

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

High blood pressure, occurs in a large percentage of the adult population. From 25 to 50% of adults in various European and North American countries have high blood pressure. The rate of high blood pressure increases with age. High blood pressure is associated with a higher risk of cardiovascular disease and kidney disease. According to the World Health Organization, more than half of strokes and heart attacks are caused by high blood pressure. Because it is associated with strokes, heart attacks, and kidney failure, high blood pressure is estimated to cause almost 13% of deaths worldwide.

There is limited information on the rate of high blood pressure in children in Europe. One study showed that approximately 25% of 11 year old children in one Greek community had high blood pressure. The rate of high blood pressure in children in the US ranges from 5 to approximately 20% depending on gender and ethnicity.

VI.2.2 Summary of treatment benefits

The benefits of losartan have been established in the treatment of essential hypertension in adults and in children and adolescents 6-18 years of age; treatment of renal disease in adult patients with hypertension and type 2 diabetes mellitus with proteinuria ≥ 0.5 g/day as part of an antihypertensive treatment; treatment of chronic heart failure in adult patients when treatment with angiotensin converting enzyme (ACE) inhibitors is not considered suitable due to incompatibility, especially cough, or contraindication; reduction in the risk of stroke in adult hypertensive patients with left ventricular hypertrophy documented by ECG.

VI.2.3 Unknowns relating to treatment benefits.

Losartan has not been studied and should not be used in patients who:

- Are allergic to any of the ingredients of the medication (listed in the product label);
- Are in the 2nd or 3rd trimester of pregnancy;
- Have severe liver impairment

VI.2.4 Summary of safety concerns

Table 23 Important identified risks

Risk	What is known	Preventability
<p>Electrolyte imbalance</p>	<p>Electrolyte imbalances are common in patients with renal impairment, with or without diabetes, and should be addressed.</p>	<p>2. What you need to know before you take <invented name</p> <p><u>Warnings and precautions</u></p> <p>It is important to tell your doctor before taking Losartan/Hydrochlorothiazide:</p> <p>If you take diuretics (water pills)</p> <p>If you are on a salt-restricted diet</p> <p>If you have or have had severe vomiting and/or diarrhoea</p> <p>If you have high calcium or low potassium levels or you are on a low potassium diet</p> <p>Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals</p> <p>4. Possible side effects</p> <p><i>Common (may affect up to 1 in 10 people):</i></p> <p>increased potassium levels (which can cause an abnormal heart rhythm), decreased haemoglobin levels</p> <p><i>Not known (frequency cannot be estimated from the available data)</i></p> <p>Low levels of sodium in the blood (hyponatraemia)</p>

Risk	What is known	Preventability
<p>Low blood pressure (Hypotension)</p>	<p>As with all antihypertensive therapy, symptomatic hypotension may occur in some patients.</p>	<p>4. Possible side effects</p> <p><i>Uncommon (may affect up to 1 in 100 people):</i> Low blood pressure, which may be associated with changes in posture (feeling light-headed or weak when you stand up, angina (chest pain), abnormal heartbeat, cerebrovascular accident (TIA, “mini-stroke”), heart attack, palpitations</p>
<p>Changes in renal function including renal failure</p>	<p>Losartan may impair kidney function, particularly in patients with preexisting kidney problems and patients with heart failure. Use of losartan together with ACE inhibitors and/or aliskiren may worsen kidney function.</p>	<p>2. What you need to know before you take <invented name</p> <p><u>Warnings and precautions</u></p> <p>Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals</p> <p>4.Possible side effects</p> <p><i>Common (may affect up to 1 in 10 people):</i> Changes in kidney function including kidney failure</p> <p><i>Uncommon (may affect up to 1 in 100 people):</i> Frequent urination including at night, abnormal kidney function including inflammation of the kidneys, urinary tract infection, sugar in the urine</p>

Risk	What is known	Preventability
<p>Serious allergic reaction which causes swelling of the face or throat (Angioedema)</p>	<p>Patients with a history of angioedema (swelling of the face, lips, throat, and/or tongue) should be closely monitored</p>	<p>What you need to know before you take <invented name</p> <p><u>Warnings and precautions</u></p> <p>If you have or have had an allergic condition, asthma or a condition that causes joint pain, skin rashes and fever (systemic lupus erythematosus)</p> <p>4.Possible side effects <i>Uncommon (may affect up to 1 in 100 people)):</i></p> <p>Hives, itching, inflammation of the skin, rash, redness of the skin, sensitivity to light, dry skin, flushing, sweating, hair loss</p>

