HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OZEMPIC® safely and effectively. See full prescribing information for OZEMPIC®.

OZEMPIC® (semaglutide) injection, for subcutaneous use

Initial U.S. Approval: 2017

——— INDICATIONS AND USAGE ———

OZEMPIC® is a glucagon-like peptide 1 (GLP-1) receptor agonist indicated as:

• an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (1).

• to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease (1).

Limitations of Use:

• Has not been studied in patients with a history of pancreatitis. Consider another antidiabetic therapy (1, 5.2).

• Not for treatment of type 1 diabetes mellitus (1).

——— DOSAGE AND ADMINISTRATION ———

Start at 0.25 mg once weekly. After 4 weeks, increase the dose to 0.5 mg once weekly. If after at least 4 weeks additional glycemic control is needed, increase to 1 mg once weekly (2.1).

Administer once weekly at any time of day, with or without meals (2.1).

If a dose is missed administer within 5 days of missed dose (2.1).

Inject subcutaneously in the abdomen, thigh, or upper arm (2.2).

——— CONTRAINDICATIONS ———

OZEMPIC® is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and symptoms of thyroid tumors (4, 5.1).

——— USE IN SPECIFIC POPULATIONS ———

Females and Males of Reproductive Potential: Discontinue OZEMPIC® in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide (8.3).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 04/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

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2 DOSAGE AND ADMINISTRATION

3 CONTRAINDICATIONS

4 WARNINGS AND PRECAUTIONS

5 DOSAGE FORMS AND STRENGTHS

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*Sections or subsections omitted from the full prescribing information are not listed.

——— DOSAGE FORMS AND STRENGTHS ———

Injection: 2 mg/1.5 mL (1.34 mg/mL) available in:

• Single-patient-use pen that delivers 0.25 mg or 0.5 mg per injection (3).

• Single-patient-use pen that delivers 1 mg per injection (3).

Injection: 4 mg/3 mL (1.34 mg/mL) available in:

• Single-patient-use pen that delivers 1 mg per injection (3).

——— ADVERSE REACTIONS ———

The most common adverse reactions, reported in ≥5% of patients treated with OZEMPIC® are:

• nausea, vomiting, diarrhea, abdominal pain and constipation (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc., at 1-888-693-6742 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

——— DRUG INTERACTIONS ———

Oral Medications: OZEMPIC® delays gastric emptying. May impact absorption of concomitantly administered oral medications (7.2).

——— USE IN SPECIFIC POPULATIONS ———

Females and Males of Reproductive Potential: Discontinue OZEMPIC® in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide (8.3).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 04/2021
**Indications and Usage**

OZEMPIC® (semaglutide) injection, for subcutaneous use is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. (See Clinical Studies [14.1]).
- 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. (See Clinical Studies [14.4]).

Limitations of Use

- OZEMPIC® has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. (See Warnings and Precautions [5.2]).
- OZEMPIC® is not indicated for use in patients with type 1 diabetes mellitus.

**Dosage and Administration**

2.1 Recommended Dosage

Start OZEMPIC® with a 0.25 mg subcutaneous injection once weekly for 4 weeks. The 0.25 mg dose is intended for treatment initiation and is not effective for glycemic control.

After 4 weeks on the 0.25 mg dose, increase the dosage to 0.5 mg once weekly.

If additional glycemic control is needed after at least 4 weeks on the 0.5 mg dose, the dosage may be increased to 1 mg once weekly. The maximum recommended dosage is 1 mg once weekly.

Administer OZEMPIC® once weekly, on the same day each week, at any time of the day, with or without meals.

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).

If a dose is missed, administer OZEMPIC® as soon as possible within 5 days after the missed dose. If more than 5 days have passed, skip the missed dose and administer the next dose on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule.

2.2 Important Administration Instructions

Administer OZEMPIC® subcutaneously to the abdomen, thigh, or upper arm. Instruct patients to use a different injection site each week when injecting in the same body region.

Inspect OZEMPIC® visually before use. It should appear clear and colorless. Do not use OZEMPIC® if particulate matter and coloration is seen.

When using OZEMPIC® with insulin, instruct patients to administer as separate injections and to never mix the products. It is acceptable to inject OZEMPIC® and insulin in the same body region, but the injections should not be adjacent to each other.

3 Dosage Forms and Strengths

Injection: clear, colorless solution available in 3 pre-filled, disposable, single-patient-use pens:

<table>
<thead>
<tr>
<th>Dose per Inj</th>
<th>Use For</th>
<th>Total Strength per Total Volume</th>
<th>Strength per mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg</td>
<td>Initiation Maintenance</td>
<td>2 mg / 1.5 mL</td>
<td>1.34 mg/mL</td>
</tr>
<tr>
<td>0.5 mg</td>
<td>Maintenance</td>
<td>2 mg / 1.5 mL</td>
<td>1.34 mg/mL</td>
</tr>
<tr>
<td>1 mg</td>
<td>Maintenance</td>
<td>4 mg / 3 mL</td>
<td>1.34 mg/mL</td>
</tr>
</tbody>
</table>

4 Contraindications

OZEMPIC® is contraindicated in patients with:

- A personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) (See Warnings and Precautions [5.1]).
- A prior serious hypersensitivity reaction to semaglutide or to any of the excipients in OZEMPIC®. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with OZEMPIC® (See Warnings and Precautions [5.7]).

5 Warnings and Precautions

5.1 Risk of Thyroid C-Cell Tumors

In mice and rats, semaglutide caused a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure at clinically relevant plasma exposures. (See Nonclinical Toxicology [13.1]). It is unknown whether OZEMPIC® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined.

Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing 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.

OZEMPIC® is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of OZEMPIC® and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with OZEMPIC® (See Contraindications [4] and Warnings and Precautions [5.1]).

5.2 Pancreatitis

In glycemic control trials, acute pancreatitis was confirmed by adjudication in 7 OZEMPIC®-treated patients (0.3 cases per 100 patient years) versus 3 in comparator-treated patients (0.2 cases per 100 patient years). One case of chronic pancreatitis was confirmed in an OZEMPIC®-treated patient. In a 2-year trial, acute pancreatitis was confirmed by adjudication in 8 OZEMPIC®-treated patients (0.27 cases per 100 patient years) and 10 placebo-treated patients (0.33 cases per 100 patient years), both on a background of standard of care.

After initiation of OZEMPIC®, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, OZEMPIC® should be discontinued and appropriate management initiated, if confirmed, OZEMPIC® should not be restarted.

5.3 Diabetic Retinopathy Complications

In a 2-year trial involving patients with type 2 diabetes and high cardiovascular risk, more events of diabetic retinopathy complications occurred in patients treated with OZEMPIC® (0.0%) compared to placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline (OZEMPIC® 8.2%, placebo 5.2%) than among patients without a known history of diabetic retinopathy (OZEMPIC® 0.7%, placebo 0.4%).

Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. The effect of long-term glycemic control with semaglutide on diabetic retinopathy complications has not been studied. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.

5.4 Never Share an OZEMPIC® Pen Between Patients

OZEMPIC® pens must never be shared between patients, even if the needle is changed. Pen-sharing poses a risk for transmission of blood-borne pathogens.

5.5 Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin

Patients receiving OZEMPIC® in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia (See Adverse Reactions [6.1] and Drug Interactions [7]).

The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogue) or insulin. Inform patients using these concomitant medications of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia.

5.6 Acute Kidney Injury

There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis, in patients treated with GLP-1 receptor agonists. Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, and dehydration. Monitor renal function when initiating or escalating doses of OZEMPIC® in patients reporting severe adverse gastrointestinal reactions.

5.7 Hypersensitivity

Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported in patients treated with OZEMPIC®. If hypersensitivity reactions occur, discontinue use of OZEMPIC®, treat promptly per standard of care, and monitor until signs and symptoms resolve. Do not use in patients with a previous hypersensitivity to OZEMPIC® (See Contraindications [4] and Adverse Reactions [6.3]).

Anaphylaxis and angioedema have been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of angioedema or anaphylaxis with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to anaphylaxis with OZEMPIC®.

6 Adverse Reactions

The following serious adverse reactions are described below or elsewhere in the prescribing information:

- Risk of Thyroid C-Cell Tumors (See Warnings and Precautions [5.1])
- Pancreatitis (See Warnings and Precautions [5.2])
- Diabetic Retinopathy Complications (See Warnings and Precautions [5.3])
- Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin (See Warnings and Precautions [5.5])
- Acute Kidney Injury (See Warnings and Precautions [5.6])
- Hypersensitivity (See Warnings and Precautions [5.7])
6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Pool of Placebo-Controlled Trials

The data in Table 1 are derived from 2 placebo-controlled trials (1 monotherapy trial and 1 trial in combination with basal insulin) in patients with type 2 diabetes [see Clinical Studies (14)]. These data reflect exposure of 521 patients to OZEMPIC® and a mean duration of exposure to OZEMPIC® of 32.9 weeks. Across the treatment arms, the mean age of patients was 56 years, 3.4% were 75 years or older and 55% were male. In these trials 71% were White, 7% were Black or African American, and 19% were Asian; 21% identified as Hispanic or Latino ethnicity. At baseline, patients had type 2 diabetes for an average of 8.8 years and had a mean HbA1c of 8.2%. At baseline, 8.9% of the population reported retinopathy. Baseline estimated renal function was normal (eGFR ≥ 60 mL/min/1.73m²) in 72.3%, mildly impaired (eGFR 60 to 90 mL/min/1.73m²) in 35.9% and moderately impaired (eGFR 30 to 60 mL/min/1.73m²) in 6.9% of patients.

