# RMP Summary

# Ozempic®

*(semaglutide)*

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**Disclaimer**

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 minimise them.

The RMP summary of Ozempict® 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 Ozempic® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Novo Nordisk Pharma AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Ozempic®.

**Summary of the risk management plan for Ozempic® (semaglutide s.c. for T2D)**

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

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

This summary of the RMP for Ozempic 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 EPAR.

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

## I. The medicine and what it is used for

Ozempic is authorised for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise (see SmPC for the full indication). It contains semaglutide as the active substance and it is injected by subcutaneous route.

Further information about the evaluation of Ozempic's benefits can be found in Ozempic's EPAR, including in its plain-language summary,available on the EMA website, under the medicine's webpage: EPAR link.

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

Important risks of Ozempic, together with measures to minimise such risks and the proposed studies for learning more about Ozempic'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 public (e.g., with or without prescription) can help to minimises its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse events is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

## II.A List of important risks and missing information

Important risks of Ozempic 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 Ozempic. 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 1 List of important risks and missing information**

| **List of important risks and missing information** | |
|---|---|
| Important identified risks | • Diabetic retinopathy complications |
| Important potential risks | • Pancreatic cancer<br>• Medullary thyroid cancer |
| Missing information | • Pregnancy and lactation<br>• Patients with severe hepatic impairment |

## II.B Summary of important risks

**Table 2 Diabetic retinopathy complications**

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| Evidence for linking the risk to the medicine | The risk of diabetic retinopathy complications was identified based on findings in the cardiovascular outcomes trial (CVOT; SUSTAIN 6), where a total of 3,297 subjects with T2D and high cardiovascular risk were included. In the CVOT (SUSTAIN 6), subjects with known proliferative retinopathy or maculopathy requiring acute treatment were not excluded. |
| Risk factors and risk groups | Patient risk factors include increasing age, long duration of diabetes, poor glycaemic control, prior history of diabetic retinopathy and rapid decline in $HbA_{1c}$. |
| Risk minimisation measures | *Routine risk minimisation measures:*<br>SmPC Sections 4.4 and 4.8and PL Sections 2 and 4.<br><br>*Additional risk minimisation measures:*<br>None |
| Additional pharmacovigilance activities | Additional pharmacovigilance activities:<br>*Study NN9535-4352 (Long-term effects of semaglutide on diabetic retinopathy in subjects with T2D [FOCUS])*<br><br>See Section II.C of this summary for an overview of the post-authorisation development plan. |

**Abbreviations:** CVOT = cardiovascular outcomes trial; PL = package leaflet; SmPC = Summary of Product Characteristics; T2D = type 2 diabetes mellitus.

**Table 3 Pancreatic cancer**

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|---|---|
| Evidence for linking the risk to the medicine | Patients with T2D, as well as patients being overweight or with obesity, have an increased risk of certain types of cancer such as pancreatic cancer. There is no evidence from clinical trials, that GLP-1-based therapies increase the risk of pancreatic cancer. However, pancreatic cancer is included as an important potential risk, based on the EC regulation 726/2004 Article 5(3) referral procedure in 2013 (EMEA/H/A-5(3)/1369). |
| Risk factors and risk groups | Patient risk factors for neoplasms include diabetes, chronic pancreatitis, obesity, physical inactivity, advanced age, smoking, alcohol abuse, environmental factors, history of neoplasms and family history of pancreatic cancer and other genetic predispositions. |
| Risk minimisation measures | No risk minimisation measures |
| Additional pharmacovigilance activities | Additional pharmacovigilance activities:<br>*Study NN9535-4447 (Epidemiological assessment of the risk for pancreatic cancer associated with the use of semaglutide in patients with T2D)*<br><br>See Section II.C of this summary for an overview of the post-authorisation development plan. |

**Abbreviations:** GLP-1 = glucagon-like peptide-1; T2D = type 2 diabetes mellitus

**Table 4 Medullary thyroid cancer**

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| Evidence for linking the risk to the medicine | This potential class risk is based on findings in mice and rats for all currently approved long–acting GLP-1 RAs. Data from the monitoring of calcitonin (a marker for MTC) in plasma in the semaglutide s.c. and oral semaglutide clinical development programmes did not support a semaglutide effect on calcitonin in humans. |
| Risk factors and risk groups | Patient risk factors for MTC include previous family history or personal medical history of multiple endocrine neoplasia 2 (MEN2), a group of medical disorders associated with tumours of the endocrine system. |
| Risk minimisation measures | *Routine risk minimisation measures:*<br>SmPC Section 5.3.<br><br>*Additional risk minimisation measures:*<br>None |
| Additional pharmacovigilance activities | Additional pharmacovigilance activities:<br>*Study MTC-22341 (Medullary Thyroid Carcinoma Surveillance Study: a Case-Series Registry)*<br><br>See Section II.C of this summary for an overview of the post-authorisation development plan. |

**Abbreviations:** MEN2 = multiple endocrine neoplasia 2; MTC = medullary thyroid cancer; s.c. = subcutaneous(-ly); SmPC = Summary of Product Characteristics.

**Table 5 Pregnancy and lactation**

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| Risk minimisation measures | *Routine risk minimisation measures:*<br>SmPC Section 4.6 and PL Section 2.<br><br>*Additional risk minimisation measures:*<br>None |

**Abbreviations:** PL = package leaflet; SmPC = Summary of Product Characteristics.

**Table 6 Patients with severe hepatic impairment**

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| Risk minimisation measures | *Routine risk minimisation measures:*<br>SmPC Sections 4.2 and 5.2.<br><br>*Additional risk minimisation measures:*<br>None |

**Abbreviations:** SmPC = Summary of Product Characteristics.

## 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 Ozempic.

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

**NN9535-4352 (FOCUS)**

Purpose of the study: The aim of this randomised clinical trial is to establish the long-term effects of semaglutide on diabetic retinopathy in subjects with type 2 diabetes mellitus (T2D) using validated and standardised ophthalmic assessments.

**NN9535-4447**

Purpose of the study: The aim of this study is to evaluate whether exposure to semaglutide increases the risk of pancreatic cancer in patients with T2D.

**MTC-22341**

Purpose of the study: This active surveillance programme for MTC has been established to evaluate further a potential association between treatment with long-acting GLP-1 RAs and the occurrence of MTC in humans. The MTC registry is an FDA post-marketing requirement for long-acting GLP-1 RA products.