WARNINGS AND PRECAUTIONS

- Personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2 (4).
- Known hypersensitivity to OZEMPIC® or any of the product components (4).

- Pancreatitis: Has been reported in clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed (5.2).
- Diabetic Retinopathy Complications: Has been reported in a clinical trial. Patients with a history of diabetic retinopathy should be monitored (5.3).
- Never share an OZEMPIC® pen between patients, even if the needle is changed (5.4).
- Hypoglycemia: When OZEMPIC® is used with an insulin secretagogue or insulin, consider lowering the dose of the secretagogue or insulin to reduce the risk of hypoglycemia (5.5).
- Acute Kidney Injury: Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions (5.6).
- Hypersensitivity Reactions: Discontinue OZEMPIC® if suspected and promptly seek medical advice (5.7).
- Macrovascular outcomes: There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with semaglutide (5.6).

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.
**1 INDICATIONS AND USAGE**

**OZEMPIC®** 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)).

**Limitations of Use**

- **OZEMPIC®** is not recommended as a first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of rodent C-cell tumor findings to humans (see Warnings and Precautions (5.1)).
- **OZEMPIC®** has not been studied in patients with a history of pancreatitis. Consider other anti-diabetic therapies in patients with a history of pancreatitis (see Warnings and Precautions (5.2)).
- **OZEMPIC®** is not a substitute for insulin. **OZEMPIC®** is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would pose a risk for transmission of blood-borne pathogens.

**2 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 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: 2 mg/1.5 mL (1.34 mg/mL) of semaglutide as a clear, colorless solution available in:
- **Pre-filled, disposable, single-patient-use pen** that delivers 0.25 mg (for treatment initiation) or 0.5 mg (for maintenance treatment) per injection
- **Pre-filled, disposable, single-patient-use pen** that delivers 1 mg (for maintenance treatment) per injection.

**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)).
- Known hypersensitivity to semaglutide or to any of the product components (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 tiraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports is 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 (0.27 cases per 100 patient years) versus 3 in comparator-treated patients (0.22 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®** (3.0%) 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**

The risk of hypoglycemia is increased when **OZEMPIC®** is used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. Patients may require a lower dose of the secretagogue or insulin to reduce the risk of hypoglycemia in this setting (see Adverse Reactions (6.1), Drug Interactions (7.1)).

**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, or 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 with GLP-1 receptor agonists. 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)).

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®**.

**5.8 Macrovascular Outcomes**

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction 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 ≥90 mL/min/1.73m²) in 57%, mildly impaired (eGFR 60 to 90 mL/min/1.73m²) in 35% 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 ≥90 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.

Common Adverse Reactions

Table 1 shows common adverse reactions, excluding hypoglycemia, associated with the use of OZEMPIC® in the pool of placebo-controlled trials. These adverse reactions occurred more commonly on OZEMPIC® than on placebo, and occurred in at least 5% of patients treated with OZEMPIC®.

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=262)</th>
<th>OZEMPIC® 0.5 mg (N=260)</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 (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>N (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>
<tr>
<td>Add-on to Basal Insulin with or without Metformin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (weeks)</td>
<td>N=132</td>
<td>N=132</td>
<td>N=131</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>15.2%</td>
<td>16.7%</td>
<td>29.8%</td>
</tr>
<tr>
<td>Severe* or Blood Glucose Confirmed Symptomatic (≤56 mg/dL glucose threshold)</td>
<td>5.3%</td>
<td>8.3%</td>
<td>10.7%</td>
</tr>
</tbody>
</table>

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

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 18 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 dippeptidyl-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 C₁₅₁H₂₁₀₁N₈₀O₃₉ and the molecular weight is 4113.58 g/mol.
Glucose dependent insulin and glucagon secretion

Semaglutide lowers high blood glucose concentrations by stimulating insulin secretion and lowering glucagon secretion in a glucose-dependent manner. With semaglutide, the insulin secretion rate in patients with type 2 diabetes was similar to that of healthy subjects (see Figure 2).

