JARDIANCE (Empagliflozin)
Filmtabletten
ZL-Nr.: 63227

Public Risk Management Plan (RMP) Summary

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Boehringer Ingelheim (Schweiz) GmbH
Hochbergerstrasse 60B
CH-4057 Basel
www.boehringer-ingelheim.ch

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary of Jardiance is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the “Arzneimittelinformation / Information sur le médicament” approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.
Please note that the reference document which is valid and relevant for the effective and safe use of Jardiance in Switzerland is the “Arzneimittelinformation/ Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic.

Boehringer Ingelheim (Schweiz) GmbH is fully responsible for the accuracy and correctness of the content of the published summary RMP of Jardiance.

PART VI SUMMARY OF THE RISK MANAGEMENT PLAN

SUMMARY OF RISK MANAGEMENT PLAN FOR JARDIANCE (EMPAGLIFLOZIN)

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

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

This summary of the RMP for Jardiance should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

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

I. THE MEDICINE AND WHAT IT IS USED FOR

Jardiance is authorised for the treatment of adults and children aged 10 years and above
- With insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise.

Jardiance is authorised for the treatment of adults
- With symptomatic chronic heart failure independent of left ventricular ejection fraction.

See SmPC for full indication. It contains empagliflozin as the active substance and it is given by oral administration.

Further information about the evaluation of Jardiance’s benefits can be found in Jardiance’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Jardiance, together with measures to minimise such risks and the proposed studies for learning more about Jardiance'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 Jardiance is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Jardiance 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 Jardiance. 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
Important potential risks	Urinary tract carcinogenicity
	Liver injury
	Amputation risk
	Pancreatitis
Missing information	None

II.B Summary of important risks

There is no missing information for Jardiance.

Table 1 Important identified risks

Complicated urinary tract infection	
Evidence for linking the risk to the medicine	Clinical trial and post-marketing data with use of empagliflozin
Risk factors and risk groups	Diabetes, diseases impairing the immune system, catheter use, asymptomatic bacteriuria, kidney stones, female gender, sexually active females, diaphragm use in females, post-menopausal females, and males with prostatic enlargement
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 and 4.8 PL sections 2 and 4 Prescription only medicine Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1245-0096 See Section II.C of this summary for an overview of the post-authorisation development plan.
Genital infection	
Evidence for linking the risk to the medicine	Clinical trial data with use of empagliflozin; post-marketing experience with use of SGLT-2 inhibitors, including empagliflozin
Risk factors and risk groups	General risk factors: diabetes, diseases impairing the immune system Female gender, sexually active females, diaphragm use, lack of oestrogen
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8 PL section 4 Prescription only medicine Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1245-0096 See Section II.C of this summary for an overview of the post-authorisation development plan.
Diabetic ketoacidosis with atypical presentation	
Evidence for linking the risk to the medicine	Post-marketing experience with use of SGLT-2 inhibitors, including empagliflozin
Risk factors and risk groups	Low beta-cell function reserve; conditions leading to restricted food intake or severe dehydration; reduced insulin doses; increased insulin requirements due to acute illness, surgery, or alcohol abuse
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 and 4.8 PL sections 2 and 4 Prescription only medicine

	Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1245-0096 See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 2 Important potential risks

Urinary tract carcinogenicity	
Evidence for linking the risk to the medicine	Clinical trial data and post-marketing experience with use of SGLT-2 inhibitors
Risk factors and risk groups	Risk factors for bladder cancer: smoking, exposure to aromatic amines or aniline dyes, history of radiation treatment of the pelvis, chemotherapy with cyclophosphamide, and long-term indwelling urinary catheterisation Risk factors for renal cancer: smoking, obesity, hypertension, exposure to substances such as asbestos, cadmium, and benzene, and genetic hereditary diseases such as von Hippel-Lindau disease, and Birt-Hogg-Dube syndrome
Risk minimisation measures	Routine risk minimisation measures: Prescription only medicine Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1245-0097 See Section II.C of this summary for an overview of the post-authorisation development plan.
Liver injury	
Evidence for linking the risk to the medicine	Clinical trial data with use of empagliflozin
Risk factors and risk groups	Hepatotoxic drugs (e.g. non-steroidal anti-inflammatories, carbamazepine, isoniazid, and statins), chronic liver disease (e.g. fatty liver disease, viral hepatitis infections), diabetes
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.2 and 4.4 Prescription only medicine Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1245-0096 See Section II.C of this summary for an overview of the post-authorisation development plan.
Amputation risk	
Evidence for linking the risk to the medicine	Clinical trial data for another SGLT-2 inhibitor

Risk factors and risk groups	Patients with diabetes with the following risk factors: smoking, history of foot ulcer or previous amputation, foot deformities including pre-ulcerative callus or corn, Charcot foot, peripheral neuropathy with loss of protective sensation, peripheral artery disease, poor glycaemic control, visual impairment due to diabetic retinopathy, and diabetic nephropathy (especially patients on dialysis)
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 PL section 2 Prescription only medicine Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1245-0137 See Section II.C of this summary for an overview of the post-authorisation development plan.
Pancreatitis	
Evidence for linking the risk to the medicine	Clinical trial and post-marketing data with use of empagliflozin In clinical trials, there was no increase in the frequency of pancreatitis AEs with empagliflozin treatment compared to placebo. However, these results are limited due to the small sample size for capturing rare events. Post-marketing experience does not provide strong evidence for a causal association between empagliflozin treatment and pancreatitis.
Risk factors and risk groups	T2DM, obesity, alcohol abuse, smoking, higher comorbidity index, hypertriglyceridaemia, any history of gallbladder disease
Risk minimisation measures	Routine risk minimisation measures: Prescription only medicine Additional risk minimisation measures: 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 Jardiance.

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

PASS 1245-0096
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 1245-0097
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 1245-0137
Purpose of the study: To assess the effect of empagliflozin on time to kidney disease progression or cardiovascular death

ABBREVIATIONS

AE	Adverse event
EMA	European Medicines Agency
EPAR	European Public Assessment Report
PASS	Post-Authorisation Safety Study
PL	Package leaflet
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
SGLT-2	Sodium-dependent glucose co-transporter 2
SmPC	Summary of Product Characteristics
T2DM	Type 2 diabetes mellitus