IMPORTANT MEDICINE INFORMATION

SECTION 36 APPROVAL – OZEMPIC® Solution for Injection 1.34 mg (1.5 ml pen) Reg. No.: 53/21.13/0497

02 December 2024

Dear Healthcare Professional

Novo Nordisk (Pty) Ltd, as directed by the South African Health Products Regulatory Authority (SAHPRA), wishes to inform you that it has obtained a section 36 exemption to distribute a designated batch of Ozempic 0.25 mg and 0.5 mg/dose pen (1.5 ml pen) registered for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise. This exemption is due to the omission on our English Professional Information (PI) of the recently approved side effect of Angioedema with an unknown frequency from post-marketing reports, which falls under the MedRA system organ class "skin and subcutaneous tissue disorder". It is important to note that the product consists of two leaflets - one in Afrikaans and one in English. While the additional Afrikaans leaflet was updated in a timely manner, the English version was impacted. The approved section 36 exemption allows for the distribution of Ozempic 0.25 mg and 0.5 mg/dose pen with a previous version of the English PI, which excludes the recently approved Angioedema side effect, with **Batch number:** PP5M559, **Expiry date:** 02/2027.

Summary

Ozempic is a Glucagon-like peptide-1 indicated

a) 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.
   - as combination therapy with oral anti-diabetic medicines (metformin, thiazoledinediones, sulphonylurea), basal insulin with or without metformin and pre-mix insulin.

b) to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

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Table 1: Noticeable labelling difference between the previous version PI and the latest approved PI:

<table>
<tr><th>SAHPRA PI heading</th><th>Previous version of the PI</th><th>Current approved details</th></tr>
<tr><td>4.8 Undesirable effects</td><td>This AE was previously not included.</td><td>Side effects from controlled phase 3a trials
<table>
<tr><th colspan="2">Skin and subcutaneous tissue disorders</th></tr>
<tr><td>Unknown</td><td>Angioedema[d]</td></tr>
</table>
[d)]From post-marketing reports.</td></tr>
</table>

Advice to healthcare professional

1. Healthcare professionals are alerted to note the difference in artwork between the previous approved PI version and the current approved PI in table 1.
2. Healthcare professionals are urged to report adverse drug reactions (ADRs), or product quality issues (including batch details) related to Ozempic 0,25 mg and 0,5 mg/dose pen to Novo Nordisk (Pty) Ltd via email: za-acandcc@novonordisk.com or call +2783 379 2104. Alternatively, healthcare professionals may complete the ADR reporting form accessible via the SAHPRA website and email it to adr@sahpra.org.za.
3. Healthcare professionals may also use eReporting link available on SAHPRA website (www.sahpra.org.za). Additionally, reporting can be done via Med Safety App. The Application can be downloaded onto a smart phone via Google play or App store. For more information on ADR reporting of products, please contact the SAHPRA vigilance unit at pvqueries@sahpra.org.za.
4. Healthcare professionals may email medical queries to MedInfo South Africa: infoza@novonordisk.com .
5. Healthcare professionals are advised to refer to the PI/PIL from the SAHPRA repository for the latest approved professional information, which can be found at this link: https://pi-pil-repository.sahpra.org.za/.

For additional information or any enquiries, please contact:
Novo Nordisk customer contact service: +27 10 500 8699

Yours Sincerely,

Euganthri Pillay

Responsible Pharmacist

Ozempic® abbreviated PI
Scheduling status: S4
Name of the medicine: OZEMPIC®
Qualitative and quantitative composition: Semaglutide 1, 34 mg/ml
Therapeutic indication: Ozempic® is indicated:

a) 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.
- as combination therapy with oral anti-diabetic medicines (metformin, thiazoledinediones, sulphonylurea), basal insulin with or without metformin and pre-mix insulin.

b) to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Posology and method of administration: Ozempic® starting dose is 0,25 mg once weekly. After 4 weeks, the dose should be increased to 0,5 mg once weekly. After at least 4 weeks with a dose of 0,5 mg once weekly, the dose can be increased to 1 mg once weekly to further improve glycaemic control. Ozempic® is to be administered once weekly at any time of the day, with or without meals. Ozempic® is to be injected subcutaneously in the abdomen, in the thigh or in the upper arm. The injection site can be changed without dose adjustment. Ozempic® should not be administered intravenously or intramuscularly. The day of weekly administration can be changed if necessary as long as the time between two doses is at least 2 days (>48 hours). When Ozempic® is added to existing sodium-glucose cotransporter 2 (SGLT2) inhibitor therapy, the current dose of SGLT2 inhibitor can be continued unchanged.
Contraindications: Hypersensitivity to semaglutide or to any of the excipients, a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2), pregnancy and lactation.
Special warnings and precautions for use: Ozempic® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Ozempic® is not a substitute for insulin. Acute pancreatitis has been observed with the use of Ozempic®. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, Ozempic® should be discontinued; if confirmed, Ozempic® should not be restarted. Patients treated with Ozempic® in combination with a sulfonylurea or insulin may have an increased risk of hypoglycaemia. The risk of hypoglycaemia can be lowered by reducing the dose of sulfonylurea or insulin when initiating treatment with Ozempic®. Risk of Thyroid C-cell Tumours: Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist have been reported in the post marketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.
Interaction with other medicines and other forms of interaction: In vitro studies have shown very low potential for Ozempic® to inhibit or induce CYP enzymes and to inhibit drug transporters. The delay of gastric emptying with Ozempic® may influence the absorption of concomitantly administered oral medicines. The potential effect of Ozempic® on the absorption of co-administered oral medicines was studied in trials at Ozempic® 1 mg steady state exposure.
Fertility, pregnancy and lactation: Ozempic® is contraindicated during pregnancy and lactation. Undesirable effects: The most frequently reported adverse reactions with Ozempic® in clinical trials were gastrointestinal disorders, including nausea, diarrhoea and vomiting. Adverse reactions by system organ class and absolute frequencies identified in all phase 3a trials listed here as Very common (≥1/10): Hypoglycaemia when used with insulin or sulfonylurea, nausea, diarrhoea; Common (≥1/100 to <1/10): Hypoglycaemia when used with other OADs, decreased appetite, dizziness, diabetic retinopathy complications, vomiting, abdominal pain, abdominal distension, constipation, dyspepsia, gastritis, gastroesophageal reflux disease, eructation, flatulence, cholelithiasis, fatigue, increased lipase, increased amylase, weight decreased; Uncommon (≥1/1,000 to <1/100): hypersensitivity, dysgeusia, increased heart rate, injection site reactions, hypersensitivity, acute pancreatitis; Rare (≥1/10,000 to <1/1,000): anaphylactic reaction; Frequency unknown: angioedema.
Overdose: There is no specific antidote for overdose with Ozempic®. In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms. A prolonged period of observation and treatment for these symptoms may be necessary, taking into account the long half-life of Ozempic® of approximately 1 week.
Reg. No.: 53/21.13/0497
For full prescribing information, refer to the Professional Information approved by the Regulatory Authority