Pool of Placebo- and Active-Controlled Trials

The occurrence of adverse reactions was also evaluated in a larger pool of patients with type 2 diabetes participating in 7 placebo- and active-controlled glycemic control trials [see Clinical Studies (14)] including two trials in Japanese patients evaluating the use of OZEMPIC® as monotherapy and add-on therapy to oral medications or insulin. In this pool, a total of 3150 patients with type 2 diabetes were treated with OZEMPIC® for a mean duration of 44.9 weeks. Across the treatment arms, the mean age of patients was 57 years, 3.2% were 75 years or older and 57% were male. In these trials, 60% were White, 6% were Black or African American, and 31% were Asian; 16% identified as Hispanic or Latino ethnicity. At baseline, patients had type 2 diabetes for an average of 8.2 years and had a mean HbA1c of 8.2%. At baseline, 7.8% of the population reported retinopathy. Baseline estimated renal function was normal (eGFR ≥ 60 mL/min/1.73m²) in 63.1%, mildly impaired (eGFR 60 to 90 mL/min/1.73m²) in 34.3%, and moderately impaired (eGFR 30 to 60 mL/min/1.73m²) in 2.5% of the patients.

Table 1. Adverse Reactions in Placebo-Controlled Trials Reported in ≥5% of OZEMPIC®-Treated Patients with Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo (N=252) %</th>
<th>OZEMPIC® 0.5 mg (N=269) %</th>
<th>OZEMPIC® 1 mg (N=261) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>6.1</td>
<td>15.8</td>
<td>20.3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.3</td>
<td>5.0</td>
<td>9.2</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1.9</td>
<td>8.5</td>
<td>8.8</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4.6</td>
<td>7.3</td>
<td>5.7</td>
</tr>
<tr>
<td>Constipation</td>
<td>1.5</td>
<td>5.0</td>
<td>3.1</td>
</tr>
</tbody>
</table>

In the pool of placebo- and active-controlled trials and in the 2-year cardiovascular outcomes trial, the types and frequency of common adverse reactions, excluding hypoglycemia, were similar to those listed in Table 1.

Gastrointestinal Adverse Reactions

In the pool of placebo-controlled trials, gastrointestinal adverse reactions occurred more frequently among patients receiving OZEMPIC® than placebo (15.3%, OZEMPIC® 0.5 mg 32.7%, OZEMPIC® 1 mg 36.4%). The majority of reports of nausea, vomiting, and/or diarrhea occurred during dose escalation. More patients receiving OZEMPIC® 0.5 mg (3.1%) and OZEMPIC® 1 mg (3.8%) discontinued treatment due to gastrointestinal adverse reactions than patients receiving placebo (0.4%). In addition to the reactions in Table 1, the following gastrointestinal adverse reactions with a frequency of <5% were associated with OZEMPIC® (frequencies listed, respectively, as: placebo; 0.5 mg: 1 mg): dyspepsia (1.9%, 3.5%, 2.7%), eructation (0%, 2.7%, 1.1%), flatulence (0.8%, 0.4%, 1.5%), gastroesophageal reflux disease (0%, 1.9%, 1.5%), and gastritis (0.8%, 0.8%, 0.4%).

Other Adverse Reactions

Hypoglycemia

Table 2 summarizes the incidence of events related to hypoglycemia by various definitions in the placebo-controlled trials.

Table 2. Hypoglycemia Adverse Reactions in Placebo-Controlled Trials in Patients with Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Placebo</th>
<th>OZEMPIC® 0.5 mg</th>
<th>OZEMPIC® 1 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>(30 weeks)</td>
<td>N=129</td>
<td>N=127</td>
<td>N=130</td>
</tr>
<tr>
<td>Severe*</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Documented symptomatic (≤70 mg/dL glucose threshold)</td>
<td>0%</td>
<td>1.6%</td>
<td>3.8%</td>
</tr>
<tr>
<td>Severe* or Blood Glucose Confirmed Symptomatic (≤56 mg/dL glucose threshold)</td>
<td>1.6%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Add-on to Basal Insulin with or without Metformin

| (30 weeks)  | N=132   | N=132          | N=131         |
| Severe*     | 0%      | 0%             | 1.5%          |
| Documented symptomatic (≤70 mg/dL glucose threshold) | 15.2% | 16.7% | 29.8% |
| Severe* or Blood Glucose Confirmed Symptomatic (≤56 mg/dL glucose threshold) | 5.3% | 8.3% | 10.7% |

*Severe* hypoglycemia adverse reactions are episodes requiring the assistance of another person.

Hypoglycemia was more frequent when OZEMPIC® was used in combination with a sulfonylurea [see Warnings and Precautions (5.5) and Clinical Studies (14)]. Severe hypoglycemia occurred in 0.8% and 1.2% of patients when OZEMPIC® 0.5 mg and 1 mg, respectively, was co-administered with a sulfonylurea. Documented symptomatic hypoglycemia occurred in 17.3% and 24.4% of patients when OZEMPIC® 0.5 mg and 1 mg, respectively, was co-administered with a sulfonylurea. Severe or blood glucose confirmed symptomatic hypoglycemia occurred in 6.5% and 10.4% of patients when OZEMPIC® 0.5 mg and 1 mg, respectively, was co-administered with a sulfonylurea.

Injection Site Reactions

In placebo-controlled trials, injection site reactions (e.g., injection-site discomfort, erythema) were reported in 0.2% of OZEMPIC®-treated patients.

Increases in Amylase and Lipase

In placebo-controlled trials, patients exposed to OZEMPIC® had a mean increase from baseline in amylase of 13% and lipase of 22%. These changes were not observed in placebo-treated patients.

Cholelithiasis

In placebo-controlled trials, cholelithiasis was reported in 1.5% and 0.4% of patients treated with OZEMPIC® 0.5 mg and 1 mg, respectively. Cholelithiasis was not reported in placebo-treated patients.

Increases in Heart Rate

In placebo-controlled trials, OZEMPIC® 0.5 mg and 1 mg resulted in a mean increase in heart rate of 2 to 3 beats per minute. There was a mean decrease in heart rate of 0.3 beats per minute in placebo-treated patients.

Fatigue, Dysgeusia and Dizziness

Other adverse reactions with a frequency of >0.4% were associated with OZEMPIC® include fatigue, dysgeusia and dizziness.

6.2 Immunogenicity

Consistent with the potentially immunogenic properties of protein and peptide pharmaceuticals, patients treated with OZEMPIC® may develop anti-semaglutide antibodies. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, the incidence of antibodies to semaglutide in the studies described below cannot be directly compared with the incidence of antibodies in other studies or to other products. Across the placebo- and active-controlled glycemic control trials, 32 (1.0%) OZEMPIC®-treated patients developed anti-drug antibodies (ADAs) to the active ingredient in OZEMPIC® (i.e., semaglutide). Of the 32 semaglutide-treated patients that developed semaglutide ADAs, 19 patients (0.6% of the overall population) developed antibodies cross-reacting with native GLP-1. The in vitro neutralizing activity of the antibodies is uncertain at this time.

6.3 Postmarketing Experience

The following adverse reactions have been reported during post-approval use of semaglutide, the active ingredient of OZEMPIC®. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Hypersensitivity: anaphylaxis, angioedema, rash, urticaria.

7 DRUG INTERACTIONS

7.1 Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin

When initiating OZEMPIC®, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia [see Warnings and Precautions (5.5) and Adverse Reactions (6)].

7.2 Oral Medications

OZEMPIC® causes a delay of gastric emptying, and thereby has the potential to impact the absorption of concomitantly administered oral medications. In clinical pharmacology trials, semaglutide did not affect the absorption of orally administered medications to any clinically relevant degree [see
Clinical Pharmacology (12.3). Nonetheless, caution should be exercised when oral medications are concomitantly administered with OZEMPIC®.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are limited data with semaglutide use in pregnant women to inform a drug-associated risk for adverse developmental outcomes. There are clinical considerations regarding the risks of poorly controlled diabetes in pregnancy (see Clinical Considerations). Based on animal reproduction studies, there may be potential risks to the fetus from exposure to semaglutide during pregnancy. OZEMPIC® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In pregnant rats administered semaglutide during organogenesis, embryofetal mortality, structural abnormalities and alterations to growth occurred at maternal exposures below the maximum recommended human dose (MRHD) based on AUC. In rabbits and cynomolgus monkeys administered semaglutide during organogenesis, early pregnancy losses and structural abnormalities were observed at below the MRHD (rabbit) and ≥5-fold the MRHD (monkey). These findings coincided with a marked maternal body weight loss in both animal species (see Data). The estimated background risk of major birth defects is 6–10% in women with pre-gestational diabetes with an HbA1c >7 and has been reported to be as high as 20–25% in women with a HbA1c >10. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

Disease associated maternal and fetal risk

Poorly controlled diabetes during pregnancy increases the maternal risk for diabetic ketoacidosis, pre-eclampsia, spontaneous abortions, preterm delivery, stillbirth and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macrosomia related morbidity.

Data

Animal Data

In a combined fertility and embryofetal development study in rats, subcutaneous doses of 0.01, 0.03 and 0.09 mg/kg/day (0.1-, 0.4-, and 1.1-fold the MRHD) were administered to males for 4 weeks prior to and throughout mating and to females for 2 weeks prior to mating, and throughout organogenesis to Gestation Day 17. In parental animals, pharmacologically mediated reductions in body weight gain and food consumption were observed at all dose levels. In the offspring, reduced growth and fetuses with visceral (heart blood vessels) and skeletal (cranial bones, vertebra, ribs) abnormalities were observed at the maternal exposure.

