

Summary of risk management plan (RMP) for Wegovy® (semaglutide 2.4 mg)

RMP Version 5.0

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The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine but also in connection with larger changes such as extension of the indication. 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 Wegovy® 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 / Informazione sul medicamento“, 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 Wegovy® in Switzerland is the „Arzneimittelinformation / Information sur le médicament / Informazione sul medicamento“ (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.

Novo Nordisk Pharma AG is fully responsible for the accuracy and correctness of the content of the here published summary RMP of Wegovy®.

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Summary of risk management plan for Wegovy® (semaglutide s.c. 2.4 mg for weight management)

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

Wegovy®'s Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Wegovy® should be used.

This summary of the RMP for Wegovy® 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 is part of the EPAR.

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

I. The medicine and what it is used for

Wegovy® is used for weight loss and weight maintenance in addition to diet and physical activity in adults who have:

- a BMI of 30 kg/m² or greater (with obesity) or
- a BMI of 27 kg/m² and less than 30 kg/m² (overweight) and weight-related health problems.

BMI (body mass index) is a measure of your weight in relation to your height. It contains semaglutide as the active substance and it is injected through subcutaneous route.

Further information about the evaluation of Wegovy®'s benefits can be found in Wegovy®'s EPAR, including 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 Wegovy[®], together with measures to minimise such risks and the proposed studies for learning more about Wegovy[®]'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 minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse events is collected continuously and analysed regularly, including the 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 Wegovy[®] 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 Wegovy[®]. 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).

Tabel 2-1 List of important risks and missing information	
Important identified risks	<ul style="list-style-type: none"> • Diabetic retinopathy complications (only for patients with T2D)
Important potential risks	<ul style="list-style-type: none"> • Pancreatic cancer • Medullary thyroid cancer • Neoplasms (malignant and non-malignant)
Missing information	<ul style="list-style-type: none"> • Pregnancy and lactation • Patients with severe hepatic impairment

Abbreviations: T2D = type 2 diabetes mellitus.

II.B Summary of important risks

Table 2-2 Diabetic retinopathy complications only for patients with T2D)	
Evidence for linking the risk to the medicine	The risk is included for semaglutide s.c. 2.4 mg for weight management in patients with T2D based on the findings in the semaglutide s.c. for T2D (Ozempic) clinical development programme. In STEP 2 trial, few diabetic retinopathy events were reported, but with higher rates and proportions with semaglutide 2.4 mg than with placebo.
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 HbA1c.
Risk minimisation measures	<p><i>Routine risk minimisation measures:</i> SmPC Sections 4.4 and 4.8 and PL Sections 2 and 4.</p> <p><i>Additional risk minimisation measures:</i> None</p>
Additional pharmacovigilance activities	<p><i>Additional pharmacovigilance activities:</i> Study NN9535-4352 (Long-term effects of semaglutide on diabetic retinopathy in subjects with T2D [FOCUS]) will also be relevant for the ongoing evaluation of the risk for semaglutide s.c. 2.4 mg for weight management in patients with T2D. See Section II.C of this summary for an overview of the post-authorisation development plan.</p>

Abbreviations: CVOT = cardiovascular outcomes trial; PL = package leaflet; s.c. = subcutaneous(-ly); SmPC = Summary of Product Characteristics; T2D = type 2 diabetes mellitus.

Table 2-3 Pancreatic cancer	
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 (EMA/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	<i>Additional pharmacovigilance activities:</i> <i>Study NN9535-4447 (Epidemiological assessment of the risk for pancreatic cancer associated with the use of Ozempic/Rybelsus (semaglutide s.c./oral semaglutide) in patients with T2DM)</i> will also be relevant for the ongoing evaluation of the risk for semaglutide s.c. 2.4 mg for weight management. See Section II.C of this summary for an overview of the post-authorisation development plan.

Abbreviations: GLP-1 = glucagon-like peptide-1; s.c. = subcutaneous(-ly); T2DM = type 2 diabetes mellitus.

Table 2-4 Medullary thyroid cancer	
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	<i>Routine risk minimisation measures:</i> SmPC Section 5.3. <i>Additional risk minimisation measures:</i> None
Additional pharmacovigilance activities	<i>Additional pharmacovigilance activities:</i> <i>Study MTC-22341 (Medullary Thyroid Carcinoma Surveillance Study: a Case-Series Registry)</i> 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 2-5 Neoplasms (malignant and non-malignant)	
Evidence for linking the risk to the medicine	Patients being overweight or with obesity as well as patients with T2D have an increased risk of certain types of cancer. There is no evidence from clinical trials that GLP-1-based therapies increase the risk of neoplasms. No imbalance was observed in the semaglutide s.c. 2.4 mg for weight management phase 3a trials with regard to the proportions of subjects with neoplasms (malignant and non-malignant). However, in the semaglutide s.c. for T2D (Ozempic) as well as oral semaglutide for T2D (Rybelsus) phase 3a trials, the proportion of subjects with neoplasms (malignant and non-malignant) was slightly higher with semaglutide than with comparator. The number of subjects exposed to semaglutide in a clinical trial setting for a longer period was considered insufficient for a thorough assessment of the risk of neoplasms, and therefore the risk is included in the RMP.
Risk factors and risk groups	Patient risk factors for neoplasm include T2DM, obesity, smoking, alcohol abuse, environmental factors, a history of neoplasm and genetic predisposition.

Risk minimisation measures	<p><i>Routine risk minimisation measures:</i> None.</p> <p><i>Additional risk minimisation measures:</i> None</p>
Additional pharmacovigilance activities	<p>Additional pharmacovigilance activities:</p> <p>Serious adverse event reporting pertaining to neoplasms from clinical trial EX9536-4388. See Section 6.3.2.3 of this summary for an overview of the post-authorisation development plan.</p>

Abbreviations: GLP-1 = glucagon-like peptide-1; s.c. = subcutaneous(-ly); T2D = type 2 diabetes mellitus; RMP = risk management plan.

Table 2-6 Pregnancy and lactation	
Risk minimisation measures	<p><i>Routine risk minimisation measures:</i> SmPC Section 4.6 and PL Section 2.</p> <p><i>Additional risk minimisation measures:</i> None</p>

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

Table 2-7 Patients with severe hepatic impairment	
Risk minimisation measures	<p><i>Routine risk minimisation measures:</i> SmPC Sections 4.2 and 5.2.</p> <p><i>Additional risk minimisation measures:</i> None</p>

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 Wegovy.

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

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.

The important potential risk Neoplasms (malignant and non-malignant) will be monitored through routine serious adverse event reporting in the following study:

EX9536-4388: SELECT – Semaglutide cardiovascular outcomes trial in patients who are overweight or with obesity.