VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Eplerenone is specifically indicated for the reduction of risk of cardiovascular death in people with heart failure and left ventricular dysfunction (the heart is unable to provide sufficient pump action to maintain blood flow to meet the needs of the body), especially after an acute myocardial infarction (heart attack).

Heart failure is a common, costly, disabling, and potentially deadly condition. In developed countries, around 2% of adults suffer from heart failure, but in those over the age of 65, this increases to 6–10%. Ischemic heart disease (reduced blood supply of the heart muscle, usually due to coronary artery disease) which includes myocardial infarction (heart attack) and heart failure when preceded by myocardial infarction) was the leading cause of death for both men and women worldwide in 2004. Important risk factors are previous cardiovascular disease, older age, tobacco smoking, high blood levels of certain lipids (low-density lipoprotein cholesterol, triglycerides) and low levels of high density lipoprotein (HDL) cholesterol, diabetes, high blood pressure, lack of physical activity and obesity, chronic kidney disease, excessive alcohol consumption, the use of illicit drugs (such as cocaine and amphetamines), and chronic high stress levels.

VI.2.2 Summary of treatment benefits

If administered as indicated in the Summary of Product Characteristics and taking into account the contra-indications, the warnings and precautions, Eplerenone 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

Risk	What is known	Preventability
Heart attack (myocardial infarction)	Although eplerenone is indicated in the treatment of chronic heart failure especially in patients following heart attack (myocardial infarction), myocardial infarction is also listed as a common side effect occurring during eplerenone treatment. High potassium level in the blood may increase the risk of developing heart attack.	It is recommended that patient starts with eplerenone therapy 3 – 14 days after an acute heart attack. Laboratory analysis should be done before the treatment starts in order to determine potassium level in the blood and should be repeated regularly in order to keep potassium level in the normal range. Treating physician should be informed about all medical products taken by the patient at the same time with eplerenone to avoid the risk of drug interactions which may lead to the increased level of potassium.

Risk	What is known	Preventability
High level of potassium in the blood (hyperkalaemia)	High level of potassium in the blood is a common side effect of eplerenone and it is considered as one of the most important identified risks due to the possible impact on the heart function. Elderly patients and those with renal impairment and diabetes are at the risk of having increased level of potassium in the blood. Some medication for hypertension and heart failure taken at the same time can increase potassium level. Interactions of eplerenone with medications indicated for other diseases (including potassium supplements) can also increase potassium level in the blood.	Treating physician should have a complete overview of all the medicinal products and supplements (including food) which are taken by the patient at the same time with eplerenone. Regular laboratory tests should be done to monitor potassium level in the blood. Patient should inform the doctor if new medication is prescribed for other indication in order to check possible interactions.
Kidney impairment	The risk of elevated potassium increases with decreasing of kidney function. Treatment with eplerenone depends on the grade of kidney impairment (mild, moderate or severe). Kidney function is decreased in elderly patients. Kidney impairment is a common side effect of eplerenone.	For patients with severe kidney impairment eplerenone is contraindicated. Treatment with eplerenone requires close monitoring of kidney function and dose adjustment according to the level of kidney impairment. Diabetic patients who have kidney impairment should also be monitored regarding potassium concentration.
Itching	Patients treated with Eplerenone may be at an increased risk of developing itching.	Not known

Important potential risks:

Risk	What is known (Including reason why it is considered a potential risk)
Allergic reactions (rash, itching,	Patients treated with Eplerenone may be at an increased risk of

swollen face, tongue or throat)	developing rash or symptoms of angioneurotic oedema (swollen face, tongue or throat with difficulties in swallowing or breathing). **If you experience swollen face, tongue or throat with difficulties in swallowing or breathing you should seek immediate medical attention.** Rash may be potentially a symptom of more serious allergic reaction on the medication, therefore, patients taking eplerenone should be advised to contact treating physician immediately if skin rash or itching develops.

Important missing information:

Risk	What is known
Use in pregnant and/or lactating women	There are no adequate data on the use of eplerenone in pregnant women. Preclinical studies on safety pharmacology, genotoxicity, carcinogenic potential and toxicity to reproduction revealed no special hazard for humans. Caution should be exercised prescribing eplerenone to pregnant women. It is unknown if eplerenone is excreted in human breast milk after oral administration. Because of the unknown potential for adverse effects on the breast fed infant, a decision should be made whether to discontinue breast-feeding or discontinue eplerenone, taking into account the importance of the medicinal product to the mother.

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 minimising 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 minimisation measures.

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

Version	Date	Safety Concerns	Comment
1.0	1 Aug 2013	Identified Risks: • Myocardial infarction • Hyperkalaemia • Renal impairment • Rash, pruritus and angioedema Potential Risks: None Missing information: None	-

Version	Date	Safety Concerns	Comment
1.1	12 Nov 2013	Pruritus is identified risk. Rash and angioedema were moved to potential risks. Use in pregnant and/or lactating women added as missing information.	Changes based on comments fromType II variation PAR: DK/H/2121/001-002/II/003/G and DK/H/2144/001-002/II/003/G To be aligned with reference product RMP.