1.4. Summary table of risk minimization measures

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
Hypersensitivity reactions	Text in the company product labelling documents as per CCDS (in sections contraindications, warning and precautions for use, and undesirable effects).	None
Important identified and potential interactions o Nelfinavir o Atazanavir o Warfarin or other vitamin K antagonists o Phenytoin o Digoxin o Methotrexate o Tacrolimus o clopidogrel	Text in the company product labelling documents as per CCDS (in sections contraindications, warning and precautions for use, and interactions with other medicinal products and other forms of interactions).	None
Risk of masking symptoms of more serious conditions	Text in the company product labelling documents as per CCDS (in section warning and precautions for use).	None
Gastrointestinal effects/infections related to acid inhibition	Text in the company product labelling documents as per CCDS (in sections warning and precautions for use, and pharmacodynamic properties/other effects related to acid inhibitions).	None
Use in pregnancy and childhood asthma	Text in the company product labelling documents as per CCDS (in section fertility, pregnancy and lactation).	None

2. ELEMENTS FOR A PUBLIC SUMMARY

2.1. Overview of disease epidemiology

Omeprazole products are used for the relief of reflux symptoms such as occasional heartburn and acid regurgitation in adults. Heartburn, also known as acid indigestion, is usually associated with regurgitation of gastric acid (reflux is the backflow of acid from the stomach into the gullet “food pipe”, which may become inflamed and painful). This may cause symptoms such as a painful burning sensation in the chest rising up to the throat (heartburn) and a sour taste in the mouth (acid regurgitation).

Heartburn occurs after eating particularly at night, and worsens when a person lies down or bends over. It may be triggered by consuming food in large quantities, or specific foods containing certain spices, high fat content, or high acid content. At any given time, approximately 40% of a population can experience heartburn. About 10% of people can have daily heartburn symptoms. Gastroesophageal reflux disease (GERD), caused by reflux of gastric acid into the oesophagus, is one of the most frequently occurring diseases in the industrialized nations of the western hemisphere with a prevalence (the total number of cases of a disease in a given population at a specific time) ranging from 10% to 20% and an overall increasing trend.

2.2. Summary of treatment benefits

Omeprazole is a well-established drug substance for both prescription and OTC use, and which is indicated and already approved worldwide for the treatment of a range of conditions associated with gastric acid production.

Omeprazole is one of the most commonly prescribed substances for the treatment of acid reflux. Omeprazole 10 mg and 20 mg tablets are recommended for once-daily use in the relief of acid-reflux-like symptoms, such as heartburn.

The efficacy and safety of omeprazole for treatment of heartburn and acid regurgitation is well established. Omeprazole and other proton pump inhibitors (a group of drugs that reduce the secretion of stomach) are currently available without prescription (as "over-the-counter" (OTC) drug products) in many countries worldwide. They are considered currently the most effective substance for the symptomatic treatment of heartburn and acid regurgitation. Compared with other therapies available without prescription for the treatment of heartburn and acid regurgitation, omeprazole offers longer periods of freedom from these uncomfortable symptoms, providing an improved quality of life with comparable tolerability.

Omeprazole has a favourable benefit- risk which justifies it use for adults as an over the counter drug in the form of a single daily dose of 20 mg for up to 14 days.

2.3. Unknowns relating to treatment benefits

Not applicable.

2.4. Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Hypersensitivity reactions	Hypersensitivity (allergic) reactions like angioedema, anaphylactic reaction /shock	Do not take omeprazole if you are allergic

	(Serious allergic reactions which causes swelling of the face or throat, difficulty in breathing or dizziness) can rarely occur with omeprazole use. The products should not be used by patients with known hypersensitivity to omeprazole, or any of the constituents of the product.	(hypersensitive) to omeprazole or any of the other ingredients of the product, or if you are allergic to medicines containing other proton pump inhibitors (e.g. pantoprazole, lansoprazole, rabeprazole, esomeprazole).