Figure 2. Mean insulin secretion rate versus glucose concentration in patients with type 2 diabetes during graded glucose infusions 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 of 1.5 times the maximum recommended dose, semaglutide does not prolong QTc intervals to any clinically relevant extent.

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 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 is 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.

Figure 3. Impact of intrinsic factors on semaglutide exposure

- **Intrinsic factor**: Relative exposure (Cavg) Ratio and 90% CI

- **Sex**: Male

- **Age**: 65-74 years

- **Race**: Black or African American

- **Ethnicity**: Hispanic or Latino

- **Body weight**: 55 kg

- **Renal impairment**: Mild

Semaglutide exposure (Cavg) relative to reference subject profile: non-Hispanic/non-Latino, White, female below 65 years, body weight 65 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

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 the evaluated medications; therefore, no dose adjustment is required when co-administered with semaglutide.

Figure 4. Impact of semaglutide on the exposure of co-administered oral medications

Relative exposure in terms of AUC and Cmax for each medication when given with semaglutide compared to without semaglutide. Metformin and oral contraceptive drug (ethinyl estradiol/levonorgestrel) were assessed at steady state. Warfarin (S-warfarin/R-warfarin), digoxin and atorvastatin were assessed after a single dose. Abbreviations: AUC: area under the curve. Cmax: maximum concentration. CI: confidence interval.

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 dose levels (≥2X 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 estrous 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 adaptive response secondary to the pharmacological effect of semaglutide on food consumption and body weight.

14 CLINICAL STUDIES

14.1 Overview of Clinical Studies

OZEMPIC® has been studied as monotherapy and in combination with metformin, metformin and sulfonylurea, metformin and/or thiazolidinedione, and basal insulin in patients with type 2 diabetes mellitus. The efficacy of OZEMPIC® was evaluated using multiple imputation. Missing data were imputed using multiple imputation based on retrieved dropouts.

Most trials evaluated the use of OZEMPIC® 0.5 mg, and 1 mg, with the exception of the trials comparing OZEMPIC® and exenatide ER where only the 1 mg dose was studied.

In patients with type 2 diabetes mellitus, OZEMPIC® produced clinically relevant reduction from baseline in HbA1c, compared to placebo. The efficacy of OZEMPIC® was not impacted by age, gender, race, ethnicity, BMI at baseline, body weight, gender, race, ethnicity, BMI at baseline, body weight.

14.2 Monotherapy Use of OZEMPIC® in Patients with Type 2 Diabetes Mellitus

In a 30-week double-blind trial (NCT02054897), 388 patients with type 2 diabetes mellitus inadequately controlled with diet and exercise were randomized to OZEMPIC® 0.5 mg or OZEMPIC® 1 mg once weekly or placebo. Patients had a mean age of 54 years and 54% were men. The mean duration of type 2 diabetes was 4.2 years, and the mean BMI was 33 kg/m². Overall, 64% were White, 8% 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 3. Results at Week 30 in a Trial of OZEMPIC® as Monotherapy in Adult Patients with Type 2 Diabetes Mellitus Inadequately Controlled with Diet and Exercise

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>OZEMPIC® 0.5 mg</th>
<th>OZEMPIC® 1 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treat (ITT) Population (N)a</td>
<td>129</td>
<td>128</td>
<td>130</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.0</td>
<td>8.1</td>
<td>8.1</td>
</tr>
<tr>
<td>Baseline (mean)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change at week 30b</td>
<td>-0.1</td>
<td>-1.4</td>
<td>-1.6</td>
</tr>
<tr>
<td>Difference from placebob [95% CI]</td>
<td>-1.2 [-1.5, -0.9]</td>
<td>-1.4 [-1.7, -1.1]</td>
<td></td>
</tr>
<tr>
<td>Patients (%) achieving HbA1c &lt;7%</td>
<td>28</td>
<td>73</td>
<td>70</td>
</tr>
<tr>
<td>FPG (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (mean)</td>
<td>174</td>
<td>174</td>
<td>179</td>
</tr>
<tr>
<td>Change at week 30b</td>
<td>-15</td>
<td>-41</td>
<td>-44</td>
</tr>
</tbody>
</table>

aIntent-to-treatment population includes all randomized and exposed patients. At week 30, the primary HbA1c endpoint was missing for 10%, 7% and 7% of patients and during the trial rescue medication was initiated by 20%, 5% and 4% of patients randomized to placebo, OZEMPIC® 0.5 mg and OZEMPIC® 1 mg, respectively. Missing data were imputed using multiple imputation based on retrieved dropouts.

bThe intent-to-treatment analysis using ANCOVA adjusted for baseline value and country.

