

Prescribing considerations for patients prescribed PPIs for greater than 1 year.

## General Principles for Appropriate Prescribing of PPIs

- **Prescribe only where there is a clear indication**
- **Prescribe treatment doses of PPIs short-term where possible.**<sup>3</sup> Treatment doses are usually only necessary for 4-8 weeks. PPIs should be reduced to maintenance doses (or stopped) when the underlying condition has been effectively treated. [NB. Stopping a PPI is not appropriate in some clinical situations, (Barrett's etc.), but reducing to a maintenance dose in other circumstances may be possible].
- **Review REGULARLY (at least annually).**<sup>5</sup> Patients should be encouraged to reduce or stop their dose of PPI. Consider PRN PPI use or alginate or antacid treatments instead. Ranitidine may be an option for some patients.
- **Offer lifestyle advice.**<sup>5</sup> Include advice on healthy eating, weight reduction, smoking cessation, and avoidance of known precipitants.
- **Counsel patients about rebound symptoms.**<sup>3</sup> Rebound acid hyper-secretion and protracted dyspepsia may occur after stopping prolonged treatment with a PPI. This is usually a short-term effect and goes within 2-4 weeks (during this period patients should be allowed to stabilize, using alginate (e.g. Peptac) to treat any symptoms, before further dose reduction is considered.

Proton Pump Inhibitors (PPIs) block the H<sup>+</sup>/K<sup>+</sup>-ATP-ase enzyme system (the 'proton pump') of gastric parietal cells causing profound suppression of gastric acid secretion. This makes PPIs very effective, but should not provide an opportunity for patients to choose less healthy lifestyles; **particularly as recent evidence has emerged suggesting problems with long term PPI use, particularly in high doses.**

## NSAIDs and PPI Gastro-Protection:

**Review need for NSAID (including coxib);** if considered essential (no available alternative), NICE guidance indicates that a PPI should routinely be co-prescribed with an NSAID (including coxibs) to reduce GI risk for anyone with:

- Osteoarthritis<sup>7</sup>
- Rheumatoid arthritis<sup>8</sup>
- Chronic low back pain ≥ 45yrs old<sup>9</sup>
- Also consider for those at high risk of GI side effects, including > 65yrs, long-term use<sup>10</sup>
- Choose PPI with lowest acquisition cost

## General Cautions

- PPIs may mask the symptoms of gastric cancer; particular care is required for those presenting with 'alarm features'.<sup>3</sup>
- Concomitant use of clopidogrel with omeprazole or esomeprazole should be avoided unless considered essential.<sup>2</sup>

## Clostridium Difficile Risk:

The FDA (USA) issued a Safety Announcement<sup>6</sup> advising:

- The weight of evidence suggests a positive association between the use of PPIs and C. difficile infection. H<sub>2</sub>-receptor antagonists like ranitidine may also be associated with C. difficile however the weight of evidence suggests that the association is probably stronger for PPIs than for H<sub>2</sub>-receptor antagonists.
- In 23 of 28 observational studies a higher (approximately 2-fold) risk of C. difficile was observed in those who had taken PPIs compared to those who had not.
- Adverse event reporting data suggested that elderly patients with chronic medical conditions, or taking broad spectrum antibiotics may have serious outcomes from C. difficile-associated diarrhoea (CDAD) with concomitant PPI use.

