Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Ozempic 2 mg solution for injection in pre-filled pen

semaglutide

PLGB 04668/0435

Novo Nordisk A/S

LAY SUMMARY

Ozempic 2 mg solution for injection in pre-filled pen
semaglutide

This is a summary of the Public Assessment Report (PAR) for Ozempic 2 mg solution for injection in pre-filled pen. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Ozempic in this lay summary for ease of reading.

For practical information about using Ozempic, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Ozempic and what is it used for?
This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 11 January 2022 (EMEA/H/C/004174/X/0021), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

Ozempic is used:

- on its own – if the blood sugar is not controlled well enough by diet and exercise alone, and the patient cannot use metformin (another diabetes medicine) or
- with other medicines for diabetes – when they are not enough to control the patient's blood sugar levels. These other medicines may include: oral antidiabetics (such as metformin, thiazolidinediones, sulfonylureas, sodium-glucose cotransporter 2 (SGLT2) inhibitor) or insulin.

It is important that the patient continues with their diet and exercise plan as told to them by their doctor, pharmacist or nurse.

How does Ozempic work?
Ozempic contains the active substance semaglutide. It helps to reduce the blood sugar level, but only when blood sugar is too high it can also help prevent heart disease.

How is Ozempic used?
The pharmaceutical form of this medicine is a solution for injection in a pre-filled pen and the route of administration is injection under the skin (subcutaneous injection).

Recommended dose
The starting dose is 0.25 mg once a week for four weeks. After four weeks your doctor will increase your dose to 0.5 mg once a week.

The patient's doctor may increase your dose to 1 mg once a week if your blood sugar is not controlled well enough with a dose of 0.5 mg once a week.

The doctor may increase their patient's dose to 2 mg once a week, if their blood sugar is not controlled well enough with a dose of 1 mg once a week.

The patient should not change how much of this medicine they take unless their doctor has told them to

For further information on how Ozempic is used, refer to the PIL and Summary/Summaries of Product Characteristics (SmPC/SmPCs) available on the Medicines and Healthcare product Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning their medicine.

What benefits of Ozempic have been shown in studies?
Ozempic is a line extension of the existing products Ozempic 0.25/0.5/1 mg. The data submitted previously for Ozempic 0.25/0.5/1 mg and the new studies that included Bioequivalence, PK studies are sufficient to demonstrate that Ozempic shows a benefit in the indications listed.

What are the possible side effects of Ozempic?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Why was Ozempic approved?
MHRA decided that the benefits are greater than the risks and recommended that this medicine/these medicines can be approved for use.

What measures are being taken to ensure the safe and effective use of Ozempic?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Ozempic. The RMP details the important risks of Ozempic, how these risks can be minimised, any uncertainties about Ozempic (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Ozempic:

Summary of safety concerns	
Important identified risks	• Diabetic retinopathy complications
Important potential risks	• Pancreatic cancer • Medullary thyroid cancer
Missing information	• Pregnancy and lactation • Patients with severe hepatic impairment

Abbreviations: s.c. = subcutaneous(-ly); T2D = type 2 diabetes mellitus.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Ozempic are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

A ~~(~~RMP~~)~~ and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Ozempic
A marketing authorisation was granted in Great Britain on 18 July 2022.

The full PAR for Ozempic follows this summary.

This summary was last updated in September 2022.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare product Regulatory Agency (MHRA) considered that the application for Ozempic 2 mg solution for injection in pre-filled pen (PLGB 04668/0435) could be approved.

The product is approved for the following indications:
Ozempic is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise

- as monotherapy when metformin is considered inappropriate due to intolerance or contraindications
- in addition to other medicinal product for the treatment of diabetes.

Semaglutide is a GLP-1 analogue with 94% sequence homology to human GLP-1. Semaglutide acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1.

GLP-1 is a physiological hormone that has multiple actions in glucose and appetite regulation, and in the cardiovascular system. The glucose and appetite effects are specifically mediated via GLP-1 receptors in the pancreas and the brain.

Semaglutide reduces blood glucose in a glucose dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. The mechanism of blood glucose lowering also involves a minor delay in gastric emptying in the early postprandial phase. During hypoglycaemia, semaglutide diminishes insulin secretion and does not impair glucagon secretion.

Semaglutide reduces body weight and body fat mass through lowered energy intake, involving an overall reduced appetite. In addition, semaglutide reduces the preference for high fat foods.

GLP-1 receptors are also expressed in the heart, vasculature, immune system and kidneys. Semaglutide had a beneficial effect on plasma lipids, lowered systolic blood pressure and reduced inflammation in clinical studies. In animal studies, semaglutide attenuates the development of atherosclerosis by preventing aortic plaque progression and reducing inflammation in the plaque.

