Summary of risk management plan for Glubrava (Pioglitazone/metformin FDC)

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

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

This summary of the RMP for Glubrava 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 the Glubrava RMP.

I. The medicine and what it is used for

Glubrava is authorized for the second line treatment of adult type II diabetes mellitus patients, particularly overweight patients, who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone.

Further information about the evaluation of pioglitazone and Glubrava's benefits can be found in the relevant EPARs, 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/glubrava

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

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

II.A List of important risks and missing information

Important risks of Glubrava 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 Glubrava. 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	Pioglitazone None Metformin Lactic acidosis
Important potential risks	None
Missing information	None

II.B Summary of important risks

Important identified risk: Lactic acidosis	
Evidence for linking the risk to the medicine	Increase of lactic acid in the blood is a rare but serious reaction which may occur in less than 1 case per 10,000 patients. The reported mortality is high (42% to 50% of patients). Reported cases of lactic acidosis in patients on metformin have occurred mainly in diabetic patients with significant kidney disease.
Risk factors and risk groups	Patients with acute alcohol intoxication, liver problems, severe kidney problems, and the use of iodinated contrast agents (these are used for some X-ray procedures), sepsis and dehydration.
Risk minimisation measures	**Routine risk minimisation measures** SmPC section 4.8 and PL section 4 SmPC section 4.2, 4.3 and PL section 2 and 3 prohibiting use in patients with acute metabolic acidosis, diabetic pre-coma, or severe renal failure.; Recommended monitoring of renal function and recommended dosing in elderly and patients with renal impairment. SmPC 4.4 & PL section 2 include special warnings and

	precautions before initiating use in patients with risk factors for renal impairment; monitoring specific signs/symptoms of acute worsening of renal function and increased risk for lactic acidosis and recommended discontinuation of Glubrava in specific clinical situations. **Additional risk minimisation measures** Not applicable
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 authorization or specific obligation of Glubrava.

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

There are no studies required for Glubrava.