The mean baseline body weight was 89.1 kg, 89.8 kg, and 96.9 kg in the placebo, OZEMPIC® 0.5 mg, and OZEMPIC® 1 mg arms, respectively. The mean changes from baseline to week 30 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].

14.3 Combination Therapy Use of OZEMPIC® in Patients with Type 2 Diabetes Mellitus

Combination with metformin and/or thiazolidinediones

In a 56-week, double-blind trial (NCT01930188), 1231 patients with type 2 diabetes mellitus were randomized to OZEMPIC® 0.5 mg, OZEMPIC® 1 mg, and exenatide extended-release (ER), and insulin glargine. The intent-to-treatment population includes all randomized and exposed patients. At week 56 the primary HbA1c endpoint was missing for 8%, 5% and 6% of patients and during the trial rescue medication was initiated by 5%, 2% and 19% of patients randomized to OZEMPIC® 0.5 mg, OZEMPIC® 1 mg and sitagliptin, respectively. Missing data were imputed using multiple imputation based on retrieved dropouts.

The mean baseline body weight was 89.2 kg, 89.3 kg in the OZEMPIC® 0.5 mg, OZEMPIC® 1 mg, and sitagliptin arms, respectively. The mean changes from baseline to week 56 were -4.2 kg, -5.5 kg, and -1.7 kg for the OZEMPIC® 0.5 mg, OZEMPIC® 1 mg, and sitagliptin arms, respectively. The difference from sitagliptin [95% CI] for OZEMPIC® 0.5 mg was -2.5 kg [-3.2, -1.8], and for OZEMPIC® 1 mg was -3.6 kg [-4.5, -3.1].

### Table 4. Results at Week 56 in a Trial of OZEMPIC® Compared to Sitagliptin in Adult Patients with Type 2 Diabetes Mellitus In Combination with Metformin and/or Thiazolidinediones

<table>
<thead>
<tr>
<th></th>
<th>OZEMPIC® 0.5 mg</th>
<th>OZEMPIC® 1 mg</th>
<th>Sitagliptin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treat (ITT) Population (N)a</td>
<td>409</td>
<td>409</td>
<td>407</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (mean)</td>
<td>8.0</td>
<td>8.0</td>
<td>8.2</td>
</tr>
<tr>
<td>Change at week 56b</td>
<td>-1.3</td>
<td>-1.5</td>
<td>-0.7</td>
</tr>
<tr>
<td>Difference from sitagliptinb [95% CI]</td>
<td>-0.6 [-0.7, -0.4]</td>
<td>-0.8 [-0.9, -0.6]</td>
<td></td>
</tr>
<tr>
<td>Patients (%) achieving HbA1c &lt;7%</td>
<td>66</td>
<td>73</td>
<td>40</td>
</tr>
<tr>
<td>FPG (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (mean)</td>
<td>168</td>
<td>167</td>
<td>173</td>
</tr>
<tr>
<td>Change at week 56b</td>
<td>-35</td>
<td>-43</td>
<td>-23</td>
</tr>
</tbody>
</table>

aThe intent-to-treatment population includes all randomized and exposed patients. At week 56 the primary HbA1c endpoint was missing for 5% and 6% of patients and during the trial rescue medication was initiated by 5% and 10% of patients randomized to OZEMPIC® 0.5 mg, OZEMPIC® 1 mg and exenatide, respectively. Missing data were imputed using multiple imputation based on retrieved dropouts.

bThe intent-to-treatment analysis using ANCOVA adjusted for baseline value and country.

