Summary of the Risk Management Plan for Losartan

VI.1 Elements for summary tables in the European Public Assessment Report (EPAR)

VI.1.1 Summary table of Safety concerns

Table 6 Summary of safety concerns

Important identified risks	Hypotension Hyperkalaemia Use during pregnancy Renal impairment and renal failure Hypersensitivity
Important potential risks	Abnormal liver function
Missing information	Use during lactation Use in paediatric population; treatment of proteinuria in children under 1 year of age and treatment of hypertension in children under 6 months of age

VI.1.2. Table of on-going and planned studies in the post-authorization pharmacovigilance development plan

Not applicable.

VI.1.3. Summary of post-authorisation efficacy development plan

Not applicable.

VI.1.4. Summary table of risk minimisation measures

Table 7 Summary table of risk minimisation measures

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
Hypotension	(Proposed) text in SmPC: Listen in section **4.4 Special warnings and precautions for use** Listen in section **4.5 Interaction with other medicinal products and other forms of interaction** Listen in section **4.6.Fertility, pregnancy and lactation** Prescription only medicine.	Not applicable.
Hyperkalaemia	(Proposed) text in SmPC: Listen in section **4.3 Contraindications** Listen in section **4.4 Special warnings and precautions for use** Listen in section **4.5.Interaction with other medicinal products and other forms of interaction** Listen in section **4.8 Undesirable effects** Prescription only medicine.	Not applicable.
Renal impairment and renal failure	(Proposed) text in SmPC: Listen in section **4.4 Special warnings and precautions for use** Prescription only medicine.	Not applicable.
Use during pregnancy	(Proposed) text in SmPC: Listen in section **4.4 Special warnings and precautions for use** Listen in section **4.6 Fertility, pregnancy and lactation**	Not applicable.

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	Prescription only medicine.	
Hypersensitivity	(Proposed) text in SmPC: Listen in section **4.3 Contraindications** Listen in section **4.4 Special warnings and precautions for use** Listen in section **4.8 Undesirable effects** Prescription only medicine.	Not applicable.
Abnormal liver function	(Proposed) text in SmPC: Listen in section **4.2 Posology and method of administration** Listen in section **4.3 Contraindications** Listen in section **4.4 Special warnings and precautions for use** Prescription only medicine.	Not applicable.
Use during lactation	(Proposed) text in SmPC: Listen in section **4.6 Fertility, pregnancy and lactation** Prescription only medicine.	Not applicable.
Use in paediatric population; treatment of proteinuria in children under 1 year of age and treatment of hypertension in children under 6 months of age.	(Proposed) text in SmPC: Listen in section **4.1 Therapeutic indications** Listen in section **4.2 Posology and method of administration** Listen in section **4.4 Special warnings and precautions for use** Listen in section **5.2 Pharmacokinetic properties** Prescription only medicine.	Not applicable.

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

High blood pressure is one of the most important causes of premature death worldwide killing nearly 9.4 million people every year globally, and the problem is growing. Over 1 billion people are living with high blood pressure. The prevalence was highest in Germany (55%), followed by Finland (49%), Spain (47%), England (42%), Sweden (38%), and Italy (38%). Prevalences in the United States and Canada were half of the rate in Germany (28% and 27%, respectively). The prevalence of hypertension for the European average was 44.2% compared with 27.6% in North America Hypertension represents a major risk factor for myocardial infarction and the most important risk factor for stroke. Two thirds of strokes and half of myocardial infarctions arise from a systolic blood pressure > 115 mmHg. The relationship between blood pressure and cardiovascular diseases is log linear. Hypertension is the leading risk factor of preventable deaths worldwide Hypertension is highly prevalent in the elderly. Several epidemiological surveys conducted in the USA and Europe conclude that hypertension prevalence in the elderly ranges between 53% and 72%.