Important potential risks

Risk	What is known (including reason why it is considered a potential risk)
Potential drug interactions	Omeprazole can affect the way some medicines work and some medicines can have an effect on omeprazole. Omeprazole should not be taken together with nelfinavir or atazanavir (medicines used to treat HIV infection). Special precautions are required for use with the following medicines, which might result in a decrease of the effects or increase of the toxicity of those interacting medicines: clopidogrel, warfarin or other vitamin K antagonists (medicines used to prevent the formation of blood clots in the blood vessels and their migration elsewhere in the body), phenytoin (used in the management of seizures), digoxin (a drug used to treat heart conditions), methotrexate (a drug used for the treatment of cancer and autoimmune diseases such as rheumatoid arthritis), tacrolimus (a drug used mainly after organ transplantation to reduce the activity of the patient's immune system and so lower the risk of organ rejection).
Risk of masking symptoms of more serious conditions	Omeprazole should not be taken for more than 14 days without consulting a doctor. The majority of patients achieve complete relief of heartburn within 7 days. Once complete relief of symptoms has occurred, treatment should be discontinued. If the patient does do not experience relief, or experience a worsening of symptoms, a doctor should consulted. Omeprazole may hide the symptoms of other diseases. Therefore, in the presence of any “alarm symptom” (such as unintentional weight loss, recurrent vomiting, swallowing problems, vomiting blood, passing black stools or blood stained faeces) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment with omeprazole may alleviate symptoms and delay diagnosis.
Gastrointestinal effects related to acid inhibition	Decreased stomach acidity due to any means including medicines such as omeprazole, increases stomach counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing medicines may lead to slightly increased risk of gastrointestinal infections and severe or persistent diarrhoea.
Use in pregnancy and childhood asthma	Reports in the literature suggested an association between exposure of the foetus in the uterus to gastric acid suppressive medications and an increased risk of developing asthma during childhood. However, there is no evidence that such association exists, and a further study is being conduct to investigate the matter. Omeprazole can be used during pregnancy after assessment of the risks and benefits of the treatment by a physician.

Missing information

Risk	What is known
None	Not applicable

2.5. Summary of additional risk minimisation measures by safety concern

There are no additional risk minimization measures.

2.6. Planned post authorization development plan

None.

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

This is the first omeprazole Risk Management Plan **(**RMP) prepared in accordance with the new format specified in guidelines on Good Pharmacovigilance Practice (GVP) adopted by the European Union (EU) in the frame of the new legislation for pharmacovigilance. This RMP is assigned the version number (V2.0), as an update & amendment of the previously created RMP in the frame of authorization of omeprazole as an OTC product (dated May 2010). Consequently, this module was amended with the rearrangement and/or addition of important identified & potential risks which were all included in the CCDs (sections 4.3, 4.4, 4.5, 4.6, and 4.8) prior to creation of this RMP V. 2.0.

Table 2-1: Major Changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1.0	25 May, 2010	**Identified Risks**: none **Potential Risks**: anaphylaxis, gastrointestinal adverse events, pregnancy and lactation **Potential interaction with drugs: e.g.** clopidogrel, ketoconazole & itraconazole, diazepam, phenytoin, warfarin and other vitamin K antagonists, clarithromycin, , digoxin, atazanavir, tacrolimus, voriconazole, **Missing information**: none	First RMP

1.2	20 December, 2010	No change to safety concerns	Editorial changes
2.0	Current RMP	Important identified risks: • hypersensitivity reactions Important potential risks: • Risk of masking symptoms of more serious conditions • Gastrointestinal effects related to acid inhibition • Use in pregnancy and childhood asthma Important identified and potential interactions • Nelfinavir, atazanavir, warfarin or other vitamin k antagonists, phenytoin, digoxin, methotrexate, tacrolimus, clopidogrel Missing information: none	Version 2.0: is an amendment of the RMP in alignment with the EU new guidelines on GVP (19 December 2013). All safety concerns were already addressed & included in the applicable sections of the CCDS.