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

SUSTAIN 6 (NCT01720446) was a 104-week, double-blind trial in which 3,257 patients with type 2 diabetes and high risk of cardiovascular events were randomized to OZEMPIC® 0.5 mg once weekly, OZEMPIC® 1 mg once weekly, or placebo in addition to standard-of-care. In total, 7,735 (83%) of the patients had a history of cardiovascular disease and 562 (17%) were at high risk but without known cardiovascular disease. The mean age at baseline was 65 years, and 61% were men. The mean duration of diabetes was 13.9 years, and mean BMI was 33 kg/m². Overall, 83% were White, 7% were Black or African American, and 8% were Asian; 16% identified as Hispanic or Latino ethnicity. Concomitant diseases of patients in this trial included, but were not limited to, heart failure (24%), hypertension (93%), history of ischemic stroke (12%) and history of a myocardial infarction (33%).

In total, 98.0% of the patients completed the trial and the vital status was known at the end of the trial for 99.6%. The primary composite endpoint was the time from randomization to first occurrence of a major adverse cardiovascular event (MACE): cardiovascular death, non-fatal myocardial infarction or non-fatal stroke. The secondary endpoint was time from randomization to first occurrence of an expanded composite cardiovascular outcome, defined as MACE, revascularization (coronary and peripheral), unstable angina requiring hospitalization or hospitalization for heart failure. The total number of primary component MACE endpoints was 254 (108 [6.6%] with OZEMPIC® and 146 [8.9%] with placebo). No increased risk for MACE was observed with OZEMPIC®.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

OZEMPIC® injection is supplied as a clear, colorless solution that contains 2 mg of semaglutide in a 1.5 mL (1.34 mg/mL) pre-filled, disposable, single-patient-use pen injector in the following packaging configurations:

- Carton of 1 Pen (NDC 0169-4132-12)
  - Pen delivers doses of 0.25 mg or 0.5 mg per injection
  - 6 NovoFine® Plus needles
  - Intended for treatment initiation at the 0.25 mg dose and maintenance treatment at the 0.5 mg dose

- Carton of 2 Pens (NDC 0169-4136-02)
  - Pen delivers doses of 1 mg per injection
  - 4 NovoFine® Plus needles
  - Intended for maintenance treatment at the 1 mg dose only

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 8). 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.

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 8:

Table 8. 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>Room Temperature</td>
</tr>
<tr>
<td>59°F to 86°F</td>
<td>59°F to 86°F</td>
</tr>
<tr>
<td>(15°C to 30°C)</td>
<td>(15°C to 30°C)</td>
</tr>
</tbody>
</table>

17 PATIENT COUNSELING INFORMATION

Advises patients 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

Advises 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)).

---

**Table 7. Results at Week 30 in a Trial of OZEMPIC® in Adult Patients with Type 2 Diabetes Mellitus in Combination with Metformin or Metformin with Sulfonylurea**

<table>
<thead>
<tr>
<th>OZEMPIC® 0.5 mg</th>
<th>OZEMPIC® 1 mg</th>
<th>Insulin Glargine</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>HbA1c (%)</td>
<td>HbA1c (%)</td>
</tr>
<tr>
<td>Baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>8.1</td>
<td>8.1</td>
<td>8.1</td>
</tr>
<tr>
<td>Baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>Change at week 30</td>
<td>-1.7</td>
<td>-0.9</td>
</tr>
<tr>
<td>Difference from insulin glargine</td>
<td>-0.3 [0.5, -0.7]</td>
<td>-0.4 [0.8, -0.4]</td>
</tr>
<tr>
<td>(%) achieving HbA1c &lt;7%</td>
<td>55%</td>
<td>56%</td>
</tr>
<tr>
<td>FPG (mg/dL)</td>
<td>172</td>
<td>174</td>
</tr>
<tr>
<td>Change at week 30</td>
<td>-35</td>
<td>-37</td>
</tr>
</tbody>
</table>

---

**Table 8. 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>Room Temperature</td>
</tr>
<tr>
<td>59°F to 86°F</td>
<td>59°F to 86°F</td>
</tr>
<tr>
<td>(15°C to 30°C)</td>
<td>(15°C to 30°C)</td>
</tr>
</tbody>
</table>

