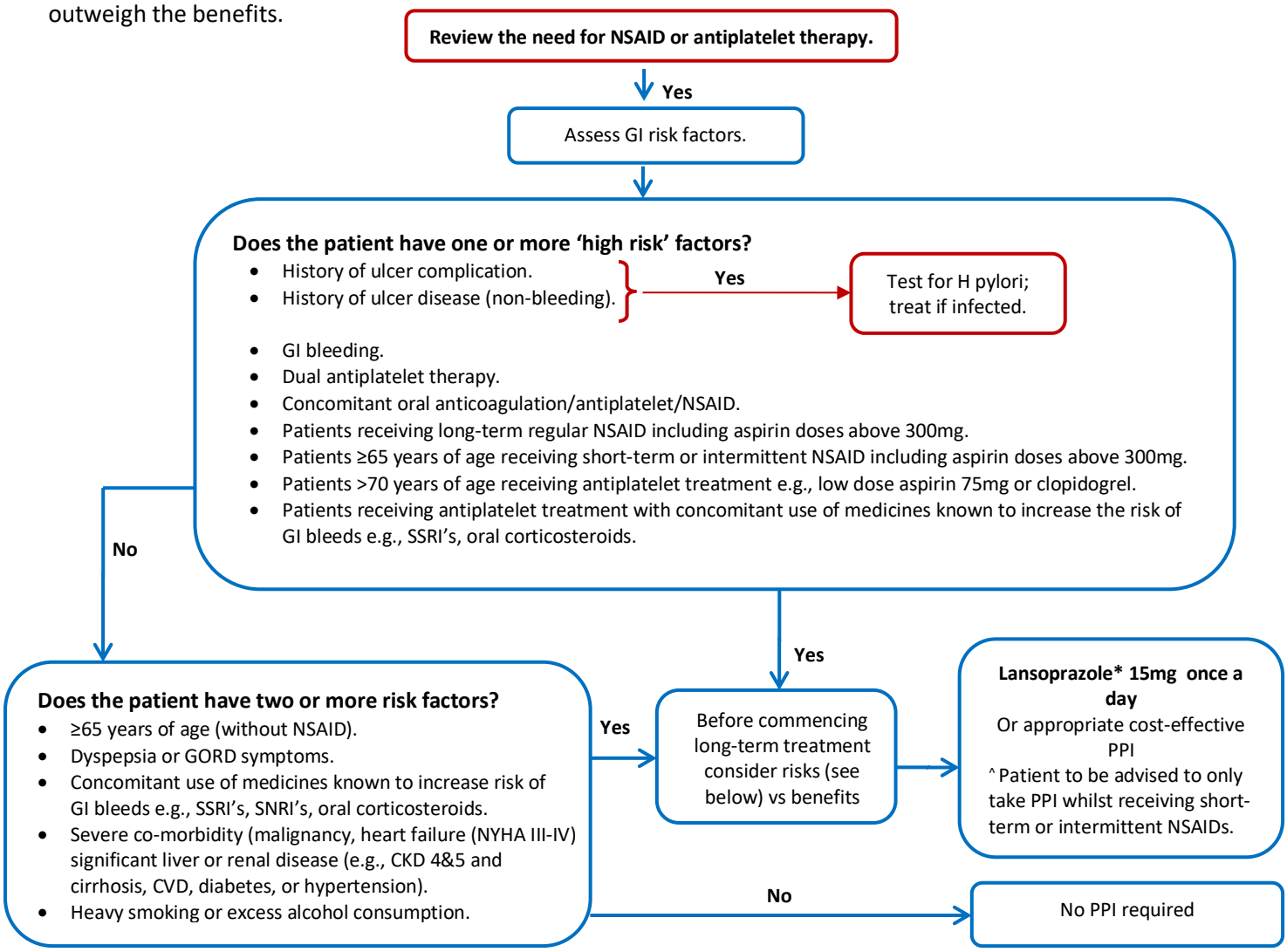
Gastroprotection (with PPI) for patients on NSAID or antiplatelet

Advisory guidance on when to initiate a PPI with a NSAID (or antiplatelet) for gastro-protection.

Where a NSAID (or antiplatelet) is indicated, and to reduce the risk of gastrointestinal adverse effects, the **lowest effective dose for the shortest duration** of treatment should be used. This document is intended as advisory, it does not replace clinical judgement which is assessed on a case-by-case basis.

As PPIs have become widely used, evidence has started to emerge regarding their long-term safety and potential for adverse effects. Clinicians when considering prescribing long-term PPIs, should consider if the risks (see below) outweigh the benefits.



*To aid bioavailability of lansoprazole it should be taken at least 30 minutes before food. If this is difficult omeprazole 20mg with or without food is an alternative, unless the patient is taking clopidogrel, when omeprazole/esomeprazole should be avoided.

Liquid omeprazole is AMBER. It is very expensive and only recommended in rare circumstances. If a patient is on liquid omeprazole or requires liquid omeprazole, please refer this algorithm

Key points

- Ensure that appropriate patients are monitored for side effects during treatment.
- PPI should be stopped when the NSAID/antiplatelet is stopped.
- For other indications of PPI usage ensure there is a set duration/review date.
- All PPIs should be reviewed between 4 and 8 weeks after starting treatment.
- **Long term PPI use should be reviewed at least annually.**
- Exercise caution in the elderly and in patients with other risk factors for *Clostridiodes difficile* infection or bone fractures. Consider need for PPI and if relevant, ensure adequate intake of calcium and vitamin D.
- A PPI is the preferred choice for gastroprotection. Other options for patients who can't tolerate, or where PPIs are contra-indicated, can include H_2-antagonists and misoprostol. Be aware of drug interactions and side effects.

