Part VI: Summary of the risk management plan

Summary of risk management plan for Candezek Combi (candesartan cilexetil/amlodipine besilate)

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

Candezek Combi's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Candezek Combi should be used.

I. The medicine and what it is used for

Candezek Combi is indicated as substitution therapy in adult patients with essential hypertension whose blood pressure is adequately controlled with amlodipine and candesartan given concurrently at the same dose level (see SmPC for the full indication). It contains candesartan cilexetil/amlodipine besilate as the active substances and it is given by orally.

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

Important risks of Candezek Combi, together with measures to minimise such risks and the proposed studies for learning more about Candezek Combi'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.

If important information that may affect the safe use of Candezek Combi is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Candezek Combi 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 Candezek Combi. 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	• Hyperkalaemia • Decreased renal function– especially in patients with renal artery stenosis, pre-existing renal impairment, heart failure, dual blockade of RAAS
Important potential risks	• None
Missing information	• None

II.B Summary of important risks

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

Important identified risk: Hyperkalaemia	
Evidence for linking the risk to the medicine	There have been reports of hyperkalaemia use of candesartan in clinical trials and post-marketing reports.

Risk factors and risk groups	Patients with renal insufficiency, heart failure patients, elderly patients and diabetes
Risk minimisation measures	Routine risk communication: SmPC sections 4.4, 4.5 and 4.8. PL section 2 and 4 Other routine risk minimisation measures beyond the Product Information: Legal status: Prescription only

Important identified risk: Decreased renal function– especially in patients with renal artery stenosis, pre-existing renal impairment, heart failure, dual blockade of RAAS	
Evidence for linking the risk to the medicine	Changes in renal function including acute renal failure can be caused by drugs that inhibit the renin-angiotensin system. Patients whose renal function may depend, in part, on the activity of the renin-angiotensin system (e.g., patient with renal artery stenosis, chronic kidney disease, severe heart failure, or volume depletion) may be at particular risk of developing oliguria, progressive azotemia or acute renal failure when treated with candesartan cilexetil. Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (including

	acute renal failure) compared to the use of a single RAAS-acting agent.
Risk factors and risk groups	Patients with renal artery stenosis, chronic kidney disease, severe heart failure, or volume depletion renal insufficiency, elderly patients and diabetes.
Risk minimisation measures	Routine risk communication: SmPC sections 4.2, 4.4, 4.5 and 4.8. PL section 2, 3 and 4 Other routine risk minimisation measures beyond the Product Information: Legal status: Prescription only

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 Candezek Combi.

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

There are no studies required for Candezek Combi.