Think Medicines!

NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

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Safety

# Safety of long term Proton Pump Inhibitors (PPIs)

The CCG currently prescribes over 800,000 items per year of PPIs costing £1.5 million. Reducing by 30% would save approximately £450,000 and would also reduce the incidence of unwanted side effects.

## Key Recommendations

- Review **medication** for possible causes of dyspepsia. These include calcium channel blockers, nitrates, theophyllines, bisphosphonates, corticosteroids, or NSAIDs. In people needing referral for endoscopy, suspend NSAID use.
- Offer lifestyle advice to manage dyspepsia, e.g. healthy eating, weight reduction, smoking cessation, managing symptoms by avoiding causes and 'using treatment only when needed at the lowest effective dose. Community pharmacists should offer initial and ongoing help for people with symptoms of dyspepsia.
- Avoid long term, frequent dose, continuous antacid therapy in functional dyspepsia (it only relieves symptoms in the short term rather than preventing them).
- Review long term PPI prescribing to reduce the potential serious adverse effects. There may be indications where the benefits of long term PPI use outweigh the risks (e.g. Barrett's oesophagus, oesophageal stricture dilation, and gastroprotection for NSAID treatment) - assess on an individual basis and review regularly.
- Offer an annual review to people needing long term management of dyspepsia. Encourage them to try stepping down to the lowest effective dose needed to control symptoms, or 'as needed'/'on demand' to manage their own symptoms, or stopping treatment completely where appropriate. Advise returning to self-treatment with antacid and/or alginate therapy where required, either prescribed or purchased over-the-counter, especially if rebound symptoms occur.

## Background

Dyspepsia is any symptom of the upper gastrointestinal (GI) tract present for 4 weeks or more, including upper abdominal pain or discomfort, heartburn, reflux, nausea or vomiting. Gastro-oesophageal disease (GORD) is a chronic condition. It can be severe/frequent enough to cause damage to the oesophagus from acid flowing back up into the oesophagus, and lead to abnormality of cells lining the oesophagus, i.e. Barrett's oesophagus. This is considered the most important risk factor for oesophageal carcinoma.

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*Reference:*
*PrescQIPP*
*MHRA Subacute cutaneous lupus erythematosus*

## Supporting Evidence

RCTs on the risks of long term use of PPIs are lacking, most are observational studies, which have limitations. Even modest increases in risks of adverse effects add up to a substantial amount of patient harm at a population level when the risk factor, i.e. PPI exposure, is widely experienced. Adverse effects of PPIs are usually mild and reversible: GI-related, headache, dizziness or skin rashes (see above for MHRA advice about subacute cutaneous lupus erythematosus). Long term PPIs have been associated with increased mortality in older patients, *Clostridium difficile* infection, bone fractures, interstitial nephritis, community acquired pneumonia, hypomagnesaemia, vitamin B12 deficiency, and rebound acid hypersecretion. Strong data supporting the risk of most of these adverse effects are lacking. However, it is advisable to exercise caution in the elderly and in patients with other risk factors for *C. difficile* infection or bone fractures, which have the strongest association with PPI use. In order to minimise the risk of adverse events, only prescribe PPIs for clearly documented indications and for the shortest possible duration.

Prescribe low acquisition cost PPIs in preference to high acquisition cost PPIs, for the shortest duration (and clearly documented indications). There is no evidence that any one PPI is more effective than another. Offer H2RA therapy (e.g. ranitidine) if the response to the PPI is inadequate.

## MHRA advice: Proton pump inhibitors (PPIs): very low risk of subacute cutaneous lupus erythematosus (September 2015)

Very infrequent cases of subacute cutaneous lupus erythematosus (SCLE) have been reported in patients taking PPIs. Drug-induced SCLE can occur weeks, months or even years after exposure to the drug.

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;
- consider SCLE as a possible diagnosis;
- consider discontinuing PPI treatment unless it is imperative for a serious acid-related condition; a patient who develops SCLE with a particular PPI may be at risk of the same reaction with another;
- in most cases, symptoms resolve on PPI withdrawal; topical or systemic steroids might be necessary for treatment of SCLE only if there are no signs of remission after a few weeks or months.

## Help with Review

Contact your Lead Pharmacist for tools to help you review your PPI prescribing.

A patient information leaflet is available at www.cambsphn.nhs.uk/CJPG/Patientresources.aspx.

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