PUBLIC SUMMARY OF RISK MANAGEMENT PLAN (RMP)

ORIDIP 10 MG FILM-COATED TABLETS
ORIDIP 20 MG FILM-COATED TABLETS

ORION CORPORATION

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VI.2 Elements for a Public Summary

Lercanidipin Orion is indicated for the treatment of mild to moderate essential hypertension. In essential hypertension blood pressure is increased without any specific identifiable cause.

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 mm Hg and/or diastolic blood pressure is over 90 mm Hg. 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

Reduction of the systolic blood pressure by 10 mm Hg and diastolic blood pressure by 5 mm Hg 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.

Lercanidipine lowers blood pressure by dilating blood vessels. In dilated vessel the blood flows with lower pressure. In two randomized clinical trials of approximately 400 patients with mild-to-moderate hypertension, lercanidipine significantly reduced systolic blood pressure and diastolic blood pressure after four weeks. In a longer trial lasting for 12 months, lercanidipine led to normalized blood pressure in 49% of patients after four weeks. A postmarketing trial of 9 050 patients corroborated the results observed in previous clinical trials, with 64% of patients achieving a diastolic blood pressure of less than 90 mm Hg and 32% attaining blood pressure control (<140/90 mm Hg).

VI.2.3 Unknowns relating to treatment benefits

Lercanidipine is not recommended for use in children below 18 years due to a lack of data on efficacy and safety.

VI.2.4 Summary of safety concerns

Important identified risk

Risk	What is known	Preventability
Allergic reactions	Lercanidipine and other ingredients of this medicine may cause allergic reactions, e.g. rash.	The product should not be used, if a patient is known to be allergic to lercanidipine or other ingredients of the medicine; or is allergic to other medicines closely related to lercanidipine, such as amlodipine, nicardipine, felodipine, isradipine, nifedipine or lacidipine.
Cardiac disorders: faster heart beat (tachycardia); a sensation in which a person is aware of an irregular, hard, or rapid heartbeat (palpitations); and chest pain caused by coronary artery disease (angina pectoris)	Lercanidipine has been reported to cause faster heart beat (tachycardia); a sensation in which a person is aware of an irregular, hard, or rapid heartbeat (palpitations); and chest pain caused by coronary artery disease (angina pectoris). Very rarely patients with pre-existing angina pectoris may experience increased frequency, duration or severity of these attacks. Isolated cases of heart attacks (myocardial infarction) have been reported in some patients using lercanidipine.	Lercanidipine should not be used in the following heart diseases: untreated heart failure, obstruction of the flow of blood from the heart, unstable angina (meaning chest pain at rest or in minimal exercise in patient with coronary artery disease) or within one month after the heart attack.
Nervous system disorders, dizziness and fainting	Disorders of the nervous system, like headache, dizziness, weakness and tiredness have been reported during lecanidipine use. Very rarely lercanidipine may also cause fainting.	Clinical experience with lercanidipine indicates that it is unlikely to impair a patient's ability to drive or use machinery. However, caution should be exercised because dizziness, asthenia, fatigue and rarely somnolence may occur.
Use in severed kidney and liver impairment	Both liver and kidneys participate in removal of lercanidipine from the body. Lercanidipine is converted in the liver to inactive substances that are excreted into the urine via kidneys.	Lercanidipine is not recommended for use in patients with severely decreased liver or kidney function. Special care is needed when lercanidipine is used in patients with mildly or moderately decreased liver or kidney function. Although the usually recommended dose may be tolerated in these patients,

Risk	What is known	Preventability
		an increase in dose must be approached with caution. The blood pressure lowering effect of lercanidipine may be enhanced in these patients.
Concomitant use with medicinal products or other products that are known to strongly inhibit the function of protein named CYP3A4, grapefruit juice or ciclosporine (a drug used after transplants to prevent organ rejection)	In liver lercanidipine is converted to inactive substances that are excreted into the urine *via* kidneys. A protein named CYP3A4 is important in this conversion of lercanipine to inactive forms. There are several medicinal products that are known to inhibit the function of CYP3A4, thereby influencing on the amount of active lercanidipine in the body. Concomitant use of other medicinal products that strongly inhibit the function of CYP3A4 increase lercanidipine plasma levels and may increase its blood pressure lowering effects. Drugs that are strong inhibitors of CYP3A4 include *e.g.* some medicines used for fungal infections (such as ketoconazole and itraconazole), some antibiotics (such as erythromycin) and some drugs used for viral infections (such as ritonavir). In addition to drugs other substances, such as grapefruit or grapefruit juice may also inhibit metabolism of lercanidipine. Concomitant use of ciclosporin (a drug used after transplants to prevent organ rejection) and lercanidipine may increase the effect of both medications.	Lercanidipine should not be administered with medicinal products that are known to strongly inhibit function of CYP3A4. Patients should not take grapefruit or grapefruit juice or a drug called ciclosporine during lercanidipine treatment.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Effects on pregnancy, breast feeding and fertility	In animal studies no evidence for harmful effects of lercanidipine on fertility or on foetus during pregnancy have been seen. However, other medicinal products with similar mechanism of action have been reported to cause foetal abnormalities in animals. There is no clinical experience in humans about the effects of lercanidipine during pregnancy and lactation and on fertility. Therefore lercanidipine should not be used during pregnancy or in women with child-bearing potential unless effective contraception is used. Lercanidipine is expected to be found in breast milk and should not be administered to nursing mothers. Lercanidipine has been reported to cause in few patients reversible biochemical changes of the sperm that may impair fertilisation. This should be kept in mind in case of in vitro fertilization treatment (one of assisted reproductive techniques used in infertility).

Missing information

Risk	What is known
Use in patients with left ventricular outflow tract obstruction	The use of lercanidipine is contraindicated in patients with left ventricular outflow tract obstruction.
Use in patients with untreated cardiac failure	Lercanidipine should not be used in patients with untreated symptomatic heart failure.
Use in coronary artery disease patients who experience chest pain at rest or in minimal exercise (so called unstable angina pectoris)	It has been suggested that lercanidipine may be associated with increased risk of cardiovascular problems in patients with ischaemic heart disease, who has a long-lasting lack of oxygen in the cardiac muscle due to coronary artery disease or some other reason. Very rarely these patients may experience increased frequency, duration or severity of chest pain attacks. Lercanidipine should not be used in coronary artery disease patients who experience chest pain already at rest or in minimal exercise (so called unstable angina pectoris).
Use in patients within one month after the heart attack (myocardial infarction)	Lercanidipine may increase the frequency, duration or severity of chest pain attacks in patients with ischaemic heart disease. Therefore lercanidipine should not be used in patients within 1 month of heart attack.

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 Lercanidipin 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.