

# OZEMPI<sup>®</sup>

## semaglutide injection 0.5mg, 1mg, 2mg

### HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OZEMPI<sup>®</sup> safely and effectively. See full prescribing information for OZEMPI<sup>®</sup>.

OZEMPI<sup>®</sup> (semaglutide) injection, for subcutaneous use

Initial U.S. Approval: 2017

#### WARNING: RISK OF THYROID C-CELL TUMORS

*See full prescribing information for complete boxed warning.*

- In rodents, semaglutide causes thyroid C-cell tumors. It is unknown whether OZEMPI<sup>®</sup> causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as the human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined (5.1, 13.1).
- OZEMPI<sup>®</sup> 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).

### RECENT MAJOR CHANGES

Indication and Usage (1)	1/2025
Dosage and Administration (2.2)	1/2025
Warnings and Precautions,	
Severe Gastrointestinal Adverse Reactions (5.7)	10/2025
Pulmonary Aspiration During General Anesthesia or Deep Sedation (5.10)	1/2025

### INDICATIONS AND USAGE

OZEMPI<sup>®</sup> 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)
- to reduce the risk of sustained eGFR decline, end-stage kidney disease and cardiovascular death in adults with type 2 diabetes mellitus and chronic kidney disease. (1)

### DOSAGE AND ADMINISTRATION

- Administer once weekly at any time of day, with or without meals. (2.1)
- Start at 0.25 mg once weekly. After 4 weeks, increase the dosage to 0.5 mg once weekly. (2.2)
- If additional glycemic control is needed, increase the dosage to 1 mg once weekly after at least 4 weeks on the 0.5 mg dose. (2.2)
- If additional glycemic control is needed, increase the dosage to 2 mg once weekly after at least 4 weeks on the 1 mg dosage. (2.2)
- To reduce the risk of sustained eGFR decline, end-stage kidney disease and cardiovascular death, increase the dosage to 1 mg once weekly after at least 4 weeks on the 0.5 mg dosage. (1, 2.2)
- If a dose is missed, administer within 5 days of missed dose. (2.1)
- Inject subcutaneously in the abdomen, thigh, or upper arm. (2.1)

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

### DOSAGE FORMS AND STRENGTHS

Injection: 2 mg/3 mL (0.68 mg/mL) available in:

- Single-patient-use pen that delivers 0.25 mg or 0.5 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)

Injection: 8 mg/3 mL (2.68 mg/mL) available in:

- Single-patient-use pen that delivers 2 mg per injection (3)

### CONTRAINDICATIONS

- Personal or family history of MTC or in patients with MEN 2. (4)
- Serious hypersensitivity reaction to semaglutide or any of the excipients in OZEMPI<sup>®</sup>. (4)

### WARNINGS AND PRECAUTIONS

- Acute Pancreatitis:** Has been observed in patients treated with GLP-1 receptor agonists, including semaglutide. Discontinue if pancreatitis is suspected. (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 OZEMPI<sup>®</sup> pen between patients**, even if the needle is changed. (5.4)
- Hypoglycemia:** Concomitant use with an insulin secretagogue or insulin may increase the risk of hypoglycemia, including severe hypoglycemia. Reducing dose of insulin secretagogue or insulin may be necessary. (5.5)
- Acute Kidney Injury Due to Volume Depletion:** Monitor renal function in patients reporting adverse reactions that could lead to volume depletion. (5.6)
- Severe Gastrointestinal Adverse Reactions:** Use has been associated with gastrointestinal adverse reactions, sometimes severe. OZEMPI<sup>®</sup> is not recommended in patients with severe gastroparesis. (5.7)
- Hypersensitivity Reactions:** Serious hypersensitivity reactions (e.g., anaphylaxis and angioedema) have been reported. Discontinue OZEMPI<sup>®</sup> if suspected and promptly seek medical advice. (5.8)
- Acute Gallbladder Disease:** If cholelithiasis or cholecystitis are suspected, gallbladder studies are indicated. (5.9)
- Pulmonary Aspiration During General Anesthesia or Deep Sedation:** Has been reported in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures. Instruct patients to inform healthcare providers of any planned surgeries or procedures. (5.10)

### ADVERSE REACTIONS

The most common adverse reactions, reported in ≥5% of patients treated with OZEMPI<sup>®</sup> 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](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

**Oral Medications:** OZEMPI<sup>®</sup> delays gastric emptying. May impact absorption of concomitantly administered oral medications. Use with caution. (7.2)

### USE IN SPECIFIC POPULATIONS

**Females and Males of Reproductive Potential:** Discontinue OZEMPI<sup>®</sup> 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: 10/2025

**FULL PRESCRIBING INFORMATION****WARNING: RISK OF THYROID C-CELL TUMORS**

- In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether OZEMPI<sup>®</sup> 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 [see Warnings and Precautions (5.1), Nonclinical Toxicology (13.1)].**
- OZEMPI<sup>®</sup> is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) [see Contraindications (4)]. Counsel patients regarding the potential risk for MTC with the use of OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> [see Contraindications (4), Warnings and Precautions (5.1)].**

**1 INDICATIONS AND USAGE**OZEMPI<sup>®</sup> is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- 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.
- to reduce the risk of sustained eGFR decline, end-stage kidney disease, and cardiovascular death in adults with type 2 diabetes mellitus and chronic kidney disease.

