VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Gastro-oesophageal reflux disease (GORD):

Gastroesophageal reflux disease (GORD) is a condition in which the stomach contents (food or liquid) leak backwards from the stomach into the esophagus. This action can irritate the esophagus, causing heartburn and other symptoms. GORD affects up to 20% of the adult population in the western world. [5]

Obesity, smoking, alcohol use and certain medications increases the possibility of GORD.

Given the link between H. pylori infection and peptic ulcer disease and gastric cancer, the infection should be looked on as a major public health issue. The prevalence of H. pylori infection has fallen quite rapidly in Western countries over the past few decades. About 20% of the population under the age of 40 years and about 50% of those over the age of 60 years carry the infection. [6] Proposed risk factors for infection include male gender, increasing age, shorter height, tobacco use, lower socioeconomic status, obesity, and lower educational status of the parents in studies conducted among children. [7]

Over 90% of duodenal ulcer and 70% of gastric ulcer patients are infected with H. pylori. [8] The incidence of duodenal ulcer increases with age and peaks at about 60 years of age. [6] There are study findings suggesting acceleration healing of duodenal ulcer as well as prevention of ulcer relapse following eradication of infection. [9,10]

Patients on continued NSAID therapy and gastric ulcers associated with NSAID therapy: Population-based studies have shown that, on any given day, 10–20% of elderly people (≥65 years old) have a current or recent NSAID prescription. Many studies have now shown that NSAIDs increase the risk of peptic ulcer complications by 3–5-fold, and in several different populations it has been estimated that 15–35% of all peptic ulcer complications are due to NSAIDs. Factors that increase the risk of serious peptic ulcer disease include older age, history of peptic ulcer disease, gastrointestinal hemorrhage, dyspepsia, and/or previous NSAID intolerance, as well as several measures of poor health. [11]

Patients with Zollinger Ellison Syndrome:

Zollinger-Ellison syndrome (ZES) is a condition in which there is increased production of the hormone gastrin. In most cases, a small tumor in the pancreas or small intestine produces the high levels of gastrin.

It is difficult to accurately predict the prevalence and the incidence of Zollinger-Ellison syndrome (ZES), because the use of proton-pump inhibitors can mask the symptoms of acid hypersecretion, preventing the diagnosis of ZES.[12] ZES is believed to be responsible for up to 1% of duodenal ulcers. Diagnosis typically occurs between the

ages of 20 to 50 years but has occurred as young as age 9 years and as old as 90 years. There is equal distribution among men and women. [13]

VI.2.2 Summary of treatment benefits

Hetero omeprazole is used to treat Gastro-oesophageal reflux disease (this is where acid from the stomach escapes into the gullet (the tube which connects throat to stomach) causing pain, inflammation and heartburn) and ulcers in the stomach or upper part of the gut (intestine) that are infected with bacteria called 'Helicobacter pylori' in adults and children and stomach ulcers caused by medicines called NSAIDs (Non-Steroidal Anti-

Inflammatory Drugs), too much acid in the stomach caused by a growth in the pancreas (Zollinger-Ellison syndrome) and prolonged treatment after prevention of rebleeding of ulcers with omeprazole in adults.

- In a non-controlled study in children (1 to 16 years of age) with severe reflux oesophagitis, omeprazole at doses of 0.7 to 1.4 mg/kg improved oesophagitis level in 90% of the cases and significantly reduced reflux symptoms. [1]
- In a single-blind study, children aged 0–24 months with clinically diagnosed gastro-oesophageal reflux disease were treated with 0.5, 1.0 or 1.5 mg omeprazole/kg. The frequency of vomiting/regurgitation episodes decreased by 50% after 8 weeks of treatment irrespective of the dose. [1]
- A randomised, double blind clinical study (Héliot study) concluded that omeprazole in combination with two antibiotics (amoxicillin and clarithromycin), was safe and effective in the treatment of *H. pylori* infection in children age 4 years old and above with gastritis: *H. pylori* eradication rate: 74.2% (23/31 patients) with omeprazole + amoxicillin + clarithromycin versus 9.4% (3/32 patients) with amoxicillin + clarithromycin. There was no evidence of any clinical benefit with respect to dyspeptic symptoms. This study does not support any information for children aged less than 4 years. [1]

However, these studies were conducted for the currently marketed product Losec, (AstraZeneca, UK) and no studies to evaluate the expected benefit were performed for Hetero omeprazole, considering its similarity to Losec.

VI.2.3 Unknowns relating to treatment benefits

Not applicable

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Reduced plasma levels of clopidogrel due to interaction	The exposure to the active metabolite of clopidogrel was decreased by 46% when clopidogrel and omeprazole were administered together. Mean inhibition of platelet aggregation was diminished by 16% when clopidogrel and omeprazole were administered together. [1]	Yes By avoiding concomitant use of omeprazole and clopidogrel. [14]
Risk of hypomagnesaemia with long-term use	Severe hypomagnesaemia has been reported in patients treated with PPIs like omeprazole for at least three months, and in most cases for a year. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI. [1]	Yes By measuring magnesium levels before starting PPI treatment and periodically during treatment for patients expected to be on prolonged treatment or who take PPIs with digoxin or drugs that may cause hypomagnesaemia. [1] If any symptoms of low magnesium are seen, tell the doctor promptly. [14]
Risk of bone fracture	Omeprazole, especially if used in high doses and over long durations (>1 year), may slightly increase the risk of hip, wrist and spine fracture, predominantly in the elderly or in presence of other recognised risk	Yes By having an adequate intake of vitamin D and calcium. Inform the doctor if you

Risk	What is known	Preventability
	factors. [1]	have osteoporosis or are receiving corticosteroids.[14]

Drug interaction with atazanavir	Co-administration of atazanavir with proton pump inhibitors is not recommended. If the combination of atazanavir with a proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g virus load) is recommended in combination with an increase in the dose of atazanavir to 400 mg with 100 mg of ritonavir; omeprazole 20 mg should not be exceeded. [1]	Yes Inform the doctor if you are on treatment with atazanavir.[14]

Important potential risks

Risk	**What is known**
Risk of decrease absorption of cyanocobalamine (vitamin B12) with long-term use	Omeprazole may reduce the absorption of vitamin B12 (cyanocobalamin). This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy [1]

Missing information

Risk	**What is known**
None	None

VI.2.5 Summary of risk minimisation measures by safety concern

Currently available information does not support the need for additional risk minimisation activities.

VI.2.6 Planned post authorisation development plan

No studies planned.

VI.2.7 Summary of changes to the risk management plan over time

Not applicable