VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Heart failure is a complex syndrome, clinically characterized by signs and symptoms secondary to abnormal cardiac function. It includes patients with impaired or preserved systolic left ventricular function. The prevalence of heart failure is estimated as 2%-3% of the adult population and increases with age. Over 26 million people suffer from heart failure around the world and over 3.5 million people are newly diagnosed with heart failure every year in Europe alone. Patients suffer disabling symptoms that often become refractory to treatment and need hospitalization, having the greatest negative impact on quality of life compared with other chronic conditions. The challenge of preventing a heart failure pandemic in the future is important for all countries, but especially those with economies in transition, where traditional healthy lifestyles are quickly changing. The only way of avoiding this new pandemic is through prevention, which is the collective responsibility of everyone: physicians, education and health authorities, and patients. **[J. López-Sendón, 2011]**

VI.2.2 Summary of treatment benefits

Eplerenone belongs to a group of medicines known as selective aldosterone blocking agents. These blocking agents inhibit the action of aldosterone, a substance produced within the body, which controls your blood pressure and heart function. High levels of aldosterone can cause changes in your body that lead to heart failure. It is used to treat your heart failure to prevent worsening and reduce hospitalisations if patient had a recent heart attack, in combination with other drugs that are used to treat your heart failure.

Eplerenone is generally well tolerated in patients with left ventricular systolic dysfunction and heart failure following acute myocardial infarction. Due to the selectivity of eplerenone for the aldosterone receptor, incidence of adverse endocrine events such as gynecomasrtia, impotence or breast pain was reported low with eplerenone compared to spironolactone in EPHESUS (<1%) study. **[CTD module 2.5]**

VI.2.3 Unknowns relating to treatment benefits

Because no information available on the use of eplerenone in patients with severe hepatic impairment and with severe renal impairment hence its use is contraindicated in these patients. There are no adequate data on the use of eplerenone in pregnant women and lactating mothers. Caution should be exercised when prescribing eplerenone to pregnant women. For a lactating mother, a decision should be made whether to discontinue breast-feeding or discontinue the drug, taking into account the importance of the drug to the mother.

Because no data are available to recommend the use of eplerenone in the paediatric population, its use in this age group is not recommended.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
High levels of potassium in the blood (Hyperkalaemia)	The use of eplerenone may increase the potassium levels in your blood.	Eplerenone should not be taken if the patients having high levels of potassium in blood (hyperkalemia) or patients taking groups of drugs which help to excrete excessive body fluid, (potassium sparing diuretics) or “salt tablets” (potassium supplements). Eplerenone must not be taken with angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) together (which are used to treat high blood pressure, heart disease or particular kidney conditions) as these drugs may increase the risk of high potassium levels in blood. Patient should inform the doctor if he/she is taking cyclosporin or tacrolimus (used to treat skin conditions such as psoriasis or eczema, and to prevent rejection after organ transplantation) or Trimethoprim (used to treat bacterial infections) these drugs may increase the risk of high potassium levels in blood.
Low blood pressure (Hypotension)	Use of eplerenone is associated with fall in blood pressure. It is a commonly	Patient should inform the doctor if he/she is taking alpha I blockers, such as

Risk	What is known	Preventability
	reported adverse event with eplerenone.	prazosin or alfuzosin (used to treat high blood pressure and particular prostate conditions) or tricyclic antidepressants such as amitryptyline or amoxapine (for treatment of depressions), antipsychotics (also known as neuroleptics) such as chlorpromazine or haloperidol (for the treatment of psychiatric disorders), amifostine (used during cancer chemotherapy) and baclofen (used to treat muscle spasm). These drugs may lead to a fall in blood pressure and dizziness upon standing.
Kidney problems (Use of eplerenone in renal impairment)	When eplerenone is used in the patients with impaired kidney functions, risk of increase in potassium levels in the blood increases with decreasing renal function.	No initial dose adjustment is required in patients with mild renal impairment. Periodic monitoring of serum potassium is recommended. Eplerenone is contraindicated in patients with moderate to severe renal insufficiency (creatinine clearance < 50 mL/min)
Use of eplerenone in mild-moderate liver problems (Use of eplerenone in mild-moderate hepatic impairment)	No elevations of serum potassium above 5.5 mmol/L observed in patients with mild to moderate hepatic impairment. Due to an increased systemic exposure to eplerenone in patients with mild-to-moderate hepatic impairment, risk of elevated potassium levels in the blood increases in patients.	No initial dosage adjustment is necessary for patients with mild-to-moderate hepatic impairment. Frequent and regular monitoring of serum potassium is recommended in these patients, especially when elderly.
Eplerenone administration	Eplerenone is associated with	Eplerenone is contraindicated

Risk	What is known	Preventability
along with drugs that potently inhibit the CYP3A4 enzyme (Concomitant administration with strong inhibitors of CYP 3A4)	risk of significant pharmacokinetic interactions when given with the drugs which are potent inhibitors of CYP3A4 enzyme	in patients receiving strong inhibitors of CYP 3A4 like itraconazole, ketoconazole, ritonavir, nelfinavir, clarithromycin, telithromycin and nefazodone.
Eplerenone administration along with drugs of class of potassium-sparing diuretics (Concomitant administration with potassium-sparing diuretics)	Eplerenone is associated with risk of hyperkalaemia when used with the drugs of class of potassium-sparing diuretics. It may potentiate the effect of anti-hypertensive agents and other diuretics.	Use of eplerenone is contraindicated in patients receiving potassium-sparing diuretics.
Eplerenone administration along with potassium supplements (Concomitant administration with potassium supplements)	Eplerenone is associated with risk of hyperkalaemia when used with potassium supplements.	Use of eplerenone is contraindicated in patients receiving potassium supplements.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
None	None

Missing information

Risk	What is known
Use of eplerenone in children (Use of eplerenone in paediatric population)	There are no data to recommend the use of eplerenone in the children and adolescents, and therefore, use in this age group is not recommended.
Use of eplerenone in pregnant women	Patient should ask doctor or pharmacist for advice before taking medicine. The effect of eplerenonehas not been evaluated during pregnancy in humans. Caution should be exercised prescribing eplerenone to pregnant women
Use of eplerenone in breast-feeding mothers (Use of eplerenone in lactating mothers)	It is not known if eplerenone is excreted in human breast milk. A decision should be made with the doctor, whether to discontinue breast-feeding or to discontinue the drug, taking into account the importance of the drug to the mother.

Risk	What is known
Use of eplerenone in severe liver problems (Use of eplerenone in severe hepatic impairment)	The use of eplerenone in patients with severe hepatic impairment has not been evaluated and its use is therefore contraindicated in these patients.

VI.2.5 Summary of risk minimization measures by safety concern

Summary of Product Characteristics (SmPC) of eplerenone 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). All these risk minimization measures are given in SmPC and PL of eplerenone.

This medicine has no additional risk minimization measures.

VI.2.6 Planned post authorisation development plan

No post authorisation study is planned for this product.

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

This section is not applicable as this is version 01 of RMP.