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 11 January 2022 (EMEA/H/C/004174/X/0021), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was approved under Regulation 50A of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A marketing authorisation was granted on 18 July 2022.

II. PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

PATIENT INFORMATION LEAFLET

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a marketing authorisation is recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation is recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation is recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, the following additional pharmacovigilance measures have been proposed:

Table 6-8 Diabetic retinopathy complications

Evidence for linking the risk to the medicine	The risk is included as an identified risk for oral semaglutide based on findings in the semaglutide s.c. clinical development programme. Based on the totality of data on diabetic retinopathy collected across the oral semaglutide phase 3a trials, there was no increased risk of diabetic retinopathy with oral semaglutide.
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:* SmPC Sections 4.4 and 4.8 and PL Sections 2 and 4. *Additional risk minimisation measures:* None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Results from the study NN9535-4352 (*Long-term effects of semaglutide on diabetic retinopathy in subjects with T2D [FOCUS]*) for semaglutide s.c. will also be relevant for the ongoing evaluation of the risk for oral semaglutide.

Abbreviations: CVOT = cardiovascular outcomes trial; MedDRA = Medical Dictionary for Regulatory Activities; PL = package leaflet; SmPC = Summary of Product Characteristics; T2D = type 2 diabetes mellitus.

Table 6-9 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 (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:* *Study NN9535-4447 (Epidemiological assessment of the risk for pancreatic cancer associated with the use of semaglutide in patients with T2D)*

Abbreviations: GLP-1 = glucagon-like peptide-1; s.c. = subcutaneous; T2D = type 2 diabetes mellitus.

Table 6-10 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	*Routine risk minimisation measures:* SmPC Section 5.3. *Additional risk minimisation measures:* None
Additional pharmacovigilance activities	*Additional pharmacovigilance activities:* *Study MTC-22341 (Medullary Thyroid Carcinoma Surveillance Study: a Case-Series Registry)* See Section 6.2.2.3 of this summary for an overview of the post-authorisation development plan.

Abbreviations: MEN2 = multiple endocrine neoplasia 2; MTC = medullary thyroid cancer; SmPC = Summary of Product Characteristics.

Table 6-11 Pregnancy and lactation

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

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

Table 6-12 Patients with severe hepatic impairment

Risk minimisation measures	*Routine risk minimisation measures:* SmPC Sections 4.2 and 5.2. *Additional risk minimisation measures:* None

Abbreviations: SmPC = Summary of Product Characteristics.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation with target patient groups, in accordance with legal requirements, on the basis of a bridging report making reference to Ozempic 0.25/0.5/1 mg. (PL 04668/0331-0332-0333; Novo Nordisk A/S). The bridging report submitted by the MAH is acceptable.

