Summary of risk management plan for rosuvastatin / perindopril / amlodipine

This is a summary of the risk management plan (RMP) for rosuvastatin / perindopril / amlodipine by Krka. The RMP details important risks of rosuvastatin / perindopril / amlodipine by Krka and how more information will be obtained about rosuvastatin / perindopril / amlodipine by Krka's risks and uncertainties (missing information).

Rosuvastatin / perindopril / amlodipine by Krka's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how rosuvastatin / perindopril / amlodipine by Krka should be used.

Important new concerns or changes to the current ones will be included in updates of rosuvastatin / perindopril / amlodipine by Krka's RMP.

I. The medicine and what it is used for

Rosuvastatin / perindopril / amlodipine by Krka is authorised for substitution therapy in patients adequately controlled with rosuvastatin, perindopril and amlodipine given concurrently at the same dose levels as in the combination for treatment of hypertension and hypercholesterolaemia (see SmPC for the full indication). It contains rosuvastatin / perindopril / amlodipine as the active substance and it is given by orally.

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

Important risks of rosuvastatin / perindopril / amlodipine by Krka together with measures to minimise such risks and the proposed studies for learning more about rosuvastatin / perindopril / amlodipine by Krka'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*.

II.A List of important risks and missing information

Important risks of rosuvastatin / perindopril / amlodipine by Krka are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. 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 rosuvastatin / perindopril / amlodipine by Krka. 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);

Summary of safety concerns	
Important identified risks	Muscle effects including potentially life threatening muscle damage (**rhabdomyolysis**) and other muscle problems such as muscular weakness (**myopathy**), muscle inflammation (**myositis**), muscle pain (**myalgia**), **increased creatine kinase in the urine**, immune-mediated necrotising myopathy (Skeletal muscle effects: rhabdomyolysis, myopathy, myositis, myalgia, creatine kinase increases, immune-mediated necortising myopathy)
	Increased levels of liver enzymes in the blood (**increased transaminases**), liver inflammation (**hepatitis**), yellowing of skin and eyes (**jaundice**) (Hepatic effects: permanently increased transaminases, hepatitis, jaundice, hepatic impairment)
	Important identified drug-drug interactions: Ciclosporin (used, for example, after organ transplant to suppress the immune

Summary of safety concerns	
	system) **Various protease inhibitor combinations with ritonavir** (used to fight HIV infection) **Gemfibrozil** (used to lower cholesterol) **Clopidogrel** (used for thinning the blood) **Eltrombopag** (used to treat abnormally low blood platelet counts) **Dronedarone** (used to treat cardiac arrhythmias) **Warfarin and other vitamin K antagonists** (or any other drug used for thinning the blood) **Fusidic acid** (used to treat bacterial infections) **Ezetimibe** (used to lower cholesterol)
	Allergic reactions incuding swelling of face, neck, lips and throat (Hypersensitivity reactions (including angioedema, intestinal angioedema, concomitant use of mTOR inhibitor, photosensitivity and anaphylactoid reactions))
	Low blood pressure (Hypotension)
	Renal dysfunction, hypotension and hyperkalaemia as consequence of dual RAAS blockade
	Use in pregnancy and breastfeeding
Important potential risks	Kidney damage/failure (Renal effects: renal failure (including acute and chronic renal failure) and renal impairment)
	Lung disease (Interstitial lung disease)
	Use of the approved medicine differs from the situation described in the Patient leaflet (Off label use)
Missing information	Use in children and adolescents
	Lack of safety data on long-term use of the combination

II.B Summary of important risks

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

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 rosuvastatin / perindopril / amlodipine by Krka.

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

There are no studies required for rosuvastatin / perindopril / amlodipine by Krka.