In an embryofetal development study in pregnant rabbits, subcutaneous doses of 0.0010, 0.0025 or 0.0075 mg/kg/day (0.03-, 0.3-, and 2.3-fold the MRHD) were administered throughout organogenesis from Gestation Day 6 to 19. Pharmacologically mediated reductions in maternal body weight gain and food consumption were observed at all dose levels. Early pregnancy losses and increased incidences of minor visceral (kidney, liver) and skeletal (sternbra) fetal abnormalities were observed at ≥0.0025 mg/kg/day, at clinically relevant exposures.

In an embryofetal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (1.0-, 5.2-, and 14.9-fold the MRHD) were administered throughout organogenesis, from Gestation Day 16 to 50. Pharmacologically mediated, marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with the occurrence of sporadic abnormalities (vertebra, sternebra, ribs) at ≥0.075 mg/kg twice weekly (≥5X human exposure).

In a pre- and postnatal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (0.7-, 3.3-, and 7.2-fold the MRHD) were administered from Gestation Day 16 to 140. Pharmacologically mediated marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with an increase in early pregnancy losses and led to delivery of slightly smaller offspring at ≥0.075 mg/kg twice weekly (≥5X human exposure).

8.2 Lactation

Risk Summary

There are no data on the presence of semaglutide in human milk, the effects on the breastfed infant, or the effects on milk production. Semaglutide was present in the milk of lactating rats, however, due to species-specific differences in lactation physiology, the clinical relevance of these data are not clear (see Data). The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for OZEMPIC® and any potential adverse effects on the breastfed infant from OZEMPIC® or from the underlying maternal condition.

Data

In lactating rats, semaglutide was detected in milk at levels 3-12 fold lower than in maternal plasma.

8.3 Females and Males of Reproductive Potential

Discontinue OZEMPIC® in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide (see Use in Specific Populations [8.1]).

8.4 Pediatric Use

Safety and efficacy of OZEMPIC® have not been established in pediatric patients (younger than 16 years).

8.5 Geriatric Use

In the pool of placebo- and active-controlled glycemic control trials, 744 (23.6%) OZEMPIC®-treated patients were 65 years of age and over and 102 OZEMPIC®-treated patients (3.2%) patients were 75 years of age and over. In SUSTAIN 6, the cardiovascular outcome trial, 788 (48.0%) OZEMPIC®-treated patients were 65 years of age and over and 157 OZEMPIC®-treated patients (9.6%) patients were 75 years of age and over.

No overall differences in safety or efficacy were detected between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment

No dose adjustment of OZEMPIC® is recommended for patients with renal impairment. In subjects with renal impairment including end-stage renal disease (ESRD), no clinically relevant change in semaglutide pharmacokinetics (PK) was observed (see Clinical Pharmacology (12.3)).

8.7 Hepatic Impairment

No dose adjustment of OZEMPIC® is recommended for patients with hepatic impairment. In a study in subjects with different degrees of hepatic impairment, no clinically relevant change in semaglutide pharmacokinetics (PK) was observed (see Clinical Pharmacology (12.3)).

10 OVERDOSAGE

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.

11 DESCRIPTION

OZEMPIC® (semaglutide) injection, for subcutaneous use, contains semaglutide, a human GLP-1 receptor agonist (or GLP-1 analog). The peptide backbone is produced by yeast fermentation. The main protraction mechanism of semaglutide is albumin binding, facilitated by modification of position 26 lysine with a hydrophilic spacer and a C18 fatty di-acid. Furthermore, semaglutide is modified in position 8 to provide stabilization against degradation by the enzyme dipeptidyl-peptidase 4 (DPP-4). A minor modification was made in position 34 to ensure the attachment of only one fatty di-acid. The molecular formula is C182H292N45O95 and the molecular weight is 4113.58 g/mol.

Structural formula:

OZEMPIC® is a sterile, aqueous, clear, colorless solution. Each pre-filled pen contains a 1.5 mL solution of OZEMPIC® equivalent to 2 mg semaglutide or a 3 mL solution of OZEMPIC® equivalent to 4 mg of semaglutide. Each 1 mL of OZEMPIC® solution contains 1.34 mg of semaglutide and the following inactive ingredients: disodium phosphate dihydrate, 1.42 mg; propylene glycol, 14.0 mg; phenol, 5.50 mg; and water for injections. OZEMPIC® has a pH of approximately 7.4. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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 on glucose, mediated by the GLP-1 receptors.

The principal mechanism of protraction resulting in the long half-life of semaglutide is albumin binding, which results in decreased renal clearance and protection from metabolic degradation. Furthermore, semaglutide is stabilized against degradation by the DPP-4 enzyme.

Semaglutide reduces blood glucose through a mechanism where it stimulates insulin secretion and lowers glucagon secretion, both in a glucose-dependent manner. Thus, when blood glucose is high, insulin secretion is stimulated, and glucagon secretion is inhibited. The mechanism of blood glucose lowering also involves a minor delay in gastric emptying in the early postprandial phase.

12.2 Pharmacodynamics

Semaglutide lowers fasting and postprandial blood glucose and reduces body weight. All pharmacodynamic evaluations were performed after 12 weeks of treatment (including dose escalation) at steady state with semaglutide 1 mg.

Fasting and Postprandial Glucose

Semaglutide reduces fasting and postprandial glucose concentrations. In patients with type 2 diabetes, treatment with semaglutide 1 mg resulted in reductions in glucose in terms of absolute change from baseline and relative reduction compared to placebo of 29 mg/dL (22%) for fasting glucose, 74 mg/dL (36%) for 2-hour postprandial glucose, and 30 mg/dL (22%) for mean 24-hour glucose concentration (see Figure 1).
compared with placebo.

210 OZEMPIC® (semaglutide) injection, for subcutaneous use  0.5 mg and 1 mg. Steady-state exposure is achieved following 4-5 weeks of

In patients with type 2 diabetes, semaglutide exposure increases in a dose-proportional manner for

Figure 2. Mean insulin secretion rate versus glucose concentration in patients with type 2 diabetes during graded glucose infusion before (baseline) and after 12 weeks of treatment with semaglutide or placebo and in untreated healthy subjects

During induced hypoglycemia, semaglutide did not alter the counter regulatory responses of increased glucagon compared to placebo and did not impair the decrease of C-peptide in patients with type 2 diabetes.

Gastric emptying
Semaglutide causes a delay of early postprandial gastric emptying, thereby reducing the rate at which glucose appears in the circulation postprandially.

Cardiac electrophysiology (QTc)
The effect of semaglutide on cardiac repolarization was tested in a thorough QTc trial. At a dose

No clinically significant drug-drug interaction with semaglutide (Figure 4) was observed based on

The delay of gastric emptying with semaglutide may influence the absorption of concomitantly

In vitro studies have shown very low potential for semaglutide to inhibit or induce CYP enzymes, and to inhibit drug transporters.

The delay of gastric emptying with semaglutide may influence the absorption of concomitantly administered oral medicinal products. The potential effect of semaglutide on the absorption of co-administered oral medications was studied in trials at semaglutide 1 mg steady-state exposure.

No clinically relevant drug-drug interaction with semaglutide (Figure 4) was observed based on clinical studies (Figure 3). The effects of intrinsic factors on the pharmacokinetics of semaglutide are shown in Figure 3.

Figure 3. Impact of intrinsic factors on semaglutide exposure

<table>
<thead>
<tr>
<th>Intrinsic factor</th>
<th>Relative exposure (Cavg)</th>
<th>Ratio and 90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>65-74 years</td>
<td></td>
</tr>
<tr>
<td>&gt;74 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>Black or African American</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Hispanic or Latino</td>
<td></td>
</tr>
<tr>
<td>Body weight</td>
<td>55 kg</td>
<td></td>
</tr>
<tr>
<td>127 kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal impairment</td>
<td>Mild</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Semaglutide exposure (Cavg) relative to reference subject profile: non-Hispanic/non-Latino, White, female below 65 years, body weight 85 kg, with normal renal function. Population PK model also included maintenance dose and injection site as covariates. Body weight test categories (55 and 127 kg) represent the 5% and 95% percentiles in the dataset. Abbreviations: Cavg, average semaglutide concentration; CI, Confidence interval.

Patients with Renal impairment - Renal impairment does not impact the pharmacokinetics of semaglutide in a clinically relevant manner. This was shown in a study with a single dose of 0.5 mg semaglutide in patients with different degrees of renal impairment (mild, moderate, severe, ESRD) compared with subjects with normal renal function. This was also shown for subjects with both type 2 diabetes and renal impairment based on data from clinical studies (Figure 3).

Patients with Hepatic impairment - Hepatic impairment does not have any impact on the exposure of semaglutide. The pharmacokinetics of semaglutide were evaluated in patients with different degrees of hepatic impairment (mild, moderate, severe) compared with subjects with normal hepatic function in a study with a single-dose of 0.5 mg semaglutide.

Pediatric Patients - Semaglutide has not been studied in pediatric patients.

Drug Interaction Studies

Absorption
Absolute bioavailability of semaglutide is 89%. Maximum concentration of semaglutide is reached

similar exposure is achieved with subcutaneous administration of semaglutide in the abdomen, thigh, or upper arm.

In patients with type 2 diabetes, semaglutide exposure increases in a dose-proportional manner for

Once-weekly administration. In patients with type 2 diabetes, the mean population-PK estimated

steady-state concentrations following once weekly subcutaneous administration of 0.5 mg and 1

mg semaglutide were approximately 65.0 ng/mL and 123.0 ng/mL, respectively.

Distribution
The mean apparent volume of distribution of semaglutide following subcutaneous administration in

patients with type 2 diabetes is approximately 12.5 L. Semaglutide is extensively bound to plasma albumin (>99%).