V2.0 Gastroprotection (with PPI) for patients on NSAID or antiplatelet
Updated: January 2025. Review date January 2028. Accessibility checked - contains flow charts that may not be accessible to screen readers.

***Clostridiodes difficile* infection (CDI)**

Observational studies have found the risk of acquiring CDI is approximately 2-3 times higher in PPI users than in non-users. PPI use during CDI treatment was associated with a 42% increased risk of recurrence. Public Health England guideline recommends that consideration be given to stopping or reviewing the need for PPIs in patients with or at high risk of CDI (antibiotic use, hospitalisation, older age & underlying morbidity and inflammatory bowel disease).

Osteoporotic fractures

Observational studies suggest there may be a modest increase in the risk of hip, wrist or spine fracture associated with high dose and long term (>1 year) PPIs. Risk increases with a longer duration of PPI use in post-menopausal women with a history of smoking, which is known to inhibit calcium absorption. Smoking and PPI use may have a synergistic effect on fracture risk mediated by impaired calcium absorption. The Medicines and Healthcare products Regulatory Agency (MHRA) advice issued in April 2012 stated "There is recent epidemiological evidence of an increased risk of 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".

Other adverse effects associated with PPI

Adverse effects of PPIs are usually mild and reversible; however, through case reports and observational studies (subject to bias and causation difficult to prove) long term PPI treatment *may* be associated with uncommon, serious adverse effects such as:

- **Hypomagnesaemia:** MHRA, 2012 have warned of the risk of hypomagnesaemia following long-term use of PPIs, which occurs most commonly after one year of PPI treatment. Serious manifestations- fatigue, tetany, delirium, convulsions, dizziness, and ventricular arrhythmia- can occur, but may begin insidiously and may be overlooked. Routinely monitoring serum magnesium levels **is not** recommended but should be **considered** prior to initiation and periodically during prolonged treatment in those taking digoxin or drugs which may cause hypomagnesaemia (such as diuretics)
  Reasons which may prompt the prescriber to check serum magnesium include when patients report signs/symptoms consistent with hypomagnesaemia (nausea, vomiting, lethargy, drowsiness, weakness, tremor, twitching, tetany , agitation, vertigo, confusion, cardiac arrythmia, seizure), have other electrolyte abnormality or have signs of digoxin toxicity.

- **Pneumonia**: There is conflicting evidence on an association between PPI use and an increased risk of pneumonia. Although there appears to be an increase in risk of developing community acquired pneumonia in patients who have recently started PPI therapy, there is a lack of evidence to show that this applies to patients on long-term treatment.

- **Rebound hypersecretion:** PPI withdrawal may induce rebound acid hypersecretion, which could present as a worsening of symptoms that could be mistaken for disease relapse. However, due to weaknesses in the studies it cannot be concluded if symptoms are clinically important in patients or lead to reuptake of acid-suppressive medication.

- **Tubulo-interstitial nephritis (TIN):** A rare association has been reported between acute tubule-interstitial nephritis (TIN) and PPIs. It can occur between several hours and four months following treatment with a PPI. The standard treatment involves early diagnosis, withdrawing the causative drug, administering steroids and clinical assessment.

- **Very low risk of subacute cutaneous lupus erythematosus** (Drug Safety Update, 2015): PPIs are associated with very infrequent cases of subacute cutaneous lupus erythematosus (SCLE), a non-scarring dermatosis that can develop in sun-exposed areas. Advise avoiding exposure to sunlight and discontinuing PPI treatment.

- **PPI-induced thrombocytopenia**: A rare autoimmune disorder.

References

- ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of proton pump inhibitors and thienopyridines: A focused update of the ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use. J Am Coll Cardiol 2010; DOI:10.1016/j.jacc2010.09.010. Available at: http://content.onlinejacc.org
- All Wales Medicines Strategy Group Safe Use of Proton Pump Inhibitors February 2018. https://www.awttc.org/safe-use-proton-pump-inhibitors
- DTB Vol 55 No 10 October 2017 Prescribing PPIs http://dx.doi.org/10.1136/dtb.2017.10.0541
- MHRA Drug Safety Update. GOV.UK. Volume 3, Issue 9 April 2010
- MHRA GOV.UK Volume 5 Issue 9 April 2012
- MHRA Drug Safety Update. GOV.UK. Volume 9, Issue 2 September 2015
- NICE Clinical Knowledge Summaries: NSAID prescribing issues, revised April 2020
- NICE Clinical Knowledge Summaries: Antiplatelet treatment for secondary prevention of CVD, revised April 2022
- NUH Guideline for the use of Proton Pump Inhibitors in Adults version 4. Review date January 2027. Nottingham City Hospital/NICE
- PINCER Query Library, Evidence-based summaries, revised July 2018. PRIMIS and The University of Nottingham.
- PrescQIPP Bulletin 92. Safety of long-term proton pump inhibitors May 2015.
- PrescQIPP Bulletin 267. PPIs long term safety and gastroprotection 2.0
- Public Health England Clostridiodes difficile infection: guidance on management and treatment. Updated July 2021

Further reading

WHO third Global Patient Safety Challenge: *Medication Without Harm*. Medication safety in High-risk Situations. https://www.who.int/initiatives/medication-without-harm

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