## **FDA advice suggests:**

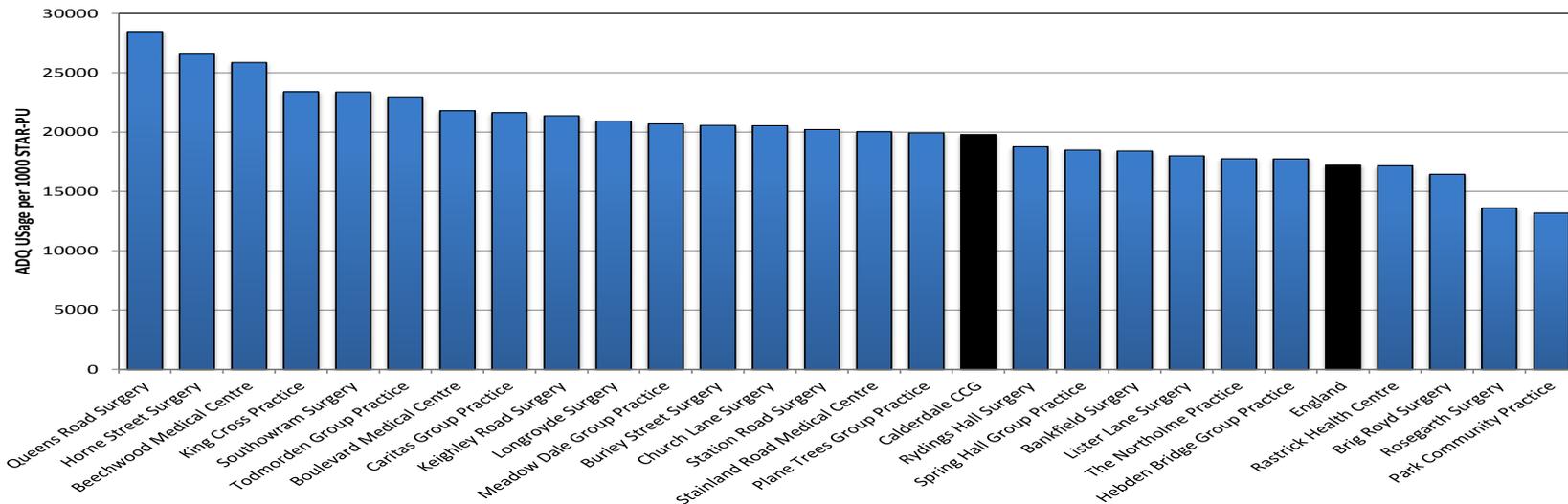
- A diagnosis of CDAD should be considered for PPI users with diarrhoea that does not improve
- PPIs should be used at the lowest dose and for the shortest duration appropriate to the condition being treated.
- Patients should be advised to seek advice from a healthcare professional if they experience watery stool (that does not go away), abdominal pain and fever whilst taking PPIs.

## **General advice**

- In patients considered to be at high risk of C. difficile infection e.g. elderly (and where it is clinically appropriate to do so) consider reducing the dose or review ongoing need for the PPI when antibiotics are co-prescribed. Cover can be provided with an alginate for those suffering from acid reflux.

# Calderdale CCG Prescribing Data

Calderdale CCG - Proton Pump Inhibitors FY 13/14  
ADQ Usage per 1000 STAR-PU



## Increased Risk of Fracture<sup>1</sup>

- 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.
- Two meta – analyses suggest the risk of fracture is increased by 10-40% above baseline (although adjustment for other potential risk factors for fracture and the use of vitamin D & calcium vary).
- Treat patients at risk of osteoporosis according to current clinical guidelines and ensure they have adequate intake of vitamin D & calcium.

## Reports of Hypomagnesaemia<sup>1</sup>

- There is a suggestion that PPIs may cause hypomagnesaemia. Symptoms are unlikely with mild deficiency; early symptoms of moderate to severe deficiency include anorexia, nausea, vomiting, lethargy and weakness. Severe hypomagnesaemia has been reported infrequently.
- The MHRA advises healthcare professionals to consider measuring magnesium levels for patients expected to be on long-term PPI treatment, especially those who take concomitant digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics).

## References

1. MHRA Drug Safety Update, Volume 5, Issue 9 April 2012
2. MHRA Drug Safety Update, Volume 3, Issue 9 April 2010
3. British National Formulary 65, April 2013
4. American Journal of Gastroenterology, April 2012, Meta-analysis of proton-pump inhibitors and risk of C difficile infection
5. NICE CG17 (2004) Dyspepsia: quick reference guide.
6. FDA Drug Safety Communication 2.8.12: <http://www.fda.gov/drugs/drugsafety/ucm290510.htm>
7. NICE CG59 (2008) Osteoarthritis: full clinical guideline.
8. NICE CG79 (2009) Rheumatoid arthritis: full clinical guideline.
9. NICE CG88 (2009) Low back pain: full clinical guideline.
10. NPC Cardiovascular and gastrointestinal safety of NSAIDs. MeReC Extra 30 (2007).

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