Elimination
The apparent clearance of semaglutide in patients with type 2 diabetes is approximately 0.05 L/h. With an elimination half-life of approximately 1 week, semaglutide will be present in the circulation for about 5 weeks after the last dose.

Metabolism
The primary route of elimination for semaglutide is metabolism following proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain.

Excretion
The primary excretion routes of semaglutide-related material are via the urine and feces. Approximately 3% of the dose is excreted in the urine as intact semaglutide.

Specific Populations
Based on a population pharmacokinetic analysis, age, sex, race, and ethnicity, and renal impairment do not have a clinically meaningful effect on the pharmacokinetics of semaglutide. The exposure of semaglutide decreases with an increase in body weight. However, semaglutide doses of 0.5 mg and 1 mg provide adequate systemic exposure over the body weight range of 40-198 kg evaluated in the clinical trials. The effects of intrinsic factors on the pharmacokinetics of semaglutide are shown in Figure 3.

12.3 Pharmacokinetics

Absorption
Absolute bioavailability of semaglutide is 89%. Maximum concentration of semaglutide is reached

1 to 3 days post dose.

Similar exposure is achieved with subcutaneous administration of semaglutide in the abdomen, thigh, or upper arm.

In patients with type 2 diabetes, semaglutide exposure increases in a dose-proportional manner for

once-weekly doses of 0.5 mg and 1 mg. Steady-state exposure is achieved following 4-5 weeks of

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In patients with type 2 diabetes, semaglutide exposure increases in a dose-proportional manner for

once-weekly doses of 0.5 mg and 1 mg. Steady-state exposure is achieved following 4-5 weeks of
In a 2-year carcinogenicity study in CD-1 mice, subcutaneous doses of 0.3, 1, and 3 mg/kg/day were administered to the males and female rats. A statistically significant increase in thyroid C-cell adenomas and a numerical increase in C-cell carcinomas were observed in males and females at all dose levels (≥2× human exposure).

In a 2-year carcinogenicity study in Sprague Dawley rats, subcutaneous doses of 0.0025, 0.01, 0.025, and 0.1 mg/kg/day were administered (below quantification, 0.4-, 1-, and 6-fold the exposure at the MRHD). A statistically significant increase in thyroid C-cell adenomas was observed in males and females at all dose levels, and a statistically significant increase in thyroid C-cell carcinomas was observed in males at ≥0.01 mg/kg/day, at clinically relevant exposures.

Human relevance of thyroid C-cell tumors in rats is unknown and could not be determined by clinical studies or nonclinical studies (see Boxed Warning and Warnings and Precautions (5.1)).

Semaglutide was not mutagenic or clastogenic in a standard battery of genotoxicity tests (bacterial mutagenicity Ames, human lymphocyte chromosome aberration, rat bone marrow micronucleus).

In a combined fertility and embryo-fetal development study in rats, subcutaneous doses of 0.01, 0.03, and 0.09 mg/kg/day (0.1-, 0.4-, and 1.1-fold the MRHD) were administered to male and female rats. Males were dosed for 4 weeks prior to mating, and females were dosed for 2 weeks prior to mating and throughout organogenesis until Gestation Day 17. No effects were observed on male fertility. In females, an increase in estrus cycle length was observed at all dose levels, together with a small reduction in numbers of corpora lutea at ≥0.03 mg/kg/day. These effects were likely an effect on male fertility. In females, an increase in estrus cycle length was observed at all dose levels, together with a small reduction in numbers of corpora lutea at ≥0.03 mg/kg/day. These effects were likely an effect on male fertility.

Overall, 68% were White, 5% were Black or African American, and 21% were Asian; 30% identified as Hispanic or Latino ethnicity.

Monotherapy with OZEMPIC® 0.5 mg and 1 mg once weekly for 30 weeks resulted in a statistically significant reduction in HbA1c compared to placebo (see Table 3).

<table>
<thead>
<tr>
<th>OZEMPIC® (semaglutide) injection, for subcutaneous use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 4. Results at Week 56 in a Trial of OZEMPIC® Compared to Sitagliptin in Adult Patients with Type 2 Diabetes Mellitus in Patients with Type 2 Diabetes Mellitus in Combination with Metformin and/or Thiazolidinediones</td>
</tr>
<tr>
<td>Intent-to-Treat (ITT) Population (N)</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>HBAlc (%)</td>
</tr>
<tr>
<td>Baseline (mean)</td>
</tr>
<tr>
<td>Change at week 56p</td>
</tr>
<tr>
<td>Difference from sitagliptin (95% CI)</td>
</tr>
<tr>
<td>Patients (%) achieving HBAlc &lt;7%</td>
</tr>
<tr>
<td>FPG (mg/dL)</td>
</tr>
<tr>
<td>Baseline (mean)</td>
</tr>
<tr>
<td>Change at week 56p</td>
</tr>
</tbody>
</table>

The mean baseline body weight was 89.1 kg, 89.2 kg, and 89.3 kg in the placebo, OZEMPIC® 0.5 mg, and OZEMPIC® 1 mg arms, respectively. The mean changes from baseline to week 56 were -1.2 kg, -3.8 kg and -4.7 kg in the placebo, OZEMPIC® 0.5 mg, and OZEMPIC® 1 mg arms, respectively. The difference from placebo (95% CI) for OZEMPIC® 0.5 mg was -2.6 kg (-3.8, -1.5), and for OZEMPIC® 1 mg was -3.5 kg (-4.8, -2.2).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 2-year carcinogenicity study in CD-1 mice, subcutaneous doses of 0.3, 1, and 3 mg/kg/day [5-, 17-, and 59-fold the maximum recommended human dose (MRHD) of 1 mg/week, based on AUC] were administered to the males, and 0.1, 0.3, and 1 mg/kg/day [2-, 5-, and 17-fold MRHD] were administered to the females. A statistically significant increase in thyroid C-cell adenomas and a numerical increase in C-cell carcinomas were observed in males and females at all doses levels (≥2× human exposure).

In a 2-year carcinogenicity study in Sprague Dawley rats, subcutaneous doses of 0.0025, 0.01, 0.025, and 0.1 mg/kg/day (below quantification, 0.4-, 1-, and 6-fold the exposure at the MRHD). A statistically significant increase in thyroid C-cell adenomas was observed in males and females at all dose levels, and a statistically significant increase in thyroid C-cell carcinomas was observed in males at ≥0.01 mg/kg/day, at clinically relevant exposures.

The mean baseline body weight was 89.1 kg, 89.2 kg, and 89.3 kg in the placebo, OZEMPIC® 0.5 mg, and OZEMPIC® 1 mg arms, respectively. The mean changes from baseline to week 56 were -1.2 kg, -3.8 kg and -4.7 kg in the placebo, OZEMPIC® 0.5 mg, and OZEMPIC® 1 mg arms, respectively. The difference from placebo (95% CI) for OZEMPIC® 0.5 mg was -2.6 kg (-3.8, -1.5), and for OZEMPIC® 1 mg was -3.5 kg (-4.8, -2.2).

In a 56-week, double-blind trial (NCT01930188), 1231 patients with type 2 diabetes mellitus were randomized to OZEMPIC® 0.5 mg once weekly, OZEMPIC® 1 mg once weekly, or sitagliptin 100 mg once daily, all in combination with metformin (94%) and/or thiazolidinediones (6%). Patients had a mean age of 55 years and 51% were men. The mean duration of type 2 diabetes was 6.8 years, and the mean BMI was 32 kg/m². Overall, 68% were White, 5% were Black or African American, and 25% were Asian; 17% identified as Hispanic or Latino ethnicity.

Treatment with OZEMPIC® 0.5 mg and 1 mg once weekly for 56 weeks resulted in a statistically significant reduction in HbA1c compared to sitagliptin (see Table 6 and Figure 5).
In a 30-week, open-label trial (NCT01885208), 813 patients with type 2 diabetes mellitus on metformin alone (49%), metformin with sulfonylurea (45%), or other (6%) were randomized to OZEMPIC® 1 mg once weekly or exenatide 2 mg once weekly. Patients had a mean age of 57 years and 55% were men. The mean duration of type 2 diabetes was 9 years, and the mean BMI was 34 kg/m². Overall, 84% were White, 7% were Black or African American, and 2% were Asian; 24% identified as Hispanic or Latino ethnicity.

Treatment with OZEMPIC® 1 mg once weekly for 56 weeks resulted in a statistically significant reduction in HbA₁c compared to exenatide 2 mg once weekly (see Table 5).

### Table 5. Results at Week 56 in a Trial of OZEMPIC® Compared to Exenatide 2 mg Once Weekly in Adult Patients with Type 2 Diabetes Mellitus in Combination with Metformin or Metformin with Sulfonylurea

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Intent-to-Treat (ITT) Population (N)</th>
<th>HbA₁c (%)</th>
<th>Change at week 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>OZEMPIC® 1 mg</td>
<td>404</td>
<td>8.4</td>
<td>-1.8</td>
</tr>
<tr>
<td>Exenatide ER 2 mg</td>
<td></td>
<td>8.3</td>
<td>-1.7</td>
</tr>
<tr>
<td><strong>Baseline (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OZEMPIC® 1 mg</td>
<td>383</td>
<td>-1.4</td>
<td>-0.9</td>
</tr>
<tr>
<td>Exenatide ER 2 mg</td>
<td>382</td>
<td>-0.9</td>
<td>-0.9</td>
</tr>
<tr>
<td><strong>Difference from exenatide</strong></td>
<td></td>
<td>-0.5</td>
<td>[-0.7, -0.3]</td>
</tr>
<tr>
<td>[95% CI]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patients (%) achieving HbA₁c &lt;7%</strong></td>
<td></td>
<td>62</td>
<td>40</td>
</tr>
<tr>
<td><strong>FFP (mg/dL)</strong></td>
<td></td>
<td>191</td>
<td>188</td>
</tr>
<tr>
<td><strong>Change at week 56</strong></td>
<td></td>
<td>-44</td>
<td>-34</td>
</tr>
<tr>
<td><strong>Intent-to-Treat analysis using ANCOVA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adjusted for baseline value, country and stratification factors.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The mean baseline body weight was 96.2 kg and 95.4 kg in the OZEMPIC® 1 mg and exenatide ER arms, respectively. The mean changes from baseline to week 56 were -4.8 kg and -2.0 kg in the OZEMPIC® 1 mg and exenatide ER arms, respectively. The difference from exenatide ER (95% CI) for OZEMPIC® 1 mg was -2.9 kg (-3.6, -2.1).