---

**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>OZEMPIC® 0.5 mg</th>
<th>OZEMPIC® 1 mg</th>
<th>Insulin Glargine</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>HbA1c (%)</td>
<td>HbA1c (%)</td>
</tr>
<tr>
<td>Baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>8.1</td>
<td>8.2</td>
<td>8.1</td>
</tr>
<tr>
<td>Baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>Change at week 30</td>
<td>-1.2</td>
<td>-1.5</td>
</tr>
<tr>
<td>Difference from insulin glargine</td>
<td>-0.3 [-0.5, -0.1]</td>
<td>-0.4 [-0.8, -0.4]</td>
</tr>
<tr>
<td>(%) achieving HbA1c &lt;7%</td>
<td>55%</td>
<td>56%</td>
</tr>
<tr>
<td>FPG (mg/dL)</td>
<td>172</td>
<td>174</td>
</tr>
<tr>
<td>Change at week 30</td>
<td>-35</td>
<td>-37</td>
</tr>
</tbody>
</table>
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 to stop taking OZEMPIC® and seek medical advice promptly if symptoms of hypersensitivity reactions 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)].

Instructions
Inform patients of the potential risks and benefits of OZEMPIC® and of alternative modes of therapy. Inform patients about the importance of adherence to dietary instructions, regular physical activity, periodic blood glucose monitoring and A1c testing, recognition and management of hypoglycemia and hyperglycemia, and assessment for diabetes complications. Advise patients to seek medical advice promptly during periods of stress such as fever, trauma, infection, or surgery as medication requirements may change.

Advise patients that the most common side effects of OZEMPIC® are nausea, vomiting, diarrhea, abdominal pain and constipation. Inform patients that nausea, vomiting and diarrhea are most common when first starting OZEMPIC®, but decreases over time in the majority of patients.

Instruct patients to reread the Medication Guide each time the prescription is renewed.

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)].
Medication Guide
OZEMPIC® (oh-ZEM-pick)
(semaglutide) injection, for subcutaneous use

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.

Read this Medication Guide before you start using OZEMPIC® and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about OZEMPIC®?
OZEMPIC® may cause serious side effects, including:

• Possible thyroid tumors, including cancer. Tell your healthcare provider if you get a lump or swelling in your neck, hoarseness, trouble swallowing, or shortness of breath. These may be symptoms of thyroid cancer. In studies with rodents, OZEMPIC® and medicines that work like OZEMPIC® caused thyroid tumors, including thyroid cancer. It is not known if OZEMPIC® will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people.
• 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 type 2 (MEN 2).

What is OZEMPIC®?
OZEMPIC® is an injectable prescription medicine for adults with type 2 diabetes mellitus that:
• along with diet and exercise may improve blood sugar (glucose).
• OZEMPIC® is not recommended as the first choice of medicine for treating diabetes.
• It is not known if OZEMPIC® can be used in people who have had pancreatitis.
• OZEMPIC® is not a substitute for insulin and is not for use in people with type 1 diabetes or people with diabetic ketoacidosis.
• 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 are allergic to semaglutide or any of the ingredients in OZEMPIC®. See the end of this Medication Guide for a complete list of ingredients in OZEMPIC®.

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 sulfonylurias.

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®?”
• 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.
• changes in vision. Tell your healthcare provider if you have changes in vision during treatment with OZEMPIC®.
• 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:
  o dizziness or light-headedness
  o sweating
  o confusion or drowsiness
  o headache
  o fast heartbeat
  o feeling jittery
• kidney problems (kidney failure). In people who have kidney problems, diarrhea, 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 itching, rash, or difficulty breathing.

