VI.2. Elements for a Public Summary

VI.2.1. Overview of Disease Epidemiology

Heart failure (HF) is a condition in which the heart can't pump enough blood to meet the body's needs for blood volume and oxygenation. Heart failure can be mild at first (you may experience no symptoms), but it can be severe or even life-threatening. Common symptoms of heart failure include feeling tired, having trouble breathing and leg swelling.

Multiple studies have reported on how often this disease occurs in the general population. A UK-based study has found that 2.3% of patients from a general population over 45 years of age were diagnosed with HF. In the US the number of people with HF has risen with an estimated 5 million patients affected (2.2% of the total US population).

Surveys throughout the world show that the risk increases in the elderly, who are 10 times more likely to suffer from HF (10%–20%), compared with the general population (1%–2%). It has also been estimated that more than 75% of patients with HF in the US are older than 65. Data from the US have also indicated that HF prevalence is 25% higher for African-Americans than estimates for the Caucasian population, with 40% higher mortality.

Healthy dietary and lifestyle changes like reducing salt intake, smoking cessation and staying active may help to make you feel better and reduce the symptoms of heart failure although drug treatment and even surgery may be needed depending on the severity of your condition.

VI.2.2. Summary of Treatment Benefits

HF is a disease that can be treated best, if it is caught early, and there are many good options for treatment. The symptoms above should not be ignored. It is important to know that, by the time the symptoms above appear, it means that your body on its own cannot help your heart. You need help from your doctor. If you have these symptoms, your doctor can help you understand how your heart is affected, and how to keep it working well. If the disease is left untreated, HF is very hard on your heart, and may lead to premature death.

Eplerenone is a medication used to help the body get rid of excess salt and fluid, while also helping the body hold onto potassium. It can be used with other medications to help manage the disease, and decrease the need for hospitalisation in some patients with HF.

VI.2.3. Unknowns Relating to Treatment Benefits

No major differences in risks or benefits of eplerenone were seen across any subgroup studied, including age, gender, or racial group.

VI.2.4. Summary of Safety Concerns

Table 62. Important Identified Risks

Risk	What is Known	Preventability
High blood potassium (Hyperkalaemia)	Approximately 1% to 10% of patients taking eplerenone will experience high blood potassium.	Physician supervision and care.

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Table 62. Important Identified Risks

Risk	What is Known	Preventability
	Symptoms of high blood potassium may show up as nausea, slow, weak or irregular pulse, or sudden collapse with a slow heartbeat. The risk of high blood potassium may increase in elderly patents, patients with renal impairment, and patients with diabetes. Some other drugs also increase the risk of high blood potassium, such as drugs which help you to excrete excessive body fluid, (potassium-sparing diuretics) or "salt tablets" (potassium supplements), and eplerenone should not be taken while being treated with these drugs. Eplerenone should not be taken if you are being treated with two kinds of medicine together, used to treat certain heart conditions or hypertension (so-called angiotensin converting enzyme (ACE) inhibitors and an angiotensin receptor blocker (ARB), because, when you are being treated with these 2 kinds of drugs together, they also increase the risk of hyperkalaemia. Some other classes of medicine such as the immunosuppressants cyclosporin and tacrolimus, and trimethoprim, and non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided while you are being treated with eplerenone, and blood potassium tested closely, if they are taken. Blood tests for serum potassium should be ordered by your doctor before starting eplerenone therapy, then within the first week and at one month after the start of treatment, and after any change in dose. The blood tests should continue to be done periodically after that, as long as you take eplerenone.	Regular medical examinations and periodic blood potassium tests. Your doctor may adjust your dose of eplerenone based on the results of periodic blood potassium tests, as described in the package insert.
Kidney problems	Decrease in the health and function of the kidney (kidney problems) occurs in 1% to 10% of patients taking eplerenone. Symptoms of kidney problems may show up as headaches, nausea, trouble sleeping, tiredness fluid swelling (oedema). The risk of kidney problems may be greater for patients with kidney problems, elderly patients, and patients on other specific drugs which may be harmful to the kidney. For this reason, certain classes of immunosuppressants such as cyclosporin and tacrolimus, and NSAIDs should be avoided with eplerenone, and kidney function tested closely, if they are taken with eplerenone. Blood tests for potassium should be done periodically in patients with kidney impairment.	Physician supervision and care. Regular medical examinations with specific kidney laboratory tests during the course of eplerenone therapy (eg, periodic monitoring of serum creatinine levels in high-risk patients, such as elderly patients, patients on certain medications (see package insert), and patients with kidney impairment).

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Table 62. Important Identified Risks

Risk	What is Known	Preventability
	Patients with moderate kidney impairment should take a reduced dosage of eplerenone, as described in the package insert, and patients with severe renal impairment should not take eplerenone.	

Table 63. Important Potential Risks

Risk	What is Known
None Identified	There is no important potential risk currently foreseen in eplerenone treatment.

Table 64. Missing Information

Risk	What is Known
There is limited information on use of eplerenone in children and adolescents	Safety and effectiveness in children and adolescents have not been established.
There is limited information on use of eplerenone in patients who are pregnant or breast feeding. Exposure to eplerenone could potentially be detrimental to the foetus or nursing infant.	Eplerenone has not been studied in patients who are pregnant or breast feeding. It is unknown if eplerenone is excreted in human breast milk after oral administration. The safety of eplerenone in these patients has not been established. 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 the drug, taking into account the importance of the drug to the mother. Animal studies did not indicate direct or indirect adverse effects on pregnancy, foetal development birth, or postnatal development. Animal studies show that eplerenone and/or metabolites are present in rat breast milk and that rat pups exposed to the drug this way developed normally.

VI.2.5. Summary of Risk Minimisation Measures by Safety Concern

This medicine has no additional risk minimisation measures.

VI.2.6. Planned Post-Authorisation Development Plan

No post-authorisation studies are planned.

VI.2.7. Summary of Changes to the Risk Management Plan Over Time

Major changes to the Risk Management Plan over time are shown in Table 65.

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Table 65. Major Changes to the Risk Management Plan Over Time

Version	Date	Safety Concerns	Comment
1.0	18 March 2011	Identified Risks: Myocardial Infarction Hyperkalaemia Renal Impairment Pruritus Potential Risk: Rash	
2.0	08 August 2016	Identified Risks: Hyperkalaemia Renal Impairment	Myocardial infarction and Pruritus were removed as Identified Risks; Rash was removed as a Potential Risk. Other risks remain unchanged.
2.1	02 February 2017	Identified Risks: Hyperkalaemia Renal Impairment	As per the RMS request, use in patients with severe renal impairment (CrCl <30 ml/min), use in patients with severe hepatic impairment (Child-Pugh Class C), and use in patients with serum potassium level >5.0 mmol/L removed as missing information. As per a CMS request, use in children and adolescents added as missing information.

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