### Combination with Metformin or Metformin with Sulfonylurea

In a 30-week, open-label trial (NCT02128932), 1089 patients with type 2 diabetes mellitus were randomized to OZEMPIC® 0.5 mg once weekly, OZEMPIC® 1 mg once weekly, or insulin glargine once daily on a background of metformin (48%) or metformin and sulfonylurea (51%). Patients had a mean age of 57 years and 53% were men. The mean duration of type 2 diabetes was 8.6 years, and the mean BMI was 33 kg/m². Overall, 77% were White, 9% were Black or African American, and 11% were Asian; 20% identified as Hispanic or Latino ethnicity.

Patients assigned to insulin glargine had a baseline mean HbA₁c of 8.1% and were started on a dose of 10 U once daily. Insulin glargine dose adjustments occurred throughout the trial period based on self-measured fasting plasma glucose before breakfast, targeting 71 to <100 mg/dL. In addition, investigators could titrate insulin glargine at their discretion between study visits. Only 26% of patients reached the target FPG of 100 mg/dL or less.

The mean baseline body weight was 93.7 kg, 94.0 kg, and 92.6 kg in the OZEMPIC® 0.5 mg, OZEMPIC® 1 mg, and insulin glargine arms, respectively. The mean changes from baseline to week 30 were -3.2 kg, -4.7 kg and 0.9 kg in the OZEMPIC® 0.5 mg, OZEMPIC® 1 mg, and insulin glargine arms, respectively. The difference from insulin glargine (95% CI) for OZEMPIC® 0.5 mg was -4.1 kg (-4.9, -3.3) and for OZEMPIC® 1 mg was -6.5 kg (-6.4, -4.8).

### Combination with Basal insulin

In a 30-week, double-blind trial (NCT02305381), 397 patients with type 2 diabetes mellitus inadequately controlled with basal insulin, with or without metformin, were randomized to OZEMPIC® 0.5 mg once weekly, OZEMPIC® 1 mg once weekly, or placebo. Patients with HbA₁c ≤ 8.0% at screening reduced their insulin dose by 20% at the start of the trial to reduce the risk of hypoglycemia. Patients had a mean age of 59 years and 56% were men. The mean duration of type 2 diabetes was 13 years, and the mean BMI was 32 kg/m². Overall, 78% were White, 5% were Black or African American, and 17% were Asian; 12% identified as Hispanic or Latino ethnicity.

Treatment with OZEMPIC® resulted in a statistically significant reduction in HbA₁c from week 30 to week 30 of treatment compared to placebo (see Table 7).

### Table 6. Results at Week 30 in a Trial of OZEMPIC® Compared to Insulin Glargine in Adult Patients with Type 2 Diabetes Mellitus in Combination with Metformin or Metformin with Sulfonylurea

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Intent-to-Treat (ITT) Population (N)</th>
<th>HbA₁c (%)</th>
<th>Change at week 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>OZEMPIC® 0.5 mg</td>
<td>362</td>
<td>8.1</td>
<td>-1.2</td>
</tr>
<tr>
<td>OZEMPIC® 1 mg</td>
<td>360</td>
<td>8.1</td>
<td>-1.5</td>
</tr>
<tr>
<td><strong>Baseline (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OZEMPIC® 0.5 mg</td>
<td>383</td>
<td>-1.4</td>
<td>-1.5</td>
</tr>
<tr>
<td>OZEMPIC® 1 mg</td>
<td>382</td>
<td>-0.9</td>
<td>-0.9</td>
</tr>
<tr>
<td><strong>Difference from insulin glargine</strong></td>
<td></td>
<td>-0.5</td>
<td>[-0.8, -0.2]</td>
</tr>
<tr>
<td>[95% CI]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patients (%) achieving HbA₁c &lt;7%</strong></td>
<td></td>
<td>55</td>
<td>66</td>
</tr>
<tr>
<td><strong>FFP (mg/dL)</strong></td>
<td></td>
<td>172</td>
<td>179</td>
</tr>
<tr>
<td><strong>Change at week 30</strong></td>
<td></td>
<td>-35</td>
<td>-46</td>
</tr>
</tbody>
</table>

The mean baseline body weight was 93.9 kg, 94.0 kg, and 92.6 kg in the OZEMPIC® 0.5 mg, OZEMPIC® 1 mg, and insulin glargine arms, respectively. The mean changes from baseline to week 30 were -3.2 kg, -4.7 kg and 0.9 kg in the OZEMPIC® 0.5 mg, OZEMPIC® 1 mg, and insulin glargine arms, respectively. The difference from insulin glargine (95% CI) for OZEMPIC® 0.5 mg was -4.1 kg (-4.9, -3.3) and for OZEMPIC® 1 mg was -6.5 kg (-6.4, -4.8).

### 14.4 Cardiovascular Outcomes Trial of OZEMPIC® in Patients with Type 2 Diabetes Mellitus and Cardiovascular Disease

SUSTAIN 6 (NCT01720446) was a multi-center, multi-national, placebo-controlled, double-blind cardiovascular outcomes trial. In this trial, 3,297 patients with inadequately controlled type 2 diabetes and atherosclerotic cardiovascular disease were randomized to OZEMPIC® (0.5 mg or 1 mg) once weekly or placebo for a minimum observation time of 2 years. The trial compared the risk of Major Adverse Cardiovascular Event (MACE) between semaglutide and placebo when these treatments were added to and used concomitantly with standard of care treatments for diabetes and cardiovascular disease. The primary endpoint, MACE, was the time to first occurrence of a three-part composite outcome which included cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

Patients eligible to enter the trial were: 50 years of age or older and had established, stable, cardiovascular, cerebrovascular, peripheral artery disease, chronic kidney disease or NYHA class II and III heart failure or were 60 years of age or older and had other specified risk factors for cardiovascular disease. In total, 1,940 patients (58.8%) had established cardiovascular disease without chronic kidney disease, 353 (10.7%) had chronic kidney disease only, and 442 (13.4%) had both cardiovascular disease and kidney disease. 562 patients (17%) had cardiovascular risk factors without established cardiovascular disease or chronic kidney disease. In the trial 453 patients (13.7%) had peripheral artery disease. The mean age at baseline was 65 years, and 61% were men. The mean...
OZEMPIC® (semaglutide) injection, for subcutaneous use

after first use of the OZEMPIC® pen, the pen can be stored for 56 days at controlled room temperature (59°F to 86°F; 15°C to 30°C) or in a refrigerator (36°F to 46°F; 2°C to 8°C). Do not freeze. Keep the pen cap on when not in use. OZEMPIC® should be protected from excessive heat and sunlight.

Always remove and safely discard the needle after each injection and store the OZEMPIC® pen without an injection needle attached. Always use a new needle for each injection.

The storage conditions are summarized in Table 9:

Table 9. Recommended Storage Conditions for the OZEMPIC® Pen

<table>
<thead>
<tr>
<th>Prior to first use</th>
<th>After first use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refrigerated</td>
<td>Refrigerated</td>
</tr>
<tr>
<td>36°F to 46°F</td>
<td>36°F to 46°F</td>
</tr>
<tr>
<td>(2°C to 8°C)</td>
<td>(2°C to 8°C)</td>
</tr>
<tr>
<td>Room Temperature</td>
<td>Refrigerated</td>
</tr>
<tr>
<td>59°F to 66°F</td>
<td>36°F to 46°F</td>
</tr>
<tr>
<td>(15°C to 30°C)</td>
<td>(2°C to 8°C)</td>
</tr>
<tr>
<td>Until expiration date</td>
<td>56 days</td>
</tr>
</tbody>
</table>

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Risk of Thyroid C-cell Tumors
Inform patients that semaglutide causes thyroid C-cell tumors in rodents and that the human relevance of this finding has not been determined. Counsel patients to report symptoms of thyroid tumors (e.g., a lump in the neck, hoarseness, dysphagia, or dyspnea) to their physician (see Boxed Warning and Warnings and Precautions (5.1)).

Pancreatitis
Inform patients of the potential risk for pancreatitis. Instruct patients to discontinue OZEMPIC® promptly and contact their physician if pancreatitis is suspected (severe abdominal pain that may radiate to the back, and which may or may not be accompanied by vomiting) (see Warnings and Precautions (5.2)).

Diabetic Retinopathy Complications
Inform patients to contact their physician if changes in vision are experienced during treatment with OZEMPIC® (see Warnings and Precautions (5.3)).

Never Share an OZEMPIC® Pen Between Patients
Advise patients that they must never share an OZEMPIC® pen with another person, even if the needle is changed, because doing so carries a risk for transmission of blood-borne pathogens (see Warnings and Precautions (5.4)).

Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin
Inform patients that the risk of hypoglycemia is increased when OZEMPIC® is used with an insulin secretagogue (such as a sulfonylurea) or insulin. Educate patients on the signs and symptoms of hypoglycemia (see Warnings and Precautions (5.5)).

