Summary of risk management plan for candesartan + amlodipine by Krka

This is a summary of the risk management plan (RMP) for candesartan + amlodipine by Krka. The RMP details important risks of candesartan + amlodipine by Krka, how these risks can be minimised, and how more information will be obtained about candesartan + amlodipine by Krka's risks and uncertainties (missing information).

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

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

I. The medicine and what it is used for

Candesartan + amlodipine by Krka is authorised for substitution therapy in adult patients with essential hypertension whose blood pressure is already adequately controlled with candesartan and amlodipine given concurrently at the same dose level (see SmPC for the full indication). It contains candesartan + amlodipine as the active substance and it is given orally.

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

Important risks of candesartan + amlodipine by Krka, together with measures to minimise such risks and the proposed studies for learning more about candesartan + 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*.

If important information that may affect the safe use of candesartan + amlodipine by Krka is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of candesartan + 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 candesartan + 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);

List of important risks and missing information	
Important identified risks	Low blood pressure (Hypotension)
	Elevated levels of potassium in the blood (Hyperkalemia)
	Excess fluid in the lungs in patients with poor heart function (Pulmonary oedema – in patients with pre-existing heart failure NYHA grades III and IV)
	Heart problems- especially in patients with poor heart function (Cardiovascular events – especially in patients with congestive heart failure)
	Kidney disorder (Decreased renal function– especially in patients with renal artery stenosis, pre-existing renal impairment, heart failure, dual blockade of RAAS)
	Concomitant use with other medicines (Drug interactions – NSAIDs, lithium, aliskiren and other RAS antihypertensives, dantrolene, drugs affecting CYP3A4, simvastatin, potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium and other substances that may increase potassium levels, tacrolimus)
	Risk of damage to your baby after 3rd month of pregnancy (Exposure during 2nd or 3rd trimester of pregnancy)
Important potential risks	Risk of damage to your baby in first months of pregnancy (Exposure during 1st trimester of pregnancy)
	Movement disorder (Extrapyramidal syndrome)
	Toxic effect on fertility (Toxic effect on fertility)
Missing information	Use during breast feeding
	Use in children below 18 years of age
	Use in patients with recent kidney transplantation or with end-stage renal impairment

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 candesartan + amlodipine by Krka.

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

There are no studies required for candesartan + amlodipine by Krka.