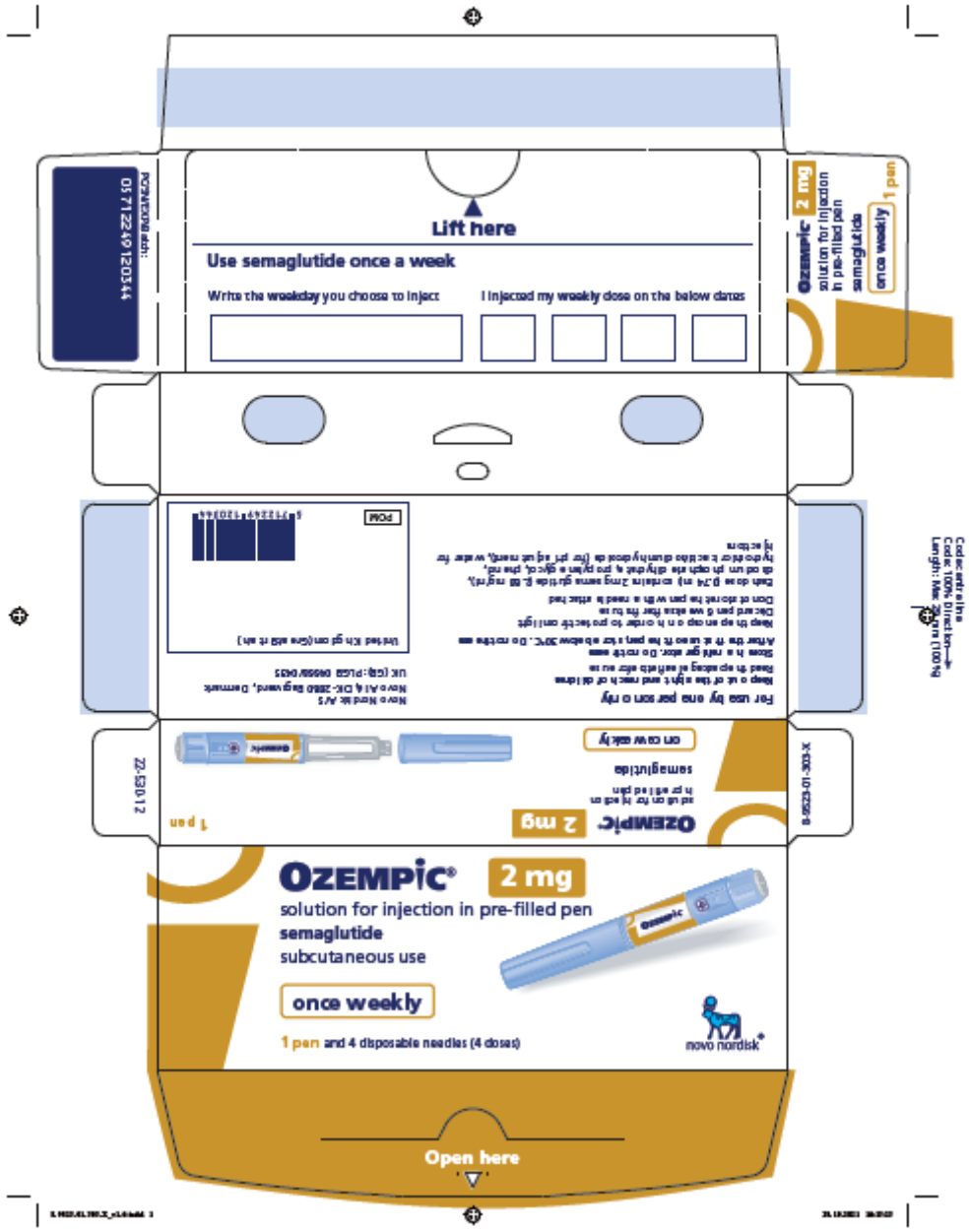
VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

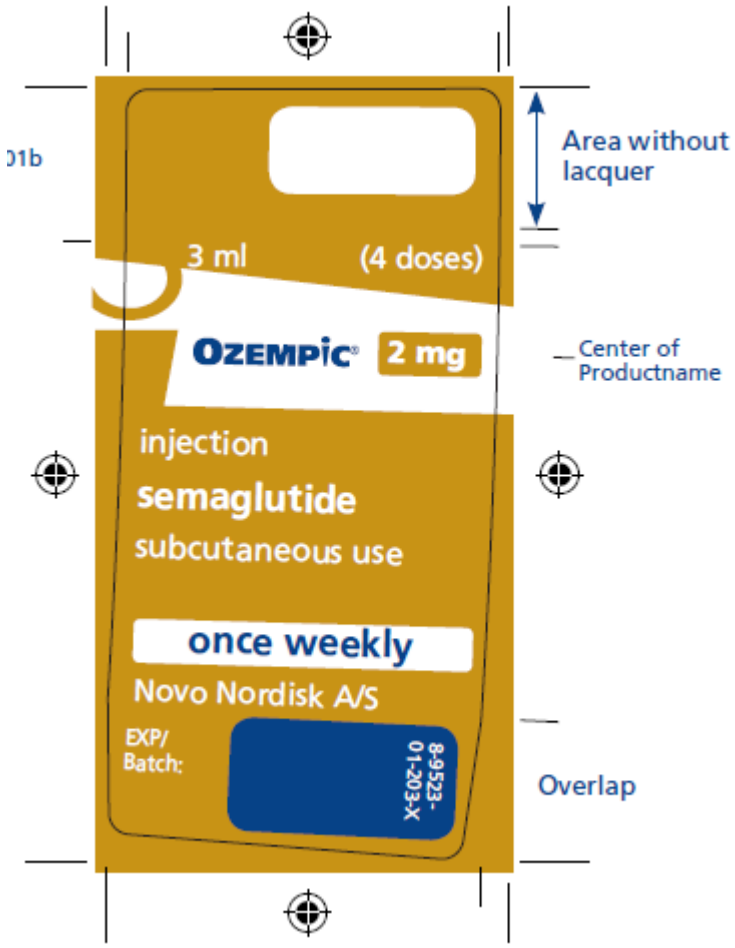
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for this product are available on the MHRA website.

Representative copies of the labels at the time of UK licensing are provided below.




01b
3 ml
(4 doses)
OZEMPIC
2 mg
injection
semaglutide
subcutaneous use
once weekly
Novo Nordisk A/S
EXP/
Batch:
8-9523-01-203-X
Area without lacquer
Center of Productname
Overlap

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**

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