

## **Part VI: Summary of the Risk Management Plan**

### **Summary of Risk Management Plan for Trulicity (Dulaglutide)**

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

Trulicity's SmPC and its package leaflet give essential information to health care professionals and patients on how Trulicity should be used.

This summary of the RMP for Trulicity should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of which are part of the EPAR.

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

#### **I - The Medicine and What It is Used for**

Trulicity is authorised for the treatment of patients aged 10 years and older with T2DM (see SmPC for the full indication). It contains dulaglutide as the active substance and it is given by injection.

Further information about the evaluation of Trulicity's benefits can be found in Trulicity'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/trulicity#overview-section>

#### **II - Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks**

Important risks of Trulicity, together with measures to minimise such risks and the proposed studies for learning more about Trulicity'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. Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions, including PSUR assessment, is collected continuously and analysed regularly 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 Trulicity is not yet available, it is listed under 'missing information' below.

## **II.A List of Important Risks and Missing Information**

Important risks of Trulicity 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 Trulicity. 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.

<b>List of Important Risks and Missing Information</b>	
<b>Important Identified Risks</b>	None
<b>Important Potential Risks</b>	Thyroid C-cell tumours Pancreatic malignancy
<b>Missing Information</b>	None

## II.B Summary of Important Risks

### 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 (rats only in the case of dulaglutide) with near lifetime exposure. This effect on rodent thyroids has been observed consistently with other long-acting GLP-1 RAs like dulaglutide. 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 dulaglutide. As cancer can take many years to develop, the database for dulaglutide is of insufficient size and exposure duration to assess the relevance of these findings in rats to dulaglutide use in patients with T2DM.
Risk factors and risk groups	Compared to the general population, patients with diabetes have a higher prevalence of thyroid disorders (6.6% vs 10.8%). 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, while other studies showed that patients with diabetes are 20% to 34% more likely to develop thyroid cancer than those without diabetes. As a result, no specific risk factors in relation to dulaglutide use have been identified.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 5.3  Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: <ul style="list-style-type: none"><li>• H9X-MC-B001: Medullary Thyroid Carcinoma (MTC) Surveillance Study</li><li>• H9X-MC-B013: Dulaglutide Retrospective Study</li></ul> See Section II.C of this summary for an overview of the post-authorisation development plan.

<b>Important Potential Risk: Pancreatic malignancy</b>	
Evidence for linking the risk to the medicine	There has been some concern that GLP-1 RA–mediated insulin secretion could promote tumour formation, including pancreatic malignancies. 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. To date, no causal relationship between dulaglutide and pancreatic malignancy has been established. From the clinical trial programme for dulaglutide, only a few cases of pancreatic malignancy were reported, even with extended exposure (up to 7 years).
Risk factors and risk groups	Except for the excess risk of pancreatic malignancy and pancreatitis associated with T2DM, no risk factors specific to dulaglutide treatment have been identified.
Risk minimisation measures	Routine risk minimisation measures: Not applicable  Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: <ul style="list-style-type: none"> <li>• H9X-MC-B013: Dulaglutide Retrospective Study</li> </ul> See Section II.C of this summary for an overview of the post-authorisation development plan.

Abbreviations: EMA = European Medicines Agency; FDA = US Food and Drug Administration; GLP-1 = glucagon-like peptide-1; RA = receptor agonist; RMP = risk management plan; 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 dulaglutide.

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

**Study short name:** Medullary Thyroid Carcinoma (MTC) Surveillance Study (H9X-MC-B001)

**Purpose of the study:** This is a prospective registry conducted through state cancer registries to determine the annual incidence of MTC in the US and to identify any possible increase related to the introduction of long-acting GLP-1 RAs, including dulaglutide, into the US market. This study addresses the important potential risk of MTC observed in rodents across all GLP-1 agonists.

**Study short name:** Dulaglutide Retrospective Study (H9X-MC-B013)

**Purpose of the study:** This study will estimate the incidence rates of events of interest among patients with T2DM treated with dulaglutide compared to other second-line anti-diabetes medications and long-acting GLP-1 RAs compared to other second-line anti-diabetes medications. It will address the safety concerns of pancreatic and thyroid cancers.