**2 DOSAGE AND ADMINISTRATION****2.1 Important Administration Instructions**

- Inspect OZEMPI<sup>®</sup> visually before use. It should appear clear and colorless. Do not use OZEMPI<sup>®</sup> if particulate matter and coloration is seen.
- Administer OZEMPI<sup>®</sup> once weekly, on the same day each week, at any time of the day, with or without meals.
- Inject OZEMPI<sup>®</sup> subcutaneously in the abdomen, thigh, or upper arm. Instruct patients to use a different injection site each week when injecting in the same body region.
- When using OZEMPI<sup>®</sup> with insulin, instruct patients to administer as separate injections and to never mix the products. It is acceptable to inject OZEMPI<sup>®</sup> and insulin in the same body region, but the injections should not be adjacent to each other.
- 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 OZEMPI<sup>®</sup> 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 Recommended Dosage****Recommended Initiation Dosage**

Initiate OZEMPI<sup>®</sup> with a dosage of 0.25 mg injected subcutaneously once weekly for 4 weeks. Follow the dosage escalation below to reduce the risk of gastrointestinal adverse reactions [see Warnings and Precautions (5.7), Adverse Reactions (6.1)].

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

**Recommended Maintenance and Maximum Dosages for Glycemic Control**

The recommended maintenance dosage is 0.5 mg, 1 mg, or 2 mg, injected subcutaneously once weekly, based on glycemic control.

If additional glycemic control is needed after at least 4 weeks on the:

- 0.5 mg dosage, the dosage may be increased to 1 mg once weekly.
- 1 mg dosage, the dosage may be increased to 2 mg once weekly.

The maximum recommended dosage is 2 mg once weekly.

**Recommended Maintenance Dosage in Patients with Type 2 Diabetes Mellitus and Chronic Kidney Disease**

Increase the dosage to the maintenance dosage, 1 mg once weekly, after at least 4 weeks on the 0.5 mg dosage.

**3 DOSAGE FORMS AND STRENGTHS**

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

Dose per Injection	Total Strength per Total Volume	Strength per mL
0.25 mg	2 mg / 3 mL	0.68 mg/mL
0.5 mg	4 mg / 3 mL	1.34 mg/mL
1 mg	8 mg / 3 mL	2.68 mg/mL
2 mg	16 mg / 3 mL	5.36 mg/mL

The 2 mg/1.5 mL (1.34 mg/mL) strength is not currently marketed by Novo Nordisk Inc.

**4 CONTRAINDICATIONS**

OZEMPI<sup>®</sup> is contraindicated in patients with:

- A personal or family history of MTC or in patients with MEN 2 [see Warnings and Precautions (5.1)].
- A serious hypersensitivity reaction to semaglutide or to any of the excipients in OZEMPI<sup>®</sup>. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with OZEMPI<sup>®</sup> [see Warnings and Precautions (5.8)].

**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 OZEMPI<sup>®</sup> causes thyroid C-cell tumors, including 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.

OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup>. Such monitoring may increase the risk of unnecessary procedures, due to the low-test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin value may indicate MTC and patients with MTC usually have calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

**5.2 Acute Pancreatitis**

Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists, including semaglutide [see Adverse Reactions (6.1)].

After initiation of OZEMPI<sup>®</sup>, observe patients carefully for signs and symptoms of acute pancreatitis which may include persistent or severe abdominal pain (sometimes radiating to the back) and which may or may not be accompanied by nausea or vomiting. If pancreatitis is suspected, discontinue OZEMPI<sup>®</sup> and initiate appropriate management.

**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 OZEMPI<sup>®</sup> (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 (OZEMPI<sup>®</sup> 8.2%, placebo 5.2%) than among patients without a known history of diabetic retinopathy (OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> Pen Between Patients**

OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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), 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 Due to Volume Depletion**

There have been postmarketing reports of acute kidney injury, in some cases requiring hemodialysis, in patients treated with semaglutide. The majority of the reported events occurred in patients who experienced gastrointestinal reactions leading to dehydration such as nausea, vomiting, or diarrhea [see Adverse Reactions (6.1)]. Monitor renal function in patients reporting adverse reactions to OZEMPI<sup>®</sup> that could lead to volume depletion, especially during dosage initiation and escalation of OZEMPI<sup>®</sup>.

