Proton pump inhibitors (PPIs) are one of the most widely used medicines in New Zealand and have changed the management of acid-related upper gastrointestinal disorders.¹

Empirical treatment is often used in general practice for managing un-investigated dyspepsia. While there is a significant placebo response when treating dyspepsia, initiating anti-secretory treatment for an uncertain indication for more than a few weeks may lead to unnecessary long-term use.²

PPIs are very effective and are generally well tolerated, but concerns about adverse effects such as increased risk of fractures, and vitamin and mineral deficiencies means they should not be prescribed indefinitely, without review.¹

Review long-term PPI patients regularly

Some patients do require PPIs long-term, and withdrawal will be inappropriate eg patients with Barrett’s oesophagus, or patients taking non-steroidal anti-inflammatory drugs long-term.

However, a substantial number of patients treated with PPIs, without a clear indication can step down or stop treatment without experiencing deteriorating symptom control.

Tapering, rather than abrupt discontinuation seems to be the most effective way of doing this.

Discontinuation without worsening symptom control can occur for up to 64% of patients, with discontinuation persisting for more than a year.

Other studies have shown that 30–50% of patients are able to lower their PPI dose without an increase in symptoms.³ Patients may also be able to switch to ‘as needed’ dosing, although this may not be effective for all patients because of the lag time to peak anti-secretory effectiveness.³

Use the STOPP/START tool to help when reviewing older patients. Consider:

- clinical appropriateness and benefit,
- duration of use,
- adherence,
- wishes of the patient, and
- the prescribing cascade.⁴
The information contained within this bulletin is to be used in conjunction with the diagnostic & clinical skills of the clinical practitioner. While the writer has taken all possible care in compiling the information contained herein, the general practitioner is responsible for the use of the information. This bulletin has been compiled by the Clinical Pharmacy Team at Te Awakairangi Health Network.

For further information please contact the clinical pharmacists on ph 04 566 5320.

### General tapering guide for acid suppressants

<table>
<thead>
<tr>
<th>PPIs - consider alternate day dosing. Capsules cannot be halved. Consider stepping down to an H2RA if a more gradual taper is required</th>
<th>Stopping PPIs suddenly can cause rebound hypersecretion of acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histamine receptor antagonists (H2RA) - taper gradually</td>
<td>Rebound dyspepsia has been described after stopping H2RA therapy abruptly</td>
</tr>
</tbody>
</table>

### PPIs linked to increased risk of heart attack

Proton pump inhibitors have previously been associated with adverse clinical outcomes in patients concurrently treated with clopidogrel.

New research using a novel, validated approach for assessing clinical data for pharmacovigilance, queried 16 million clinical documents representing 2.9 million individuals treated for gastro-oesophageal reflux disease (GORD). The investigation was to determine whether PPI use was associated with an increased cardiovascular risk in patients without any history of cardiovascular disease.

Patients who were exposed to PPIs had a 1.16-fold (95% CI 1.09–1.24) increased association with myocardial infarction (MI) and a 2-fold (95% CI 1.07–3.78; p=0.031) increased association with cardiovascular mortality regardless of clopidogrel use. The findings are also independent of high-risk (elderly) patients.

This study suggests that there may be a general adverse effect of PPIs independent of other therapy, although the results cannot eliminate possible confounding. By comparison, no association was found between H2RAs such as ranitidine and increased MI risk.

### Rebound acid secretion

Some patients may experience rebound hyperacidity when PPIs are stopped after one month or more continuous use. Serum markers suggest that acid secretion one week following PPI cessation can be significantly elevated above pre-treatment levels but should return to normal within two weeks.¹

Other studies suggest gastric acid secretion returns to baseline over a three to five day period.⁴

If rebound hyperacidity is mistaken for a return of the underlying condition, acid suppressants may be restarted unnecessarily.⁵

### References: