

## **Summary of activities in the risk management plan by product**

### **VI.1 Elements for summary tables in the EPAR**

#### ***VI.1.1 Summary table of Safety concerns***

Not applicable.

#### ***VI.1.2 Table of on-going and planned additional PhV studies/activities in the Pharmacovigilance Plan (if applicable)***

Not applicable.

#### ***VI.1.3 Summary of Post authorisation efficacy development plan (if applicable)***

Not applicable.

#### ***VI.1.4 Summary table of risk minimisation measures***

Not applicable.

### **VI.2 Elements for a public summary**

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

Not applicable. This is a generic application. Our SmPC comply with the innovator product regarding indications and adverse events.

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

Not applicable. This is a generic application. Our SmPC comply with the innovator product regarding indications and adverse events.

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

Not applicable. This is a generic application. Our SmPC comply with the innovator product regarding indications and adverse events.

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

**Important identified risks:**

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
Interaction with atazanavir	A drug interaction is a situation in which a substance (usually another drug) affects the activity of a <b>drug</b> when both are administered together.	Do not take rabeprazole if you are taking a medicine containing atazanavir (for the treatment of HIV-infection)
Low magnesium in the blood (Hypomagnesaemia)	If you are on rabeprazole 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, increased heart rate.	If you get any of these symptoms, please tell your doctor promptly. Low levels of magnesium can also lead to a reduction in potassium or calcium levels in the blood. Your doctor may decide to perform regular blood tests to monitor your levels of magnesium.
Risk of hip, wrist and spine fracture	Taking a proton pump inhibitor like Rabeprazole especially over a period of more than one year, may slightly increase your risk of fracture in the hip, wrist or spine.	Tell your doctor if you have osteoporosis or if you are taking corticosteroids (which can increase the risk of osteoporosis).
Drug interaction (Drug interaction between PPIs and clopidogrel)	A drug interaction is a situation in which a substance (usually another drug) affects the activity of a <b>drug</b> when both are administered together.	Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.
Decreased absorption of vitamin B12 (Chronic treatment with PPIs decreases absorption of cyanocobalamin (vitamin B12))	There are several medications that can interfere with how well your body absorbs vitamin B12, possibly increasing your risk of vitamin B12 deficiency. Among the drugs that may reduce your body's level of vitamin B12 are medicines used to treat ulcers.	Talk to your doctor before taking vitamin B12 supplements or any dietary supplement. Always be sure that your doctor is aware of all of the medications and supplements you take.
Vision disturbance (Visual disturbances)	Any disturbance to one's vision is vision disturbance. Like all medicines, rabeprazole can cause side effects such as vision disturbance, although not everybody gets it. It is known that vision disturbance is a rare side effect.	If you experience vision disturbances or the side effect gets serious please tell your doctor or pharmacist.

Risk	What is known	Preventability

**Important potential risks:**

Risk	What is known (Including reason why it is considered a potential risk)
Increased risk of pneumonia	Pneumonia is an inflammatory condition of the lung. It is usually caused by infection with viruses or bacteria and less commonly other microorganisms, certain drugs and other conditions such as autoimmune diseases. Pneumonia is a common illness affecting approximately 450 million people a year and occurring in all parts of the world. It is a major cause of death among all age groups resulting in 4 million deaths (7% of the world's total death) yearly.

