

## VI.2 Elements for a public summary

### VI.2.1 *Overview of disease epidemiology*

#### **Peptic ulcer disease (PUD)**

PUD is the most common ulcer of an area of the gastrointestinal tract that is usually acidic and thus extremely painful. The lifetime risk for developing a peptic ulcer is approximately 10%. *Helicobacter pylori* (bacterium associated with changes of gastric mucosa) may be detected in approximately 90% of individuals with PUD.<sup>3,4</sup> In Western countries the prevalence of *Helicobacter pylori* infections roughly

matches age. Prevalence is higher in third world countries where it is estimated at about 70% of the population, whereas developed countries show a maximum of 40% ratio.

### **Reflux oesophagitis/Gastroesophageal reflux disease (GERD)**

Reflux oesophagitis, characterized by heartburn and acid regurgitation, is an esophageal mucosal inflammation due to retrograde flux of stomach contents into the esophagus. Clinically, this is referred to as GERD. GERD is a very common disorder. About 14% of adults suffered from heartburn or acid regurgitation on a weekly basis, and 7% noticed it once a day.<sup>5</sup>

### **Zollinger-Ellison syndrome (ZES)**

ZES is caused by a tumour of the pancreas that stimulates the acid-secreting cells of the stomach to maximal activity, with consequent gastrointestinal mucosal ulceration. ZES occurs in approximately 0.1-1% of all patients with duodenal ulcers.<sup>6</sup>

#### **VI.2.2 Summary of treatment benefits**

Lansoprazole belongs to a group of drugs called proton pump inhibitors (PPIs) whose main action is a pronounced and long-lasting reduction of gastric acid production. Based on the available data from clinical studies and clinical experience of several years, Lansoprazole represents an effective drug in the treatment of peptic ulcer disease, reflux oesophagitis / gastroesophageal reflux disease (GERD), and Zollinger-Ellison syndrome.

If administered as indicated in the Summary of Product Characteristics and taking into account the contraindications, the warnings and precautions, Lansoprazole can be considered effective in the approved indications and generally well tolerated.

#### **VI.2.3 Unknowns relating to treatment benefits**

Not applicable.

#### **VI.2.4 Summary of safety concerns**

#### **Important identified risks**

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
Low blood levels of sodium, potassium, calcium or magnesium. (Electrolyte disturbances like - hyponatraemia - hypokalaemia or - hypocalcaemia in association with hypomagnesaemia)	If you are on Lansoprazole for more than three months it is possible that the levels of sodium, potassium, calcium or magnesium in your blood may fall. Low levels of magnesium can be seen as fatigue, involuntary muscle contractions, disorientation, convulsions, dizziness, increased heart rate	Your doctor may decide to perform regular blood tests to monitor your levels of magnesium. If you get any of these symptoms, please tell your doctor immediately.
Hip, wrist and spine fractures	Taking a proton pump inhibitor like Lansoprazole, especially over a period of more than one year, may slightly increase the risk of fracture in the hip, wrist or spine.	Talk to your doctor or pharmacist before taking Lansoprazole if you have osteoporosis or if you are taking corticosteroids (which can increase the risk of

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
		osteoporosis).
Drug interaction with atazanavir, a drug used to treat human immunodeficiency virus (HIV) infection	A study has shown that co-administration of Lansoprazole (60 mg once daily) with atazanavir 400 mg to healthy volunteers resulted in a substantial reduction in atazanavir exposure, which means decreased effect of atazanavir.	Do not take Lansoprazole if you are taking a medicine containing the active substance atazanavir.
Drug interaction with tacrolimus, a drug used to prevent rejection of a transplant	Co-administration of Lansoprazole increases the blood level of tacrolimus and therefore the risk of tacrolimus-induced adverse drug reactions.	Tell your doctor if you are taking medicines containing tacrolimus. Monitoring of tacrolimus blood level is advised when concomitant treatment with Lansoprazole is initiated or ended.
Drug interaction with digoxin, a drug used to treat chronic heart insufficiency	Co-administration of Lansoprazole and digoxin may lead to increased digoxin blood level and therefore increased risk of digoxin-induced adverse drug reactions.	Tell your doctor if you are taking medicines containing digoxin. The blood level of digoxin should be monitored and the dose of digoxin adjusted if necessary when initiating and ending Lansoprazole treatment.
Bowel inflammatory disease which causes abdominal pain or diarrhoea (colitis)	Colitis is a very rare side effect of Lansoprazole.	If diarrhoea occurs during the treatment with Lansoprazole contact your doctor immediately. In the case of severe and/or persistent diarrhoea, discontinuation of therapy should be considered.
Agranulocytosis (severe reduction in number of white blood cells which may decrease your resistance to infection) / Pancytopenia (reduction in number of white blood cells, red blood cells, and platelets)	Agranulocytosis or pancytopenia are very rare side effects of Lansoprazole.	If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems, you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells.
Severe adverse reactions affecting the skin (including Stevens-Johnson syndrome, toxic epidermal necrolysis)	Severe skin reactions with reddening, blistering, severe inflammation and skin loss are very rare side effects of Lansoprazole.	Not applicable.
Infections of stomach and intestines (Gastrointestinal infections)	Decreased gastric acidity due to Lansoprazole might be expected to increase gastric counts of bacteria	Not preventable. If diarrhoea occurs during the treatment contact your doctor

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
	normally present in the stomach and intestines. Treatment with Lansoprazole may lead to a slightly increased risk of gastrointestinal infections such as <i>Salmonella</i> and <i>Campylobacter</i> (related to food poisoning).	immediately, as your medicine has been associated with a small increase in infectious diarrhoea.

### **Important potential risks**

<b>Risk</b>	<b>What is known (Including reason why it is considered a potential risk)</b>
Rhabdomyolysis	Based on available data there is a potential that this adverse effect occurs with lansoprazole.
Pneumonia	Based on available data there is a potential that this adverse effect occurs with lansoprazole.
Interaction with methotrexate	Based on available data there is a potential that this adverse effect occurs with lansoprazole.

### **Missing information**

<b>Risk</b>	<b>What is known</b>
Treatment longer than 1 year (Long-term treatment)	There are limited safety data for patients treated for longer than 1 year.
Use during pregnancy and breastfeeding	There are no data available on Lansoprazole use during pregnancy. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, developing offspring, delivery or postnatal development. It is not known whether Lansoprazole is excreted in human breast milk. Animal studies have shown excretion of Lansoprazole in milk.

#### **VI.2.5 Summary of additional risk minimisation measures by safety concern**

No additional risk minimisation measures are proposed.

#### **VI.2.6 Planned post authorisation development plan (if applicable)**

Not applicable.

#### **VI.2.7 Summary of changes to the Risk Management Plan over time**

Not applicable. No previously approved RMP version available.