Mounjaro®

(tirzepatide)

2.5 mg / 5 mg / 7.5 mg / 10 mg / 12.5 mg / 15 mg,

solution for injection

Summary of Risk Management Plan (RMP)

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Based on EU-RMP Version 0.1

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 minimize them.

The RMP summary of Mounjaro 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 Mounjaro in Switzerland is the „Arzneimittelinformation/ Information sur le médicament“ (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.

Eli Lilly is fully responsible for the accuracy and correctness of the content of this published summary RMP of Mounjaro.

I - The Medicine and What It Is Used for

Mounjaro is authorised for T2DM (see SmPC for the full indication). It contains tirzepatide as the active substance and it is given by injection.

Further information about the evaluation of Mounjaro's benefits can be found in Mounjaro'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 Mounjaro, together with measures to minimise such risks and the proposed studies for learning more about Mounjaro'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, and
- 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 periodic safety update report 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 Mounjaro is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Mounjaro are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered.

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 Mounjaro. 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	None
Important Potential Risks	Thyroid C-cell tumours Pancreatic malignancy
Missing Information	None

II.B Summary of Important Risks

Important potential risk: Thyroid C-cell tumours	
Evidence for linking the risk to the medicine	The only evidence for this potential risk comes from rodents with near-lifetime exposure. This effect on rodent thyroids has been observed consistently with other long-acting GLP-1 RAs, including liraglutide, exenatide once weekly, dulaglutide, and semaglutide, in near-lifetime exposure carcinogenicity studies. The relevance to humans cannot be determined from clinical and nonclinical studies. At this time, there is insufficient evidence to attribute thyroid C-cell disease to tirzepatide. Given the latency for cancer, the database for tirzepatide is of insufficient size and exposure duration to assess definitively for any particular type of cancer. Nonclinical data suggest that there is a risk for thyroid C-cell tumours, and this has been determined to be a key safety finding from the nonclinical development programme.
Risk factors and risk groups	Medullary thyroid carcinoma develops from the C (parafollicular) cells and accounts for 5% to 10% of all thyroid cancers (Brady 2018), and up to 25% of MTC cases develop under multiple endocrine neoplasia-2A (IARC 2018). Compared to the general population (6.6%), patients with diabetes have a higher prevalence of thyroid disorders (10.8%) (Shih et al. 2012). However, the link between T2DM and thyroid cancer is arguable. Some studies did not show an association between diabetes, including T2DM and thyroid cancer risk (Kitahara et al. 2012; Shih et al. 2012; Seo et al. 2017). Other studies showed that patients with diabetes are 20% to 34% more likely to develop thyroid cancer compared to those without diabetes (Yeo et al. 2014; Li and Qian 2017).
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC Section 5.3 **Additional risk minimisation measures:** • None

Summary of Important Risks

Important potential risk: Pancreatic malignancy	
Evidence for linking the risk to the medicine	There is no evidence from clinical trials that GLP-1-based therapies increase the risk of pancreatic cancer. Some reports indicate a causal association with these agents, while others have failed to show such an association. A joint FDA and EMA publication states that, data demonstrate conflicting opinions about the strength of the association (Egan et al. 2014).
Risk factors and risk groups	Patients with long-standing T2DM are twice more likely to have pancreatic cancer than patients without T2DM (Yadav and Lowenfels 2013). About 0.5% of patients newly diagnosed with T2DM develop pancreatic cancer within 6 years of follow-up. Being the fourth leading cause of cancer mortality, pancreatic cancer is a highly mortal malignancy, with 75% of patients dying within the first year of diagnosis (Bracci 2012). The 5-year survival rate among patients with pancreatic malignancy is about 6% (Yadav and Lowenfels 2013).
Risk minimisation measures	**Routine risk minimisation measures:** • None **Additional risk minimisation measures:** • None

Abbreviations: EMA = European Medicines Agency; FDA = US Food and Drug Administration; GLP-1 = glucagon-like peptide 1; MTC: medullary thyroid cancer; RA = receptor agonist; SmPC = summary of product characteristics; T2DM = type 2 diabetes mellitus.

II.C Post-Authorisation Development Plan

II.C.1 Studies that are Conditions of the Marketing Authorisation

There are no studies that are conditions of the marketing authorisation or specific obligation of Mounjaro.

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

There are no studies required for Mounjaro post-authorisation.