**5.7 Severe Gastrointestinal Adverse Reactions**

Use of OZEMPI<sup>®</sup> has been associated with gastrointestinal adverse reactions, sometimes severe [see Adverse Reactions (6)]. In OZEMPI<sup>®</sup> clinical trials, severe gastrointestinal adverse reactions were reported more frequently among patients receiving OZEMPI<sup>®</sup> (0.5 mg 0.4%, 1 mg 0.8%) than placebo (0%). Severe gastrointestinal adverse reactions have also been reported postmarketing with GLP-1 receptor agonists.

OZEMPI<sup>®</sup> is not recommended in patients with severe gastroparesis.

**5.8 Hypersensitivity Reactions**

Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported in patients treated with OZEMPI<sup>®</sup>. If hypersensitivity reactions occur, discontinue use of OZEMPI<sup>®</sup>; treat promptly per standard of care, and monitor until signs and symptoms resolve. Do not use in patients with a previous hypersensitivity to OZEMPI<sup>®</sup> [see Contraindications (4), Adverse Reactions (6.2)].

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 OZEMPI<sup>®</sup>.

**5.9 Acute Gallbladder Disease**

Acute events of gallbladder disease such as cholelithiasis or cholecystitis have been reported in GLP-1 receptor agonist trials and postmarketing. In placebo-controlled trials, cholelithiasis was reported in 1.5% and 0.4% of patients-treated with OZEMPI<sup>®</sup> 0.5 mg and 1 mg, respectively. Cholelithiasis was not reported in placebo-treated patients. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

**5.10 Pulmonary Aspiration During General Anesthesia or Deep Sedation**

OZEMPI<sup>®</sup> delays gastric emptying [see Clinical Pharmacology (12.2)]. There have been rare postmarketing reports of pulmonary aspiration in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation who had residual gastric contents despite reported adherence to preoperative fasting recommendations.

Available data are insufficient to inform recommendations to mitigate the risk of pulmonary aspiration during general anesthesia or deep sedation in patients taking OZEMPI<sup>®</sup>, including whether modifying preoperative fasting recommendations or temporarily discontinuing OZEMPI<sup>®</sup> could reduce the incidence of retained gastric contents. Instruct patients to inform healthcare providers prior to any planned surgeries or procedures if they are taking OZEMPI<sup>®</sup>.

**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)]
- Acute 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 Due to Volume Depletion [see Warnings and Precautions (5.6)]
- Severe Gastrointestinal Adverse Reactions [see Warnings and Precautions (5.7)]
- Hypersensitivity Reactions [see Warnings and Precautions (5.8)]
- Acute Gallbladder Disease [see Warnings and Precautions (5.9)]
- Pulmonary Aspiration During General Anesthesia or Deep Sedation [see Warnings and Precautions (5.10)]

## 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 OZEMPI<sup>®</sup> and a mean duration of exposure to OZEMPI<sup>®</sup> 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 HbA<sub>1c</sub> of 8.2%. At baseline, 8.9% of the population reported retinopathy. Baseline estimated renal function was normal (eGFR ≥ 90 mL/min/1.73m<sup>2</sup>) in 57.2%, mildly impaired (eGFR 60 to 90 mL/min/1.73m<sup>2</sup>) in 35.9% and moderately impaired (eGFR 30 to 60 mL/min/1.73m<sup>2</sup>) 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 HbA<sub>1c</sub> of 8.2%. At baseline, 7.8% of the population reported retinopathy. Baseline estimated renal function was normal (eGFR ≥ 90 mL/min/1.73m<sup>2</sup>) in 63.1%, mildly impaired (eGFR 60 to 90 mL/min/1.73m<sup>2</sup>) in 34.3%, and moderately impaired (eGFR 30 to 60 mL/min/1.73m<sup>2</sup>) in 2.5% of the patients.

### Common Adverse Reactions

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

**Table 1. Adverse Reactions in Placebo-Controlled Trials Reported in ≥5% of OZEMPI<sup>®</sup>-Treated Patients with Type 2 Diabetes Mellitus**

Adverse Reaction	Placebo (N=262) %	OZEMPI <sup>®</sup> 0.5 mg (N=260) %	OZEMPI <sup>®</sup> 1 mg (N=261) %
Nausea	6.1	15.8	20.3
Vomiting	2.3	5	9.2
Diarrhea	1.9	8.5	8.8
Abdominal pain	4.6	7.3	5.7
Constipation	1.5	5	3.1

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**.

In a clinical trial with 959 patients treated with OZEMPI<sup>®</sup> 1 mg or OZEMPI<sup>®</sup> 2 mg as add-on to metformin with or without sulfonylurea treatment for 40 weeks, no new safety signals were identified.

