Summary of the risk management plan for Segluromet (ertugliflozin/metformin)

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

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

This summary of the RMP for Segluromet 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 Segluromet's RMP.

I. The Medicine and What It Is Used For

Segluromet is authorized for treatment of type 2 diabetes mellitus in adult patients as an adjunct to diet and exercise (see SmPC for the full indication).

It contains ertugliflozin/metformin as the active substances and it is given by orally.

Further information about the evaluation of Segluromet’s benefits can be found in Segluromet’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/segluromet.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

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

II.A List of Important Risks and Missing Information

Important risks of Segluromet 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 Segluromet. 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);

Table II.A.1: List of Important Risks and Missing Information

List of important risks and missing information	
Important identified risks	DKA with atypical presentation Lactic acidosis
Important potential risks	None
Missing information	Use in pregnancy and breastfeeding Use in patients with CHF Class IV

II.B Summary of Important Risks

Table II.B.1: Important Identified Risk: DKA with Atypical Presentation

Evidence for linking the risk to the medicine	The important identified risk of DKA with atypical presentation is an ertugliflozin specific safety concern. It is not an identified or potential risk for metformin. Review of ertugliflozin clinical trial data regarding DKA with Atypical Presentation and recognition of this as an SGLT2 inhibitor class effect represents sufficient evidence of a causal association with ertugliflozin exposure.
Risk factors and risk groups	Factors predisposing patients to DKA include situations of decreased insulin and/or increase glucagon such as T1DM, pancreatic insulin deficiency, decreased caloric intake, insulin dose reduction, or increased insulin requirements due to acute medical illness or surgery, and alcohol abuse.
Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.4 Special warnings and precautions for use SmPC Section 4.8 Undesirable effects Additional risk minimisation measures None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study 8835-062/Post-authorization safety study (PASS) to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus patients treated with ertugliflozin compared to patients treated with other antihyperglycaemic agents

Table II.B.2: Important Identified Risk: Lactic Acidosis

Evidence for linking the risk to the medicine	The important identified risk of lactic acidosis is a metformin specific safety concern. It is not an identified or potential risk for ertugliflozin. Lactic acidosis is a rare, but serious, metabolic complication that can occur due to metformin accumulation during treatment with sitagliptin/metformin FDC; when it occurs, it is fatal in approximately 50% of cases.
Risk factors and risk groups	The most common risk factor is renal insufficiency. Lactic acidosis may occur in association with other risk factors including poorly controlled diabetes, ketosis, prolonged fasting, excessive alcohol intake, hepatic insufficiency and any condition associated with hypoxia.
Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.2 Posology and method of administration (Special populations) SmPC Section 4.3 Contraindications SmPC Section 4.4 Special warnings and precautions for use SmPC Section 4.5 Interaction with other medicinal products and other forms of interaction SmPC Section 4.8 Undesirable effects SmPC Section 4.9 Overdose Additional risk minimisation measures None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None

Table II.B.3: Important Missing Information: Use in Pregnancy and Breastfeeding

Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.6 Fertility, pregnancy and lactation Additional risk minimisation measures None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None

Table II.B.4: Important Missing Information: Use in Patients with CHF Class IV

Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 Special warnings and precautions for use Additional risk minimisation measures: None
Additional pharmacovigilance activities	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 Segluromet.

II.C.2 Other Studies in Post-Authorisation Development Plan

Study Title:

Study 8835-062/Post-authorization safety study (PASS) to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus patients treated with ertugliflozin compared to patients treated with other antihyperglycaemic agents

Purpose of the study:

To assess the risk of DKA in new users of ertugliflozin, compared with new users of other non-SGLT2-inhibitor antihyperglycaemic agents.