Part VI: Summary of the risk management plan

Summary of risk management plan for DALTEX (vildagliptin and metformin hydrochloride)

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

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

I. The medicine and what it is used for

Daltex is authorised for type II diabetes mellitus (see SmPC for the full indication). It contains vildagliptin and metformin hydrochloride as the active substance and it is given by mouth (orally).

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

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

II.A List of important risks and missing information

Important risks of Daltex 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 Daltex. 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	Transaminase elevations and drug induced liver injury (DILI) Lactic acidosis
Important potential risks	None
Missing information	None

II.B Summary of important risks

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

Important identified risk: Transaminase elevations and drug induced liver injury (DILI)	
Evidence for linking the risk to the medicine	Abnormal liver function including a special type of liver abnormality called hepatitis is rare in treatment with vildagliptin, treated patients and may affect between 1 in 10,000 up to 1 in 1,000 people.
Risk factors and risk groups	In patients with abnormal liver function.
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.2, 4.3, 4.4, 4.5 and 4.8 and in PL sections 2 and 4. • Section 4.4 of the SmPC contains the recommendation to monitor liver functions and in PL section 2 a warning that a test to determine the liver function to be performed before the start treatment. • Legal status: medical prescription.

Important identified risk: Lactic acidosis	
Evidence for linking the risk to the medicine	A review of metformin containing medicines, under Article 31 of Directive 2001/83/EC, was carried out by the CHMP. The referral evaluated the recommendations regarding their use in patients with renal impairment and precautions regarding lactic acidosis.
Risk factors and risk groups	Lactic acidosis seems to occur more frequently with higher exposure, however other conditions (e.g., severe infection, respiratory disease, liver disease) increase the risk of lactic acidosis.

	Other important risk factors for renal impairment and lactic acidosis include diarrhea, vomiting and dehydration, alcohol, iodinated contrast media, other medicinal products.
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.2, 4.3, 4.4, 4.5 and 4.8. • SmPC sections 4.2 and 4.4 where advice to review factors that may increase the risk of lactic acidosis. • PL sections 2 and 4. • Legal status: medical prescription.

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 Daltex.

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

There are no studies required for Daltex.