Dehydration and Renal Failure
Advise patients treated with OZEMPIC® of the potential risk of dehydration due to gastrointestinal adverse reactions and take precautions to avoid fluid depletion. Inform patients of the potential risk for worsening renal function and explain the associated signs and symptoms of renal impairment, as well as the possibility of dialysis as a medical intervention if renal failure occurs (see Warnings and Precautions (5.6)).

Hypersensitivity Reactions
Inform patients that serious hypersensitivity reactions have been reported during postmarketing use of OZEMPIC®. Advise patients on the symptoms of hypersensitivity reactions and instruct them to stop taking OZEMPIC® and seek medical advice promptly if such symptoms occur (see Warnings and Precautions (5.7)).

Pregnancy
Advise a pregnant woman of the potential risk to a fetus. Advise women to inform their healthcare provider if they are pregnant or intend to become pregnant [see Use in Specific Populations (8.1), (8.3)].

Inform patients if a dose is missed, it should be administered as soon as possible within 5 days after the missed dose. If more than 5 days have passed, the missed dose should be skipped and the next dose should be administered on the regularly scheduled day. In each case, inform patients to resume their regular once weekly dosing schedule [see Dosage and Administration (2.1)].

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied
Injection: clear, colorless solution of 1.34 mg/mL of semaglutide available in pre-filled, disposable, single-patient-use pens in the following packaging configurations.

<table>
<thead>
<tr>
<th>Dose per Injection</th>
<th>Use For</th>
<th>Total Strength per Total Volume</th>
<th>Doses per Pen</th>
<th>Carton Contents</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg</td>
<td>Initiation</td>
<td>2 mg/1.5 mL</td>
<td>4 doses of 0.25 mg or 2 doses of 0.5 mg</td>
<td>1 pen 6 NovoFine® Plus needles</td>
<td>0169-4132-12</td>
</tr>
<tr>
<td>0.5 mg</td>
<td>Maintenance</td>
<td>2 mg/1.5 mL</td>
<td>2 doses of 1 mg</td>
<td>2 pens 4 NovoFine® Plus needles</td>
<td>0169-4136-02</td>
</tr>
<tr>
<td>1 mg</td>
<td>Maintenance</td>
<td>4 mg/3 mL</td>
<td>4 doses of 1 mg</td>
<td>1 pen 4 NovoFine® Plus needles</td>
<td>0169-4130-13</td>
</tr>
</tbody>
</table>

Each OZEMPIC® pen is for use by a single patient. An OZEMPIC® pen must never be shared between patients, even if the needle is changed (see Warnings and Precautions (5.4)).

Recommended Storage
Prior to first use, OZEMPIC® should be stored in a refrigerator between 36°F to 46°F (2°C to 8°C) (Table 9). Do not store in the freezer or directly adjacent to the refrigerator cooling element. Do not freeze OZEMPIC® and do not use OZEMPIC® if it has been frozen.

Refrigerated
36°F to 46°F (2°C to 8°C)

Room Temperature
59°F to 66°F (15°C to 30°C)

Until expiration date
56 days

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PATENT INFORMATION:

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US21OZM00313 5/2021
What is OZEMPIC®?

OZEMPIC® is an injectable prescription medicine used:
- along with diet and exercise to improve blood sugar (glucose) in adults with type 2 diabetes mellitus.
- to reduce the risk of major cardiovascular events such as heart attack, stroke or death in adults with type 2 diabetes mellitus with known heart disease.

It is not known if OZEMPIC® can be used in people who have had pancreatitis. OZEMPIC® is not for use in people with type 1 diabetes. It is not known if OZEMPIC® is safe and effective for use in children under 18 years of age.

Do not use OZEMPIC® if:
- you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC), or if you have an endocrine system condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
- you have had a serious allergic reaction to semaglutide or any of the ingredients in OZEMPIC®.

See the end of this Medication Guide for a complete list of ingredients in OZEMPIC®, Symptoms of a serious allergic reaction include:
- swelling of your face, lips, tongue or throat
- severe rash or itching
- problems breathing or swallowing
- very rapid heartbeat

Before using OZEMPIC®, tell your healthcare provider if you have any other medical conditions, including if you:
- have or have had problems with your pancreas or kidneys.
- have a history of diabetic retinopathy.
- are pregnant or plan to become pregnant. It is not known if OZEMPIC® will harm your unborn baby. You should stop using OZEMPIC® 2 months before you plan to become pregnant. Talk to your healthcare provider about the best way to control your blood sugar if you plan to become pregnant or while you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if OZEMPIC® passes into your breast milk. You should talk with your healthcare provider about the best way to feed your baby while using OZEMPIC®.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. OZEMPIC® may affect the way some medicines work and some medicines may affect the way OZEMPIC® works.

Before using OZEMPIC®, talk to your healthcare provider about low blood sugar and how to manage it. Tell your healthcare provider if you are taking other medicines to treat diabetes, including insulin or sulfonylureas. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use OZEMPIC®?

- Read the Instructions for Use that comes with OZEMPIC®.
- Use OZEMPIC® exactly as your healthcare provider tells you to.
- Your healthcare provider should show you how to use OZEMPIC® before you use it for the first time.
- OZEMPIC® is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm. Do not inject OZEMPIC® into a muscle (intramuscularly) or vein (intravenously).
- Use OZEMPIC® 1 time each week, on the same day each week, at any time of the day.

- You may change the day of the week you use OZEMPIC® as long as your last dose was given 2 or more days before.
- If you miss a dose of OZEMPIC®, take the missed dose as soon as possible within 5 days after the missed dose. If more than 5 days have passed, skip the missed dose and take your next dose on the regularly scheduled day.
- OZEMPIC® may be taken with or without food.
- Do not mix insulin and OZEMPIC® together in the same injection.
- You may give an injection of OZEMPIC® and insulin in the same body area (such as your stomach area), but not right next to each other.
- Change (rotate) your injection site with each injection. Do not use the same site for each injection.
- Check your blood sugar as your healthcare provider tells you to.
- Stay on your prescribed diet and exercise program while using OZEMPIC®.
- Talk to your healthcare provider about how to prevent, recognize and manage low blood sugar (hypoglycemia), high blood sugar (hyperglycemia), and problems you have because of your diabetes.
- Your healthcare provider will check your diabetes with regular blood tests, including your blood sugar levels and your hemoglobin A1C.
- Do not share your OZEMPIC® pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

Your dose of OZEMPIC® and other diabetes medicines may need to change because of:
- change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, fever, trauma, infection, surgery or because of other medicines you take.

What are the possible side effects of OZEMPIC®?

OZEMPIC® may cause serious side effects, including:
- See “What is the most important information I should know about OZEMPIC®?”
- See “Inflammation of your pancreas (pancreatitis)”. Stop using OZEMPIC® and call your healthcare provider right away if you have severe pain in your stomach area (abdomen) that will not go away, with or without vomiting. You may feel the pain from your abdomen to your back.
- See “Changes in vision”. Tell your healthcare provider if you have changes in vision during treatment with OZEMPIC®.
- See “Low blood sugar (hypoglycemia)”. Your risk for getting low blood sugar may be higher if you use OZEMPIC® with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin. Signs and symptoms of low blood sugar may include:
  - dizziness or light-headedness
  - blurred vision
  - anxiety, irritability, or mood changes
  - sweating
  - confusion or drowsiness
  - headache
  - fast heartbeat
  - weakness
  - feeling jittery

- Kidney problems (kidney failure). In people who have kidney problems, diabetes, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse. It is important for you to drink fluids to help reduce your chance of dehydration.
- Serious allergic reactions. Stop using OZEMPIC® and get medical help right away if you have any symptoms of a serious allergic reaction including:
  - swelling of your face, lips, tongue or throat
  - severe rash or itching
  - problems breathing or swallowing
  - very rapid heartbeat

The most common side effects of OZEMPIC® may include:
- nausea, vomiting, diarrhea, stomach (abdominal) pain and constipation.

Talk to your healthcare provider about any side effect that bothers you or does not go away. These are not all the possible side effects of OZEMPIC®.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of OZEMPIC®.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use OZEMPIC® for a condition for which it was not prescribed. Do not give OZEMPIC® to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about OZEMPIC® that is written for health professionals.

For more information, go to OZEMPIC.com or call 1-888-693-6742.

What are the ingredients in OZEMPIC®?

Active Ingredient: semaglutide

Inactive Ingredients: disodium phosphate dihydrate, propylene glycol, phenol and water for injection

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 04/2021
Instructions for Use
OZEMPIC® (oh-ZEM-pick) (semaglutide) injection 0.25 mg or 0.5 mg doses
(pen delivers doses of 0.25 mg or 0.5 mg)

- Read these instructions carefully before using your OZEMPIC® pen.
- Do not use your pen without proper training from your healthcare provider. Make sure that you know how to give yourself an injection with the pen before you start your treatment.
- Do not share your OZEMPIC® pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

⚠️ If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the OZEMPIC® pen.

- Start by checking your pen to make sure that it contains OZEMPIC®, then look at the pictures below to get to know the different parts of your pen and needle.
- Your pen is a prefilled, single-patient-use, dial-a-dose pen. Your pen is made to be used with NovoFine® Plus or NovoFine® disposable needles up to a length of 8 mm.
- NovoFine® Plus 32G 4 mm disposable needles are included with your OZEMPIC® pen.
- Always use a new needle for each injection.

