Lisinopril/Hydrochlorothiazide Orion 20 mg/12,5 mg tablets

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PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Hypertension is a chronic disease in which the blood pressure is sustainly elevated. Systolic blood pressure means the pressure inside the arteries (blood vessels that carry blood from heart into the tissues) during the contraction of the heart, whereas diastolic blood pressure can be described as the pressure inside the arteries during the relaxation and filling of the heart. Blood pressure is considered elevated, when systolic blood pressure in repeated blood pressure measurements exceeds 140 mmHg and/or diastolic blood pressure is over 90 mmHg. Hypertension has been estimated to affect approximately 26 % of the adult population and this proportion is considered to be increasing. Untreated hypertension increases risk of other diseases, such as stroke, heart attack, heart failure and impaired function of the kidneys. High blood pressure is also associated with a shortened life expectancy. Thus, treatment of hypertension is essential in terms of public health.

VI.2.2 Summary of treatment benefits

In patients with increased blood pressure, lisinopril and hydrochlorothiazide have additive blood pressure lowering effects.

Reduction of the systolic blood pressure by 10 mmHg and diastolic blood pressure by 5 mmHg in hypertensive patients has been shown to decrease incidence of stroke by 35-40% and events of severe coronary artery disease by 20-25%, respectively. Similarly, reduction of isolated systolic blood pressure (meaning that the diastolic blood pressure is normal while the systolic blood pressure is high) leads to reduction on incidence of stroke and events of severe coronary artery disease by 30% and 23%, respectively.

VI.2.3 Unknowns relating to treatment benefits

Safety and effectiveness of Lisinopril/Hydrochlorothiazide OrionLisinopril/Hydrochlorothiazide Orion in children have not been established. There is no experience on the safe use of Lisinopril/Hydrochlorothiazide OrionLisinopril/Hydrochlorothiazide Orion with patients recently transplanted with a kidney.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Low blood pressure, which causes symptoms to the patient	Low blood pressure is a known adverse effect of therapy with Lisinopril/Hydrochlorothiazide Orion. Symptoms of low blood pressure include, e.g., dizziness, weakness and fainting. Especially patients who have impaired function of the heart, have had diarrhoea or have been vomiting, are at increased	Lisinopril/Hydrochlorothiazide Orion therapy is started under medical supervision. The patient should be followed when the dose is adjusted. In case of too low blood pressure, the dose of Lisinopril/Hydrochlorothiazide Orion may be reduced or the treatment discontinued.

Risk	What is known	Preventability
	risk for this adverse effect.	
Hypersensitivity/ angioedema	Hypersensitivity to lisinopril or hydrochlorothiazide exists and is a contraindication for use of Lisinopril/Hydrochlorothiazide Orion. In addition, hypersensitivity to substances having a similar chemical structure with hydrochlorothiazide (so called sulfonamide–derived active substances) is a contraindication for use of Lisinopril/Hydrochlorothiazide Orion. Cases of angioedema (a severe allergic reaction with swelling of the hands, feet, ankles, face, lips, tongue or throat) have been reported in association with the use of ACE-inhibitors, such as lisinopril.	Lisinopril/Hydrochlorothiazide Orion should not be used in patients with known hypersensitivity to lisinopril, hydrochlorothiazide, other sulfonamide-derived medicinal products or to any of the excipients. In cases of hypersensitivity reactions/angioedema, Lisinopril/Hydrochlorothiazide Orion should be discontinued and appropriate medical care and monitoring should be instituted.
Impaired function of the kidneys	Impairment of the function of the kidneys has been reported during the use of Lisinopril/Hydrochlorothiazide Orion, especially in patients with previous renal failure or impaired function of the heart.	Lisinopril/Hydrochlorothiazide Orion is contraindicated in patients with severe renal impairment. Use of Lisinopril/Hydrochlorothiazide Orion in patients with mild to moderate renal impairment should be carefully monitored.
High blood levels of potassium	There is a risk of elevated blood levels of potassium with the use of Lisinopril/Hydrochlorothiazide Orion. Patients with impaired function of the kidneys, patients with diabetes mellitus and patients who concomitantly use medicines which increase the potassium levels are at higher risk of this adverse effect.	Patients at risk should have their potassium levels monitored at appropriate intervals.
Use during pregnancy and lactation	Currently available information implies that the use of ACE-inhibitors such as lisinopril during the first trimester of pregnancy may increase the risk	Alternative treatments should be used, if possible, when the patient is planning pregnancy. If the patient becomes pregnant during the treatment, the use of

Risk	What is known	Preventability
	of abnormalities of the embryo. The use during the second or third trimester of pregnancy can be harmful to the development of the embryo and to the development of the newborn infant. There is not enough information available on the use of hydrochlorothizide during pregnancy. There is not enough information and experience on use of lisinopril during lactation. Theoretically, risk for adverse effects of the heart, blood vessels or kidneys on newborn infant exists. Hydrochlorothiazide is excreted in human milk in small amounts.	Lisinopril/Hydrochlorothiazide Orion should be immediately discontinued and alternative drug treatment used, if needed. The use of Lisinopril/Hydrochlorothiazide Orion during the first trimester of pregnancy is not recommended. Lisinopril/Hydrochlorothiazide Orion should not be used during the second and third trimesters of pregnancy (contraindication for use). The use of Lisinopril/Hydrochlorothiazide Orion during lactation is not recommended. If Lisinopril/Hydrochlorothiazide Orion treatment is necessary for the mother, the doses should be kept as low as possible.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Impaired function of the liver	Lisinopril/Hydrochlorothiazide Orion should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alteration of water and electrolyte balance may precipitate a condition called hepatic coma. Lisinopril/Hydrochlorothiazide Orion is contraindicated in patients with severe hepatic impairment.
Abnormally low count of neutrophils in the blood	Abnormally low count of white-blood cells called neutrophils in the blood (neutropenia/agranulocytosis) has been reported for patients receiving ACE inhibitors such as lisinopril. However, this adverse effect is rare in patients whose kidneys are functioning normally. Abnormally low levels of neutrophils in the blood may predispose the patient to serious infections. Accordingly, the signs of abnormally low numbers of neutrophils may include fever, sore throat, chills and other signs of infection.
Concomitant use of antidiabetic medicines	Treatment with hydrochlorothiazide may impair glucose tolerance. Dose adjustment of antidiabetic medicinal products, including insulin, may be required during Lisinopril/Hydrochlorothiazide Orion treatment.
Concomitant use of medicines	There is a risk for elevated potassium levels in concomitant use of

Risk	What is known (Including reason why it is considered a potential risk)
which increase the blood levels of potassium	Lisinopril/Hydrochlorothiazide Orion and other medications which increase the serum levels of potassium. These medications include certain diuretics (so called potassium-sparing diuretics), potassium supplements or potassium-containing salt substitutes. Monitoring of potassium should be undertaken as appropriate.

Missing information

Risk	What is known
Use in children	The safety and efficacy of Lisinopril/Hydrochlorothiazide Orion have not been studied in children and thus no information on the use of Lisinopril/Hydrochlorothiazide Orion in children is available.
Use in patients with kidney transplantation	There is currently no experience regarding the administration of Lisinopril/Hydrochlorothiazide Orion in patients with recent kidney transplantation.

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. The Summary of Product Characteristics and the Package leaflet for Lisinopril/Hydrochlorothiazide Orion can be found in the national authority's web 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.