SUMMARY OF RISK MANAGEMENT PLAN FOR SYNJARDY (EMPAGLIFLOZIN + METFORMIN)- VERSION 12

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

Synjardy's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Synjardy should be used.

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

I. The medicine and what it is used for

Synjardy is authorized the treatment of adults with insufficiently controlled type 2 diabetes mellitus (see SmPC for the full indication). It contains empagliflozin and metformin as the active substances and it is given by oral administration.

II. Risks associated with the medicine and activities to minimize or further characterize the risks.

Important risks of Synjardy, together with measures to minimize such risks and the proposed studies for learning more about Synjardy's risks, are outlined below.

Measures to minimize 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 public (e.g. with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

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

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II.A List of important risks and missing information

Important risks of Synjardy are risks that need special risk management activities to further investigate or minimize 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 Synjardy. 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	Complicated urinary tract infection Genital infection Diabetic ketoacidosis with atypical presentation Lactic acidosis
Important potential risks	Urinary tract carcinogenicity Liver injury Amputation risk Pancreatitis
Missing information	None

II.B Summary of important risks

The safety information in the proposed Summary of product characteristics, Labelling and Package information leaflet is aligned to the reference medicinal product.

II.C Post-authorization development plan

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

No studies are conditions of the marketing authorization or specific obligations of Synjardy.

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

PASS 1245.96

Purpose of the study: To evaluate the risk of urinary tract and genital infection, acute renal and hepatic injury, and diabetic ketoacidosis resulting in hospitalisations, in empagliflozin treated patients, compared to users of other antidiabetic treatment.

PASS 1245.97

Purpose of the study: To evaluate the risk of renal and bladder cancer in empagliflozin treated patients, compared to users of other antidiabetic treatment.

PASS 1245.171

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Purpose of the study: Meta-analysis to evaluate amputation risk in trials 1245.25, 1245.110, 1245.121