Part VI: Summary of the risk management plan

RMP Part VI is valid for all products in this RMP: Dapaglifozin Devatis 5 mg & 10 mg film-coated tablets.

Summary of risk management plan for Dapaglifozin Devatis 5 mg & 10 mg film-coated tablets (Dapaglifozin)

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

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

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

I. The medicine and what it is used for

Dapaglifozin Devatis is authorised in adult patients for treatment of type 2 diabetes mellitus as an adjunct to diet and exercise, for treatment of symptomatic chronic heart failure with reduced ejection fraction and patients with chronic kidney disease. It contains dapagliflozin 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 Dapaglifozin Devatis, together with measures to minimise such risks and the proposed studies for learning more about Dapaglifozin Devatis'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 Dapaglifozin Devatis 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 Dapaglifozin Devatis. 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.

List of important risks and missing information	
Important identified risks	• Diabetic Ketoacidosis including events with atypical presentation
Important potential risks	• Bladder cancer • Breast cancer • Prostate cancer • Lower limb amputation
Missing information	• Use in patients with NYHA class IV

II.B Summary of important risks

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

Important identified risk: Diabetic Ketoacidosis including events with atypical presentation	
Risk minimisation measures:	**Routine risk minimisation measures:** SmPC sections 4.4, 4.8 PL sections 2, 4 Information includes that dapagliflozin should be interrupted in relation to major surgical procedures or acute serious medical illnesses, or if DKA is suspected (SmPC section 4.4, PL section 2). Before initiating dapagliflozin, factors in the patient history that may predispose to ketoacidosis should be considered. (SmPC section 4.4). **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	Monitor the Nonclinical mechanistic model studies (postdoc project). (dapagliflozin).

Important potential risk: Bladder cancer	
Risk minimisation measures	**Routine risk minimisation measures:** None. **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	Monitor MB102118: Cancer in Patients on Dapagliflozin and Other Antidiabetic Treatment.
Important potential risk: Breast cancer	
Risk minimisation measures	**Routine risk minimisation measures:** None. **Additional risk minimisation measures:** None.
Additional Pharmacovigilance Activities	Monitor MB102118: Cancer in Patients on Dapagliflozin and Other Antidiabetic Treatment.
Important potential risk: Prostate cancer	
Risk minimisation measures	**Routine risk minimisation measures:** None. **Additional risk minimisation measures:** None.
Additional Pharmacovigilance Activities	Monitor MB102118: Cancer in Patients on Dapagliflozin and Other Antidiabetic Treatment.
Important potential risk: Lower limb amputation	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section 4.4: Guidance provided on potential class effect PL section 2: Counsel on routine preventative foot care. **Additional risk minimisation measures:** None.
Additional Pharmacovigilance Activities	Dedicated eCRF for Lower Limb Amputation is evaluated in studies D169AC00001, D169CC00001, D169EC00001, D169EC00002.
Missing information: Use in patients with NYHA class IV	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section: 4.4

	Additional risk minimisation measures: None.
Additional Pharmacovigilance Activities	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 Dapaglifozin Devatis.

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

Study short name: Nonclinical mechanistic model studies [Postdoc project].

Purpose of the study: Studies aimed to elucidate the metabolic adaptations in term of glucose flux, lipolysis, and ketogenesis following insulin withdrawal in subjects with diabetes mellitus and absolute or relative endogenous insulin deficiency, when treated with dapagliflozin.

Study short name: MB102118 (D1690R00007) – Cancer in Patients on Dapagliflozin [Observational study].

Purpose of the study: (1) To compare the incidence of breast cancer, by insulin use at cohort entry, among females with T2DM who are new initiators of dapagliflozin and females who are new initiators of antidiabetic drugs in classes other than SGLT2 inhibitors, insulin, metformin monotherapy, or SU monotherapy and (2) To compare the incidence of bladder cancer, by insulin use and pioglitazone use, among male and female patients with T2DM who are new initiators of dapagliflozin and those who are new initiators of antidiabetic drugs in classes other than SGLT2 inhibitors, insulin monotherapy, metformin monotherapy, or SU monotherapy.

Study short name: D169CC00001 Deliver

Purpose of the study: Evaluate the effect of dapagliflozin on reducing cardiovascular death or worsening heart failure in patients with heart failure with preserved ejection fraction (HFpEF).