<p>Liver function tests are abnormal</p> <p>(Hepatic enzyme abnormalities)</p>	<p>The liver plays a central role in transforming and clearing chemicals and is susceptible to the toxicity from these agents. Certain medicinal agents, when taken in overdoses and sometimes even when introduced within <b>therapeutic ranges</b>, may injure the organ.</p> <p>One of the most obvious abnormal liver function symptoms is jaundice. Jaundice is a condition where the skin appears yellowish and the whites of the eyes appear yellowish in color. Because the liver is associated with so many different body functions, there are many other abnormal liver function symptoms that can be detected. Fecal matter is normally brown in color. If the fecal matter is excessively dark or excessively light, it may indicate a problem with the liver. Dark colored urine is also a sign of liver problems. The liver is located in the upper right hand side of the abdomen. This area may be sore, particularly if the liver is inflamed. The individual may also suffer from more generic symptoms such as diarrhea, vomiting, fatigue, fever and loss of appetite. These symptoms are considered to be secondary as they are useful for a confirmation of the condition rather than a diagnosis of it. If you experience any of these side effects please tell your doctor or pharmacist.</p> <p>Your doctor may do tests to measure certain chemicals produced by the liver. These tests can help your doctor check how well your liver is working.</p>
<p>Gastrointestinal infections caused by bacteria</p> <p>(Increased risk of Clostridium difficile-associated diarrhea (CDAD) with PPIs)</p>	<p>Decreased gastric acidity, due to any means - including medicines used treat ulcers – can increase gastric counts of bacteria normally present in the gastrointestinal tract.</p> <p>Tell your doctor immediately if you notice any of the following symptoms: severe and/or persistent diarrhoea, as rabeprazole can be associated with a small increase in infectious diarrhoea.</p>
<p>Decreased absorption of iron</p> <p>(Decrease in absorption of iron)</p>	<p>Many medications may interfere with your body's ability to absorb iron. Not being able to properly absorb iron may lead to anemia. Common symptoms of anemia include fatigue and weakness, which happens because blood cells aren't getting enough oxygen. If you need to use a medication that interferes with iron absorption, you may need to take additional iron supplements or alter your medication's dosage or dosing schedule to prevent anemia. Always talk to your doctor if you are concerned you are not getting enough iron.</p>
<p>Congenital heart birth defects</p> <p>(Congenital cardiac malformation following in utero exposure)</p>	<p>Congenital heart defects are problems with the heart's structure that are present at birth and change the normal flow of blood through the heart. A heart defect can result in blood flow:</p> <ul style="list-style-type: none"> <li>Slowing down</li> <li>Going to the wrong place or in the wrong direction</li> <li>Being blocked completely</li> </ul> <p>There are many types of congenital heart defects. Some are simple, such as a hole in the septum, a narrowed valve that blocks blood flow, or a patent ductus arteriosus. Other heart defects are more complex. They include</p>

	<p>combinations of simple defects, problems with the location of blood vessels leading to and from the heart, and more serious problems with how the heart develops or structural alterations.</p> <p>Multiple environmental and genetic factors influence development of body organs during this first trimester of pregnancy. Some potential causes of congenital heart defects include exposure to certain drugs/pharmacotherapeutic agents, industrial chemicals, during the first trimester.</p>
<p>Blood disorder (Blood dyscrasias- thrombocytopenia and neutropenia)</p>	<p>A <b>blood disorder</b> is where one part of the blood is not present in normal supply.</p> <p>Blood problems have been seen in some patients but often get better when rabeprazole treatment is stopped.</p> <p>Like all medicines, rabeprazole can cause side effects, although not everybody gets them.</p> <p>Neutropenia is a rare side effect (decrease of neutrophils, a type of white blood cell). It causes reductions in white blood cells resulting in frequent infections, such as sore throat or high temperature (fever), or ulcers in your mouth or throat.</p> <p>Thrombocytopenia is also a rare side effect (decrease of blood platelets). It causes reduction in blood platelets resulting in bleeding or bruising more easily than normal.</p>
<p>Exposure during pregnancy</p>	<p>Some drugs may be harmful to a growing baby.</p> <p>Do not take rabeprazole if you are pregnant, you think you might be pregnant or if you are breastfeeding.</p> <p>Ask your doctor or pharmacist for advice before taking any medicine.</p>
<p>Exposure through human milk</p>	<p>It is not known whether rabeprazole sodium is excreted in human breast milk. Therefore rabeprazole should not be used during breast feeding.</p>
<p>Drug interaction (Interaction with pH dependent medication, reducing their effectiveness)</p>	<p>Tell your doctor or pharmacist if you are taking atazanavir (a drug used to treat HIV) as the absorption of atazanavir is pH dependent and in interaction with drugs whose absorption is pH dependent may occur.</p>

### Important missing information

Risk	What is known
<p>Limited information on use in patients with kidney impairment  (Patient with renal impairment)</p>	<p>No dose reduction is recommended when rabeprazole is given to patients with impaired renal function (including patients on dialysis, which removes only negligible amounts of rabeprazole).</p>
<p>Use in pregnancy and lactating woman</p>	<p>If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.</p> <p>Do not take rabeprazole if you are pregnant, think you may</p>

	be pregnant, or are breast-feeding.
Use in children and adolescents below 18 years of age	Do not take rabeprazole if you are under 18 years of age.

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

No additional risk minimisation measures are considered necessary.

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

Not applicable. No postauthorisation studies are planned.