel disease and hospitalisation. Other medication considered as risk factors for *Clostridium difficile* infection are laxatives, enemas, enteral nutrition, anti-motility drugs, anti-emetics, corticosteroids and chemotherapy.

PPIs and increased risk of bone fractures – MHRA 2012

- There is evidence of a modest increased risk of fracture with PPIs especially if used in high doses and over long durations (>1year). Two meta-analyses suggest the risk of fracture is increased by 10-40% above baseline. PPIs should be used with caution in patients with other risk factors for bone fractures.
- Treat patients at risk of osteoporosis according to the current clinical guidelines and ensure they have an adequate intake of vitamin D and calcium.

PPIs and hypomagnesaemia – MHRA 2012

- Severe hypomagnesaemia has been reported infrequently in patients treated with PPIs, although the exact incidence is unknown.
- For patients expected to be on prolonged treatment, and especially for those who take PPIs with digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics), healthcare professionals should consider measuring magnesium levels before starting PPI treatment and repeat measurements periodically during treatment.

PPIs and clopidogrel: interaction – MHRA 2010

- MHRA updated guidance advises against the use of clopidogrel and omeprazole or esomeprazole to avoid an interaction but does not support extending this advice to other PPIs.
- Concomitant use of clopidogrel and omeprazole or esomeprazole should be discouraged unless considered essential. The potential risk of a slight reduction in efficacy of clopidogrel should be weighed against the potential gastrointestinal benefit of the PPI.

PPIs and very low risk of subacute cutaneous lupus erythematosus (SCLE) - MHRA 2015

- SCLE can occur weeks, months, or years after exposure to a PPI.
- If a patient treated with a PPI develops lesions, especially in sun-exposed areas of the skin and it is accompanied by arthralgia:
    - Advise them to avoid exposing the skin to sunlight
    - If SCLE is suspected discontinue the PPI and seek specialist advice if needed

References

1. NICE CKS, NSAIDs - prescribing issues. May 2020. https://cks.nice.org.uk/nsaids-prescribing-issues#!scenarioRecommendation:4
2. NICE CKS, Antiplatelet treatment. May 2020. https://cks.nice.org.uk/antiplatelet-treatment#!scenarioRecommendation:3
3. PrescQIPP Bulletin 92. Safety of long term proton pump inhibitors (PPIs). May 2015. https://www.prescqipp.info/umbraco/surface/authorisedmediasurface/index?url=%2fmedia%2f1574%2fattachment-2-proton-pump-inhibitor-desprescribing-algorithm-21.pdf
4. 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. Ailment Pharmacol Ther 2006; 24(6): 945-954
5. UKMI. Medicines Q&As. Clostridium difficile infection - is use of proton pump inhibitors a risk factor? November 2015. https://www.sps.nhs.uk/wp-content/uploads/2016/02/NW-QA244.3-C-difficile-and-PPIs-.pdf

The original document was produced by Rotherham CCG, and also referenced the following:

- "*Guidance for the safe and Effective use of Proton Pump inhibitors*", produced by NHS Barnsley CCG in conjunction with the gastroenterologists at Barnsley Hospital.
- All Wales Therapeutics and Toxicology Centre. All Wales Proton Pump Inhibitor and dyspepsia resource pack. Material to support appropriate prescribing of Proton Pump Inhibitors across Wales. April 2013 http://www.awmsg.org/docs/awmsg/medman/All%20Wales%20Proton%20Pump%20Inhibitor%20and%20Dyspepsia%20Resource%20Pack.pdf

- WeMeRec Bulletin. Proton pump inhibitors. November 2015. https://www.wemerec.org/Documents/Bulletins/PPIBulletinOnline.pdf

Appendix A:[3]

Proton Pump Inhibitor (PPI): Deprescribing algorithm (adults)