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

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.
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 dial-a-dose pen. Your pen is trained to use the OZEMPIC® pen. Without help.
- You can select doses of 0.25 mg or 0.5 mg for each dose. When your pen is clear and colorless, you can select doses of 0.25 mg or 0.5 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 enclosed.
- 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
  - alcohol swab
  - 1 sharps 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)**

<table>
<thead>
<tr>
<th>Pen window</th>
<th>Dose counter</th>
<th>Dose selector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pen cap</td>
<td>Dose pointer</td>
<td>Dose button</td>
</tr>
<tr>
<td>Flow check symbol</td>
<td>Dashed line used to guide to your dose</td>
<td></td>
</tr>
<tr>
<td>Outer needle cap</td>
<td>Inner needle cap</td>
<td>Needle</td>
</tr>
<tr>
<td>Paper tab</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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 that OZEMPIC® in your pen is clear and colorless. Look through the pen window. If OZEMPIC® looks cloudy, do not use the pen.
- Take a new needle, and tear off the paper tab.
- Push the needle straight onto the pen. Turn until it is on tight.
- Pull off the outer needle cap. Do not throw it away.

**Step 3. Select your dose**

- Pull off the inner needle cap and throw it away. A drop of OZEMPIC® may appear at the needle tip. This is normal, but you must still check the OZEMPIC® flow, if you use a new pen for the first time.
- 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 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.
- Contact Novo Nordisk at 1-888-693-6742.

**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.

Do not attach a new needle to your pen until you are ready to take your injection.

**Step 4. Injection**

- 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.

**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 must 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, backwards or past the number of mg left. Do not count the pen clicks.

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OZEMPIC®, OH-ZEM-pick®, OZEMPIC® Plus or OZEMPIC® Plus needle (example)}
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.

Always watch the dose counter to know how many mg you inject. Hold the dose button down until the dose counter shows 0.

How to identify a blocked or damaged needle?
- If it 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”. Make sure you select the full dose you need.

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 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.

- Place the needle in a sharps 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.

- Put the pen cap on your pen after each use to protect OZEMPIC® from light.

- If you do not have a sharps container, follow a 1-handed needle recap method. Carefully slip the needle into the outer needle cap. Dispose of the needle in a sharps container as soon as possible.

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.
- Safely 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 at 36°F to 46°F (2°C to 8°C).
- Store your pen in use for 56 days below 86°F (30°C) or in a refrigerator at 36°F to 46°F (2°C to 8°C).
- The OZEMPIC® pen you are using should be thrown away after 56 days, even if it still has OZEMPIC® left in it.
- Do not freeze OZEMPIC®. Do not use OZEMPIC® if it has been frozen.
- Unused OZEMPIC® pens may be used until the expiration date printed on the label, if kept in the refrigerator.
- 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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For information about OZEMPIC® contact:
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This Instructions for Use has been approved by the U.S. Food and Drug Administration.

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Instructions for Use

OZEMPIC® (oh-ZEM-pick) (semaglutide) injection

- 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 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 NovoFine® Plus or NovoFine® disposable needles up to a length of 8 mm.
- NovoFine® Plus 32G 4 mm disposable needles are enclosed.
- 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
  - alcohol swab
  - 1 sharps container for throwing away used OZEMPIC® pens and needles.

See “Disposing of used OZEMPIC® pens and needles” at the end of these instructions.

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 that OZEMPIC® in your pen is clear and colorless. Look through the pen window. If OZEMPIC® looks cloudy, do not use the pen.
- Take a new needle, and tear off the paper tab.
- Pull off the outer needle cap. Do not throw it away.
- Pull off the inner needle cap and throw it away. A drop of OZEMPIC® may appear at the needle tip. This is normal, but you must still check the OZEMPIC® flow, if you use a new pen for the first time.
- Pull the needle straight onto the pen. Turn until it is on tight.

Step 3.
Select your dose

- 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® 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. 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.

- Continue turning the dose selector until the dose counter stops and 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 must 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, backwards or past 1 mg. 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.

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”. Make sure you select the full dose you need.

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. 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.

Dispensing 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
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  - properly labeled to warn of hazardous waste inside the container

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• The OZEMPIC® pen you are using should be thrown away after 56 days, even if it still has OZEMPIC® left in it.
• Do not freeze OZEMPIC®. Do not use OZEMPIC® if it has been frozen.
• Unused OZEMPIC® pens may be used until the expiration date printed on the label, if kept in the refrigerator.
• 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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