Supplies you will need to give your OZEMPIC® injection:
- OZEMPIC® pen
- a new NovoFine® Plus or NovoFine® needle
- 1 alcohol swab
- 1 gauze pad or cotton ball
- 1 sharps disposal container for throwing away used OZEMPIC® pens and needles. See "Disposing of used OZEMPIC® pens and needles" at the end of these instructions.

OZEMPIC® pen and NovoFine® Plus needle (example)

Step 1. Prepare your pen with a new needle

- Wash your hands with soap and water.
- Check the name and colored label of your pen, to make sure that it contains OZEMPIC®.
- This is especially important if you take more than 1 type of medicine.
- Pull off the pen cap.

Step 2. Check the OZEMPIC® flow with each new pen

- Check the OZEMPIC® flow before your first injection with each new pen.
- If your OZEMPIC® pen is already in use, go to Step 3 "Select your dose".
- Turn the dose selector until the dose counter shows the flow check symbol (•••). Do not reuse or share your needles with other people. You may give other people a serious infection, or get a serious infection from them.

Never use a bent or damaged needle.

Step 3. Select your dose

- Turn the dose selector until the dose counter shows your dose (0.25 mg or 0.5 mg).

The dashed line in the dose counter (1) will guide you to your dose. Make sure you know the dose of OZEMPIC® you should use. If you select the wrong dose, you can turn the dose selector forward or backwards to the correct dose.

Step 4. Hold the pen with the needle pointing up. Press and hold in the dose button until the dose counter shows 0. The 0 must line up with the dose pointer. A drop of OZEMPIC® will appear at the needle tip.

If no drop appears, repeat Step 2 above as shown in Figure G and Figure H up to 6 times. If there is still no drop, change the needle and repeat Step 2 as shown in Figure G and Figure H 1 more time.

Do not use the pen if a drop of OZEMPIC® still does not appear. Contact Novo Nordisk at 1-888-693-6742.

⚠️ Always make sure that a drop appears at the needle tip before you use a new pen for the first time. This makes sure that OZEMPIC® flows.

A small drop may remain at the needle tip, but it will not be injected.

Only check the OZEMPIC® flow before your first injection with each new pen.

Always make sure that a drop appears at the needle tip before you use a new pen for the first time. This makes sure that OZEMPIC® flows.

If no drop appears, you will not inject any OZEMPIC®, even though the dose counter may move. This may mean that there is a blocked or damaged needle.

Always use a new needle for each injection. This will reduce the risk of contamination, infection, leakage of OZEMPIC®, and blocked needles leading to the wrong dose.

Do not reuse or share your needles with other people. You may give other people a serious infection, or get a serious infection from them.

Never use a bent or damaged needle.

Always use the dose counter and the dose pointer to see how many mg you select.

You will hear a “click” every time you turn the dose selector. Do not set the dose by counting the number of clicks you hear.

Only doses of 0.25 mg or 0.5 mg can be selected with the dose selector. The selected dose must line up exactly with the dose pointer to make sure that you get a correct dose.

The dose selector changes the dose. Only the dose counter and dose pointer will show how many mg you select for each dose.

You can select 0.25 mg or 0.5 mg for each dose. When your pen contains less than 0.5 mg or 0.25 mg, the dose counter stops before 0.5 mg or 0.25 mg is shown.

The dose selector clicks differently when turned forward or backward. Do not count the pen clicks.
How much OZEMPIC® is left?

- To see how much OZEMPIC® is left in your pen, use the dose counter:
  - Turn the dose selector until the dose counter stops.
  - If it shows 0.5, at least 0.5 mg is left in your pen. If the dose counter stops before 0.5 mg, there is not enough OZEMPIC® left for a full dose of 0.5 mg.
  - If it stops at 0.25, then 0.25 mg is left in your pen. If the dose counter stops before 0.25 mg, there is not enough OZEMPIC® left for a full dose of 0.25 mg.

If there is not enough OZEMPIC® left in your pen for a full dose, do not use it. Use a new OZEMPIC® pen.

Step 4.

Inject your dose

- Choose your injection site and wipe the skin with an alcohol swab. Let the injection site dry before you inject your dose (See Figure K).

- Insert the needle into your skin as your healthcare provider has shown you.

- Make sure you can see the dose counter. Do not cover it with your fingers. This could stop the injection.

- Press and hold down the dose button until the dose counter shows 0.

  The O must line up with the dose pointer. You may then hear or feel a click.

- Keep the needle in your skin after the dose counter has returned to 0 and count slowly to 6.

  If the needle is removed earlier, you may see a stream of OZEMPIC® coming from the needle tip. If this happens, the full dose will not be delivered.

- Remove the needle from your skin.

  If blood appears at the injection site, press lightly with a gauze pad or cotton ball. Do not rub the area.

- Never try to put the inner needle cap back on the needle. You may stick yourself with the needle.

  Always remove the needle from your pen.

  This will reduce the risk of contamination, infection, leakage of OZEMPIC®, and blocked needles leading to the wrong dose. If the needle is blocked, you will not inject any OZEMPIC®.

- Always dispose of the needle after each injection.

- Disposing of used OZEMPIC® pens and needles:
  - Put your used OZEMPIC® pen in the sharps disposal container right away to prevent accidental needle stick injuries and prevent passing (transmission) of infection.
  - Do not use a syringe to withdraw OZEMPIC® from your pen.
  - Always carry an extra pen and new needles with you, in case of loss or damage.
  - Always keep your pen and needles out of reach of others, especially children.
  - Always keep your pen with you. Do not leave it in a car or other place where it can get too hot or too cold.

Caring for your pen

- Do not drop your pen or knock it against hard surfaces. If you drop it or suspect a problem, attach a new needle and check the OZEMPIC® flow before you inject.

- Do not try to repair your pen or pull it apart.

- Do not expose your pen to dust, dirt or liquid.

- Do not wash, soak, or lubricate your pen.

  If necessary, clean it with mild detergent on a moistened cloth.

How should I store my OZEMPIC® pen?

- Store your new, unused OZEMPIC® pens in the refrigerator between 36°F to 46°F (2°C to 8°C).

- Store your pen in use for 56 days at room temperature between 59°F to 86°F (15°C to 30°C) or in a refrigerator between 36°F to 46°F (2°C to 8°C).

- The OZEMPIC® pen you are using should be disposed of (thrown away) after 56 days, even if it still has OZEMPIC® left in it. Write the disposal date on your calendar.

- Do not freeze OZEMPIC®. Do not use OZEMPIC® if it has been frozen.

- Unused OZEMPIC® pens may be used until the expiration date (“EXP”) printed on the label, if kept in the refrigerator.

- When stored in the refrigerator, do not store OZEMPIC® pens directly next to the cooling element.

- Keep OZEMPIC® away from heat and out of the light.

- Keep the pen cap on when not in use.

- Keep OZEMPIC® and all medicines out of the reach of children.

For more information go to www.OZEMPIC.com

Manufactured by:
Novo Nordisk A/S
DK-2880 Bagsvaerd
Denmark
For information about OZEMPIC® contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainboro, NJ 08536
1-888-693-6742

Revised: 3/2020
Version: 3
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This Instructions for Use has been approved by the U.S. Food and Drug Administration.

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US21OZM00313 5/2021
Instructions for Use

OZEMPIC® (oh-ZEM-pick) (semaglutide) injection 1 mg dose (each pen delivers doses of 1 mg only)

- Read these instructions carefully before using your OZEMPIC® pen.
- Do not use your pen without proper training from your healthcare provider. Make sure that you know how to give yourself an injection with the pen before you start your treatment.
- Do not share your OZEMPIC® pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the OZEMPIC® pen.

- Start by checking your pen to make sure that it contains OZEMPIC®, then look at the pictures below to get to know the different parts of your pen and needle.

Your pen is a prefilled, single-patient-use, dial-a-dose pen. It contains 2 mg of semaglutide, and you can only select doses of 1 mg. Your pen is made to be used with OZEMPIC® Plus or NovoFine® disposable needles up to a length of 8 mm.

- NovoFine® Plus 32G 4 mm disposable needles are included with your OZEMPIC® pen.
- Always use a new needle for each injection.

Supplies you will need to give your OZEMPIC® injection:
- OZEMPIC® pen 1 mg dose
- a new NovoFine® Plus or NovoFine® needle
- 1 alcohol swab
- 1 gauze pad or cotton ball
- 1 sharps disposal container for throwing away used OZEMPIC® pens and needles. See “Disposing of used OZEMPIC® pens and needles” at the end of these instructions.

OZEMPIC® pen and NovoFine® Plus needle (example)

Step 1. Prepare your pen with a new needle

- Wash your hands with soap and water.
- Check the name and colored label of your pen, to make sure that it contains OZEMPIC®. This is especially important if you take more than 1 type of medicine.
- Pull off the pen cap.

Step 2. Check the OZEMPIC® flow with each new pen

- Check the OZEMPIC® flow before your first injection with each new pen.
- If your OZEMPIC® pen is already in use, go to Step 3 “Select your dose”.
- Turn the dose selector until the dose counter shows the flow check symbol (••••).

Step 3. Select your dose

- Turn the dose selector until the dose counter stops and shows your 1 mg dose.

The dashed line in the dose counter (•) will guide you to 1 mg.

- Hold the pen with the needle pointing up. Press and hold in the dose button until the dose counter shows 0. The 0 must line up with the dose pointer.
- A drop of OZEMPIC® will appear at the needle tip.
- If no drop appears, repeat Step 2 above as shown in Figure G and Figure H up to 6 times. If there is still no drop, change the needle and repeat Step 2 as shown in Figure G and Figure H 1 more time.

Always make sure that a drop appears at the needle tip before you use a new pen for the first time. This makes sure that OZEMPIC® flows. If no drop appears, you will not inject any OZEMPIC®, even though the dose counter may move. This may mean that there is a blocked or damaged needle.

