	Dose adjustment is not required in patients with impaired renal function. Due to limited experience in patients with severe renal insufficiency, such patients should be treated with caution. Section 5.2: No studies have been performed in patients with decreased renal function. Since the kidney is responsible for the excretion of the metabolites of esomeprazole but not for the elimination of the parent compound, the metabolism of esomeprazole is not expected to be changed in patients with impaired renal function.	

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

GERD or commonly known as acid reflux is a public health concern defined by troublesome and frequent symptoms of heartburn or regurgitation and affecting up to 20% of the adult population in the western world. It is estimated that acid reflux affects 18.6 million people in the United States. There appears to be a lower prevalence of acid reflux (defined by at least weekly heartburn and/or regurgitation) in Europe compared to North America.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are well recognized as causing peptic ulceration and ulcer complications. Based on a widely quoted population study, it can be

estimated that there are 8528 hospitalizations for gastric and duodenal ulcer bleeding per annum in the UK. NSAIDs cause approximately 3500 hospitalizations for and 400 deaths from ulcer bleeding per annum in the UK in those aged 60 years and above.

VI.2.2 Summary of treatment benefits

Esomeprazole is recommended for the treatment of GERD (acid from the stomach escapes into the gullet (the tube which connects your throat to your stomach) causing pain, inflammation and heartburn.), healing of stomach ulcers caused by medicines called NSAID, prevention of rebleeding in adults following therapeutic endoscopy for acute bleeding gastric or duodenal ulcers.

GERD or acid reflux

In a study, patients with peptic ulcer bleeding received either esomeprazole (n=375) or placebo (n=389). After the initial 72 hour period, all the patients received 40 mg oral esomeprazole for 27 days for acid suppression. The occurrence of rebleeding within 3 days was 5.9% in the esomeprazole treated group compared to 10.3% for the placebo group. At 30 days post-treatment, the occurrence of rebleeding in the esomeprazole treated versus the placebo treated group was 7.7% vs 13.6%.

However, these studies were conducted for the reference product (Nexium, AstraZeneca UK) and no studies were performed for Accord esomeprazole to evaluate the expected benefit, considering its similarity to the reference product.

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**
Risk of reduced plasma	Use of medicines that are used to	Yes

levels of clopidogrel due to interaction with esomeprazole	thin your blood can have an effect on esomeprazole.	Inform doctor if you are taking clopidogrel to prevent blood clots
Infections of stomach or gut (Gastrointestinal infections)	Treatment with esomeprazole may lead to slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter.	Yes Inform doctor if you lose a lot of weight for no reason and have problems swallowing, get stomach pain, vomit food or blood or pass black stools.
Interaction of esomeprazole with atazanavir/nelfinavir	Decreased levels of atazanavir and nelfinavir have been reported when given together with omeprazole.	Yes Do not take esomeprazole if you are taking a medicine containing nelfinavir (used to treat HIV) Inform doctor if you are taking atazanavir for HIV.
Liver (Hepatic) impairment	Possible side effects: Uncommon: Increased liver enzymes Rare: Hepatitis with or without jaundice Very rare: Hepatic failure, encephalopathy in patients with pre-existing liver disease	Yes Check with doctor if you have severe liver problems before starting therapy with esomeprazole.
Thinning of the bones, with reduction in bone	Taking esomeprazole, especially over a period of more than one	Yes Inform doctor if have

mass, due to depletion of calcium and bone protein which may lead to fractures (Osteoporosis/osteoporotic fractures)	year, may slightly increase your risk of fracture in the hip, wrist or spine.	osteoporosis or if you are taking corticosteroids (which can increase the risk of osteoporosis)
Low levels of magnesium in blood (Hypomagnesaemia)	If you are on esomeprazole for more than three months it is possible that the levels of magnesium in your blood may fall. Low levels of magnesium can be seen as fatigue, involuntary muscle contractions, disorientation, convulsions, dizziness or increased heart rate.	Yes Inform doctor if you experience any symptoms such as fatigues, convulsions, etc. Regular blood tests should be performed to monitor levels of magnesium.

Important potential risks

Risk	**What is known**
Increased risk of pneumonia	None
Use in pregnancy and risk of childhood asthma	For esomeprazole, limited data on exposed pregnancies are available. Animal studies with esomeprazole do not indicate direct or indirect harmful effects with respect to embryonal/foetal development.

Missing information

Risk	**What is known**
Limited information on the	It is not known if esomeprazole passes into breast milk.

use in lactating females	Therefore, you should not be given esomeprazole if you are breastfeeding.
Limited information on the use in patients with renal impairment	Check with doctor if you have severe kidney problems before starting therapy with esomeprazole.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimizing them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimization measures.

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

No studies planned.

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

Version	Date	Safety Concerns	Comment
2.0	12 February 2014	Important identified risks: 'Gastrointestinal infections', 'Interaction with atazanavir/nelfinavir', 'Hepatic impairment', Osteoporosis/osteoporotic fractures', 'Hypomagnesaemia' have been added.	

Version	Date	Safety Concerns	Comment
		Important potential risks: 'Increased risk of pneumonia', 'Use in pregnancy and risk of childhood asthma' have been added. Missing information: 'Patients with renal impairment' has been included under missing information.	