Risk	What is known	Preventability
<p>Toxic to the foetus (Foetotoxicity)</p>	<p>Losartan belongs to a group of medicines known as angiotensin-II receptor antagonists. Exposure to this class of medicines during the second and third trimesters is known to induce serious harm to foetus and neonatal toxicity.</p>	<p>2.What you need to know before you take Losartan/Hydrochlorothiazide</p> <p><u>Do not take Losartan/Hydrochlorothiazide</u> If you are more than 3 months pregnant.</p> <p>Warnings and precautions You must tell your doctor if you think you are (or might become) pregnant. Losartan/Hydrochlorothiazide is not recommended in early pregnancy, and must not be taken if you are more than 3 months pregnant, as it may cause serious harm to your baby if used at that stage</p> <p>Pregnancy and breast-feeding You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking Losartan/Hydrochlorothiazide before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Losartan/Hydrochlorothiazide. Losartan/Hydrochlorothiazide is not recommended in during 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</p>

Risk	What is known	Preventability
<p>Increased risk of adverse events in patients with hepatic impairment</p>	<p>Blood levels of losartan may be increased in liver impairment. A lower dose should be considered for patients with a history of liver impairment. There is no therapeutic experience in patients with severe liver impairment. Therefore, losartan is contraindicated in patients with severe liver impairment. Losartan is also not recommended in children with liver impairment.</p>	<p>2.What you need to know before you take Losartan/Hydrochlorothiazide <u>Do not take Losartan/Hydrochlorothiazide.</u> If you have severely impaired liver function</p> <p><u>Warnings and precautions</u></p> <p>It is important to tell your doctor before taking Losartan/ Hydrochlorothiazide: If your liver function is impaired</p> <p>4.Possible side effects Rare (may affect up to 1 in 1,000 people):</p> <p>Hepatitis (inflammation of the liver), abnormal liver function tests</p>
<p>Inflammation of the pancreas (Pancreatitis)</p>	<p>Losartan/HCTZ can induce pancreatitis. It is a uncommon side effect</p>	<p>4.Possible side effects Uncommon (may affect up to 1 in 100 people)): inflammation of the pancreas</p>
<p>Combination with lithium</p>	<p>As with other medicines which affect the excretion of sodium, lithium excretion may be reduced. If lithium excretion is reduced it is possible a high risk of lithium toxicity</p>	<p>2.What you need to know before you take Losartan/Hydrochlorothiazide <u>Other medicines and Losartan/Hydrochlorothiazide</u></p> <p>Tell your doctor or pharmacist if you are taking,have recently taken, or might take any other medicines.</p> <p>Preparations containing lithium should not be taken with Losartan/ Hydrochlorothiazide without close supervision by your doctor</p>

Table 24 Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
<p>Severe low blood pressure in patients with narrowing of the renal artery that can impede blood flow to the kidney</p> <p>(Severe hypotension in patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney)</p>	<p>Losartan should be used with caution in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney.</p>
<p>Special caution in patients with abnormal narrowing of the aortic and mitral valve in the heart, disease in which the heart muscle (myocardium) becomes abnormally thick</p> <p>(Special caution in patients with aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy)</p>	<p>As with other vasodilators, special caution is indicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy.</p>
<p>Thiazide-related impaired glucose tolerance in diabetic patients</p>	<p>Thiazide therapy may impair glucose tolerance. In diabetic patients, dosage adjustments of insulin or oral hypoglycaemia agents may be required. Latent diabetes mellitus may become manifest during thiazide therapy</p>
<p>Thiazide-related increases in cholesterol and triglyceride levels</p>	<p>Increases in cholesterol and triglyceride levels have been associated with thiazide diuretic therapy.</p>
<p>High level of blood uric acid (Hyperuricaemia)</p>	<p>Hyperuricaemia or frank gout may be precipitated in some patients receiving thiazide therapy.</p>
<p>Thiazide-related aggravation of chronic autoimmune disease (systemic lupus erythematosus)</p>	<p>Exacerbation or activation of systemic lupus erythematosus has been reported with the use of thiazides.</p>
<p>Less efficacious in black</p>	<p>As observed for angiotensin converting enzyme inhibitors,</p>

Risk	What is known (Including reason why it is considered a potential risk)
patients	losartan and the other angiotensin antagonists are apparently less effective in lowering blood pressure in black patients than in non-blacks, possibly because of higher prevalence or low-renin states in the black hypertensive population.

Important missing information

Table 25 Important missing information

Risk	What is known
Paediatric population (<18 year)	There is no experience with the use of Losartan / Hydrochlorothiazide in children. Therefore, Losartan/Hydrochlorothiazide should not be given to children and teenagers.
Pregnant woman and breast feeding	Losartan/Hydrochlorothiazide is not recommended during 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. Losartan/Hydrochlorothiazide is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed.
Patients with severe renal and hepatic impairment	Patients that have severely impaired kidney function or whose kidneys are not producing any urine, should be monitored. Blood levels of losartan may be increased in liver impairment. A lower dose should be considered for patients with a history of liver impairment. There is no therapeutic experience in patients with severe liver impairment. Therefore, losartan is contraindicated in patients with severe liver impairment. Losartan is also not recommended in children with liver impairment.

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 minimizing 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/ hydrochlorothiazide can be found in the Losartan/ hydrochlorothiazide EPAR page.

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

Not applicable.