A small drop may remain at the needle tip, but it will not be injected.

Only check the OZEMPIC® flow before your first injection with each new pen.

OZEMPIC® (semaglutide) injection, 1 mg dose, Instructions For Use
How much OZEMPIC® is left?

- To see how much OZEMPIC® is left in your pen, use the dose counter:
  - Turn the dose selector until the dose counter stops.
  - If it shows 1, at least 1 mg is left in your pen. If the dose counter stops before 1 mg, there is not enough OZEMPIC® left for a full dose of 1 mg.
  - If there is not enough OZEMPIC® left in your pen for a full dose, do not use it. Use a new OZEMPIC® pen.

How to identify a blocked or damaged needle?

- If 0 does not appear in the dose counter after continuously pressing the dose button, you may have used a blocked or damaged needle.
- If this happens you have not received any OZEMPIC® even though the dose counter has moved from the original dose that you have set.

How to handle a blocked needle?

- Change the needle as described in Step 5, and repeat all steps starting with Step 1. “Prepare your pen with a new needle”.
- Never touch the dose counter when you inject. This can stop the injection.
- You may see a drop of OZEMPIC® at the needle tip after injecting. This is normal and does not affect your dose.

Step 4.
Inject your dose

- Choose your injection site and wipe the skin with an alcohol swab. Let the injection site dry before you inject your dose (See Figure K).
- Insert the needle into your skin as your healthcare provider has shown you.
- Make sure you can see the dose counter. Do not cover it with your fingers. This could stop the injection.
- Press and hold down the dose button until the dose counter shows 0.
  - The 0 must line up with the dose pointer. You may then hear or feel a click.
- Keep the needle in your skin after the dose counter has returned to 0 and count slowly to 6.
  - If the needle is removed earlier, you may see a stream of OZEMPIC® coming from the needle tip. If this happens, the full dose will not be delivered.
- Remove the needle from your skin.
  - If blood appears at the injection site, press lightly with a gauze pad or cotton ball. Do not rub the area.

How to inject your dose

- Put the pen cap on your pen after each use to protect OZEMPIC® from light.
- Place the needle in a sharps disposal container right away to reduce the risk of needle sticks. See “Disposing of used OZEMPIC® pens and needles” below for more information about how to dispose of used pens and needles the right way.
- If you do not have a sharps disposal container, follow a 1-handed needle recap method. Carefully slip the needle into the outer needle cap. Dispose of the needle in a sharps disposal container as soon as possible.

Step 5.
After your injection

- Carefully remove the needle from the pen. Do not put the needle caps back on the needle to avoid needle sticks.
- Never try to put the inner needle cap back on the needle. You may stick yourself with the needle.
- Always remove the needle from your pen.
  - This will reduce the risk of contamination, infection, leakage of OZEMPIC®, and blocked needles leading to the wrong dose. If the needle is blocked, you will not inject any OZEMPIC®.
- Always dispose of the needle after each injection.

Disposing of used OZEMPIC® pens and needles:

- Put your used OZEMPIC® pen and needle in a FDA-cleared sharps disposal container right away after use.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out
  - upright and stable during use
  - leak-resistant
  - properly labeled to warn of hazardous waste inside the container
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at http://www.fda.gov/safesharpsdisposal
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.
- Always dispose of OZEMPIC® that is out of date or no longer needed.

Important

- Caregivers must be very careful when handling used needles to prevent accidental needle stick injuries and prevent passing (transmission) of infection.
- Never use a syringe to withdraw OZEMPIC® from your pen.
- Always carry an extra pen and new needles with you, in case of loss or damage.
- Always keep your pen and needles out of reach of others, especially children.
- Always keep your pen with you. Do not leave it in a car or other place where it can get too hot or too cold.

Caring for your pen

- Do not drop your pen or knock it against hard surfaces. If you drop it or suspect a problem, attach a new needle and check the OZEMPIC® flow before you inject.
- Do not try to repair your pen or pull it apart.
- Do not expose your pen to dust, dirt or liquid.
- Do not wash, soak, or lubricate your pen. If necessary, clean it with mild detergent on a moistened cloth.

How should I store my OZEMPIC® pen?

- Store your new, unused OZEMPIC® pens in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Store your pen in use for 56 days at room temperature between 59°F to 86°F (15°C to 30°C) or in a refrigerator between 36°F to 46°F (2°C to 8°C).
- The OZEMPIC® pen you are using should be disposed of (thrown away) after 56 days, even if it still has OZEMPIC® left in it. Write the disposal date on your calendar.
- Do not freeze OZEMPIC®. Do not use OZEMPIC® if it has been frozen.
- Unused OZEMPIC® pens may be used until the expiration date (“EXP”) printed on the label, if kept in the refrigerator.
- When stored in the refrigerator, do not store OZEMPIC® pens directly next to the cooling element.
- Keep OZEMPIC® away from heat and out of the light.
- Keep the pen cap on when not in use.
- Keep OZEMPIC® and all medicines out of the reach of children.

For more information go to www.OZEMPIC.com

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Instructions for Use
OZEMPIC® (oh-ZEM-pick) (semaglutide) injection
1 mg dose
(Pen delivers 4 doses of 1 mg only)

- Read these instructions carefully before using your OZEMPIC® pen.
- Do not use your pen without proper training from your healthcare provider. Make sure that you know how to give yourself an injection with the pen before you start your treatment.
- Do not share your OZEMPIC® pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the OZEMPIC® pen.

- Start by checking your pen to make sure that it contains OZEMPIC®, then look at the pictures below to get to know the different parts of your pen and needle.
- Your pen is a prefilled, single-patient-use, dial-a-dose pen. It contains 4 mg of semaglutide, and you can only select doses of 1 mg. Your pen is made to be used with NovoFine® Plus or NovoFine® disposable needles up to a length of 8 mm.
- NovoFine® Plus 32G 4 mm disposable needles are included with your OZEMPIC® pen.
- Always use a new needle for each injection.

Supplies you will need to give your OZEMPIC® injection:
- OZEMPIC® pen 1 mg dose
- a new NovoFine® Plus or NovoFine® needle
- 1 alcohol swab
- 1 gauze pad or cotton ball
- 1 sharps disposal container for throwing away used OZEMPIC® pens and needles. See “Disposing of used OZEMPIC® pens and needles” at the end of these instructions.

OZEMPIC® pen and NovoFine® Plus needle (example)

Step 1.
Prepare your pen with a new needle
- Wash your hands with soap and water.
- Check the name and colored label of your pen, to make sure that it contains OZEMPIC®. This is especially important if you take more than 1 type of medicine.
- Pull off the pen cap.

Step 2.
Check the OZEMPIC® flow with each new pen
- Check the OZEMPIC® flow before your first injection with each new pen.
  If your OZEMPIC® pen is already in use, go to Step 3 "Select your dose".
- Turn the dose selector until the dose counter shows the flow check symbol (•••••).

Step 3.
Select your dose
- Turn the dose selector until the dose counter shows your 1 mg dose.
  The dashed line in the dose counter (1) will guide you to 1 mg.

Always use the dose counter and the dose pointer to see that 1 mg has been selected.
You will hear a “click” every time you turn the dose selector. Do not set the dose by counting the number of clicks you hear.
Only doses of 1 mg can be selected with the dose selector. 1 mg must line up exactly with the dose pointer to make sure that you get a correct dose.
The dose selector changes the dose. Only the dose counter and dose pointer will show that 1 mg has been selected.
You can only select 1 mg for each dose. When your pen contains less than 1 mg, the dose counter stops before 1 mg is shown.
The dose selector clicks differently when turned forward or backward. Do not count the pen clicks.
How much OZEMPIC® is left?
• To see how much OZEMPIC® is left in your pen, use the dose counter:
  Turn the dose selector until the dose counter stops.
  • If it shows 1, at least 1 mg is left in your pen. If the dose counter stops before 1 mg, there is not enough OZEMPIC® left for a full dose of 1 mg.

If there is not enough OZEMPIC® left in your pen for a full dose, do not use it. Use a new OZEMPIC® pen.

Step 4.
Inject your dose
• Choose your injection site and wipe the skin with an alcohol swab. Let the injection site dry before you inject your dose (See Figure K).

How much OZEMPIC® is left?
• Insert the needle into your skin as your healthcare provider has shown you.

How to identify a blocked or damaged needle?
• Make sure you can see the dose counter.
  • Do not cover it with your fingers. This could stop the injection.

Always carry an extra pen and new needles with you, in case of loss or damage.
Always keep your pen and needles out of reach of others, especially children.
Always keep your pen with you. Do not leave it in a car or other place where it can get too hot or too cold.

Caring for your pen
• Do not drop your pen or knock it against hard surfaces.
  • If you drop it or suspect a problem, attach a new needle and check the OZEMPIC® flow before you inject.
• Do not try to repair your pen or pull it apart.
• Do not expose your pen to dust, dirt or liquid.
• Do not wash, soak, or lubricate your pen. If necessary, clean it with mild detergent on a moistened cloth.

How should I store my OZEMPIC® pen?
• Store your new, unused OZEMPIC® pens in the refrigerator between 36°F to 46°F (2°C to 8°C).
• Store your pen in use for 56 days at room temperature between 59°F to 86°F (15°C to 30°C) or in a refrigerator between 36°F to 46°F (2°C to 8°C).
• The OZEMPIC® pen you are using should be disposed of (thrown away) after 56 days, even if it still has OZEMPIC® left in it. Write the disposal date on your calendar.
• Do not freeze OZEMPIC®. Do not use OZEMPIC® if it has been frozen.
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