Part VI: Summary of the risk management plan

Summary of risk management plan for Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion

(Levosimendan)

This is a summary of the risk management plan (RMP) for Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion. The RMP details important risks of the product and how these risks can be minimised.

The summary of product characteristics (SmPC) for Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion and its package leaflet give essential information to healthcare professionals and patients on how the product should be used.

Important new concerns or changes to the current ones will be included in updates of the product's RMP.

I. The medicine and what it is used for

Levosimendan Carinopharm is authorised for the short-term treatment of acutely decompensated severe chronic heart failure (ADHF) in situations where conventional therapy is not sufficient, and in cases where inotropic support is considered appropriate (see SmPC for the full indication). It contains levosimendan as the active substance and it is given as intravenous infusion following reconstitution and dilution.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion, together with measures to minimise such risks and the proposed studies for learning more about the product's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size − the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status − the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	• Hypotension • Supraventricular tachyarrhythmias • Ventricular tachyarrhythmias and use in patients with Torsade de Pointes • Ischaemic heart disease • Hypokalaemia
Important potential risks	• Hepatic disorder • Haemorrhage • Overdose • QT prolongation • Erroneous handling during preparation of diluted solution for infusion
Missing information	• Use in children and adolescents under 18 years of age • Use in patients with impaired renal function • Exposure during pregnancy • Repeated administration of levosimendan • Use of levosimendan in the following disorders: restrictive cardiomyopathy, hypertrophic cardiomyopathy, severe mitral valve insufficiency, myocardial rupture, cardiac tamponade and right ventricular infarction

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

There is a difference in the pharmaceutical form between Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion and the pharmaceutical form for the originator product (Simdax 2.5 mg/ml concentrate for solution for infusion) or its generic version Zimino 2.5 mg/ml concentrate for solution for infusion. Levosimendan Carinopharm is a lyophilized powder which must be reconstituted and diluted prior to intravenous infusion. This is important since the reference medicinal product Simdax and its generic version Zimino do not need to be reconstituted prior to dilution. Erroneous handling during the preparation of the diluted solution for infusion is therefore an additional important potential risk for Levosimendan Carinopharm, which is described below.

Erroneous handling during preparation of diluted solution for infusion	
Evidence for linking the risk to the medicine	There is a difference in the pharmaceutical form between Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion and the pharmaceutical form for the originator product (Simdax 2.5 mg/ml concentrate for solution for infusion) or its generic version Zimino 2.5 mg/ml concentrate for solution for infusion. Levosimendan Carinopharm is a lyophilized powder which must be reconstituted and diluted prior to intravenous infusion. This is important since the reference medicinal product Simdax and its generic version Zimino do not need to be reconstituted prior to dilution. Erroneous handling during the preparation of the diluted solution for infusion is therefore an additional important potential risk for Levosimendan Carinopharm.
Risk factors and risk groups	Not applicable.
Risk minimisation measures	<u>Routine risk minimisation measures:</u> Routine risk communication in SmPC Sections 4.2 and 6.6 / PL Sections 1 and Information for Healthcare Professionals Only Prescription only <u>Additional risk minimisation measures:</u> None

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Levosimendan Carinopharm 12.5 mg powder for concentrate for solution for infusion.