VI.2.2 Summary of treatment benefits

Losartan is a synthetic oral angiotensin-II receptor (type AT1) antagonist. Angiotensin II, that decreases local blood flood, is the primary active hormone of the renin/angiotensin system and an important determinant of the pathophysiology of hypertension. Angiotensin II binds to the AT1 receptor found in many tissues (e.g. vascular smooth muscle, adrenal gland, kidneys and the heart) that cause several important biological actions, including vasoconstriction and the release of aldosterone. Losartan selectively blocks the AT1 receptor. Losartan does not have an agonist effect nor does it block other hormone receptors or ion channels important in cardiovascular regulation Losartan potassium is effective as a once-daily antihypertensive agent.

VI.2.3 Unknowns relating to treatment benefit

Losartan is not recommended for mothers who are breast feeding because no information is available regarding the use of this product during breastfeeding. Losartan is not recommended for use in children suffering from kidney or liver problems, as limited data are available in these patient groups. Losartan is not recommended for use in children under 6 years old, as it has not been shown to work in this age group.

VI.2.4 Summary of safety concerns

Table 8 Important Identified Risk

Important Identified Risk	What is known	Preventability
Low blood pressure **(Hypotension)**	As with all antihypertensive therapy, symptomatic hypotension may occur in some patients	**3. How to take** **If you take more losartan than you should** If you accidentally take too many tablets, or a child swallows some, contact your doctor immediately. Symptoms of overdose are low blood pressure, increased heartbeat, possibly decreased heartbeat **4. Possible side effects** *Common* (may affect up to 1 in 10 people)*:* • low blood pressure, (especially after excessive loss of water from the body within blood vessels e.g. in patients with severe heart failure or under treatment with high dose diuretics).
Increase in mineral (potassium) in the blood (hyperkalaemia)	Electrolyte imbalances are common in patients with renal impairment, with or without diabetes, and should be addressed.	**2. What you need to know before you take losartan** **Warning and precautions** It is important to tell your doctor before taking losartan • if you suffer from excessive vomiting or diarrhoea leading to an extreme loss of fluid and/or salt in your body, • if you receive diuretics (medicines that increase the amount of

		water that you pass out through your kidneys) or are under dietary salt restriction leading to an extreme loss of fluid and salt in your body (see section 3 'Dosage in special patient groups'). Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals **4.Posible side effects** *Common* (may affect up to 1 in 10 people)*:* • too much potassium in the blood (hyperkalaemia)
Kidney damage (Renal impairment and renal failure)	Losartan may impair kidney function, particularly in patients with pre-existing kidney problems and patients with heart failure. Use of losartan together with ACE inhibitors and/or aliskiren may worsen kidney function	**2.What you need to know before you take** **Do not take Losartan** • if you have diabetes or impaired kidney function **Warning and precautions** Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals **Other medicines and losartan** If your kidney function is impaired, the concomitant use of these medicines may lead to a worsening of the kidney function. 4. **Possible side effects** *Common* (may affect up to 1 in 10 people)*:*

		• changes in kidney function including kidney failure
Use during pregnancy	The use of losartan is not recommended during the first trimester of pregnancy. The use of losartan is contra-indicated during the 2nd and 3rd trimester of pregnancy.	**2.What you need to know before you take** You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking Losartan before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of <invented name>. Losartan is not recommended in early pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy.
Hypersensitivity	Hypersensitivity is a rare side effect.	The use of losartan is not recommended in patient with history of hypersensitivity

Table 14 Important potential risk

Risk	What is known
Abnormal liver function	There is no therapeutic experience with losartan in patients with severe hepatic impairment. Therefore losartan must not be administered in patients with severe hepatic impairment.

Table 9 Missing information

Risk	What is known
Use during lactation	No information is available regarding the use of losartan during breastfeeding, losartan is not recommended and alternative treatments with better established safety profiles during breastfeeding are preferable, especially while

	nursing a newborn or preterm infant.
Paediatric population (6 months to less than six years)	There are limited data on the efficacy and safety of losartan in children and adolescents aged 6-18 years old for the treatment of hypertension

VI.2.5 Summary of additional 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.

The Summary of Product Characteristics and the Package leaflet for Losartan can be found on the web pages of the national competent authorities in the EU.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable.

List of studies in post authorisation development plan

Not applicable.

Studies which are a condition of the marketing authorisation

Not applicable.

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

Not applicable