In the FLOW trial [see Clinical Studies 14.3] in patients with type 2 diabetes mellitus and chronic kidney disease, safety data collection was limited to serious adverse events and selected predefined categories of adverse events regardless of seriousness. There were no new serious or severe adverse reactions identified in this trial.

### Gastrointestinal Adverse Reactions

In the pool of placebo-controlled trials, gastrointestinal adverse reactions occurred more frequently among patients receiving OZEMPI<sup>®</sup> than placebo (placebo 15.3%, OZEMPI<sup>®</sup> 0.5 mg 32.7%, OZEMPI<sup>®</sup> 1 mg 36.4%). The majority of reports of nausea, vomiting, and/or diarrhea occurred during dose escalation. More patients receiving OZEMPI<sup>®</sup> 0.5 mg (3.1%) and OZEMPI<sup>®</sup> 1 mg (3.8%) discontinued treatment due to gastrointestinal adverse reactions than patients receiving placebo (0.4%).

In the trial with OZEMPI<sup>®</sup> 1 mg and 2 mg, gastrointestinal adverse reactions occurred more frequently among patients receiving OZEMPI<sup>®</sup> 2 mg (34%) vs OZEMPI<sup>®</sup> 1 mg (30.8%).

In addition to the reactions in **Table 1**, the following gastrointestinal adverse reactions with a frequency of <5% were associated with OZEMPI<sup>®</sup> (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**

	Placebo	OZEMPI <sup>®</sup> 0.5 mg	OZEMPI <sup>®</sup> 1 mg
<b>Monotherapy</b>			
<b>(30 weeks)</b>	<b>N=129</b>	<b>N=127</b>	<b>N=130</b>
Severe <sup>†</sup>	0%	0%	0%
Documented symptomatic (≤70 mg/dL glucose threshold)	0%	1.6%	3.8%
Severe <sup>†</sup> or Blood Glucose Confirmed Symptomatic (≤56 mg/dL glucose threshold)	1.6%	0%	0%
<b>Add-on to Basal Insulin with or without Metformin</b>			
<b>(30 weeks)</b>	<b>N=132</b>	<b>N=132</b>	<b>N=131</b>
Severe <sup>†</sup>	0%	0%	1.5%
Documented symptomatic (≤70 mg/dL glucose threshold)	15.2%	16.7%	29.8%
Severe <sup>†</sup> or Blood Glucose Confirmed Symptomatic (≤56 mg/dL glucose threshold)	5.3%	8.3%	10.7%

<sup>†</sup> "Severe" hypoglycemia adverse reactions are episodes requiring the assistance of another person.

Hypoglycemia was more frequent when OZEMPI<sup>®</sup> was used in combination with a sulfonylurea [see Warnings and Precautions (5.5), Clinical Studies (14)]. Severe hypoglycemia occurred in 0.8% and 1.2% of patients when OZEMPI<sup>®</sup> 0.5 mg and 1 mg, respectively, was coadministered with a sulfonylurea.

Documented symptomatic hypoglycemia occurred in 17.3% and 24.4% of patients when OZEMPI<sup>®</sup> 0.5 mg and 1 mg, respectively, was coadministered with a sulfonylurea. Severe or blood glucose confirmed symptomatic hypoglycemia occurred in 6.5% and 10.4% of patients when OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup>-treated patients.

### Increases in Amylase and Lipase

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

### Acute Pancreatitis

In glycemic control trials, acute pancreatitis was confirmed by adjudication in 7 OZEMPI-treated patients (0.3 cases per 100 patient years) versus 3 in comparator-treated patients (0.2 cases per 100 patient years).

### Cholelithiasis

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

### Increases in Heart Rate

In placebo-controlled trials, OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> include fatigue, dysgeusia and dizziness.

## 6.2 Postmarketing Experience

The following adverse reactions have been reported during post-approval use of semaglutide, the active ingredient of OZEMPI<sup>®</sup>. 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.

**Gastrointestinal:** ileus, intestinal obstruction, severe constipation including fecal impaction

**Hypersensitivity:** anaphylaxis, angioedema, rash, urticaria

**Hepatobiliary:** cholecystitis, cholecystectomy

**Neurologic:** dysesthesia, headache

**Pulmonary:** Pulmonary aspiration has occurred in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation.

**Renal:** acute kidney injury

**Skin and Subcutaneous Tissue:** alopecia

## 7 DRUG INTERACTIONS

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

OZEMPI<sup>®</sup> stimulates insulin release in the presence of elevated blood glucose concentrations. Patients receiving OZEMPI<sup>®</sup> in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. When initiating OZEMPI<sup>®</sup>, 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), Adverse Reactions (6)].

### 7.2 Oral Medications

OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup>.



**Insulin Secretion**

Both first-and second-phase insulin secretion are increased in patients with type 2 diabetes treated with OZEMPI® compared with placebo.

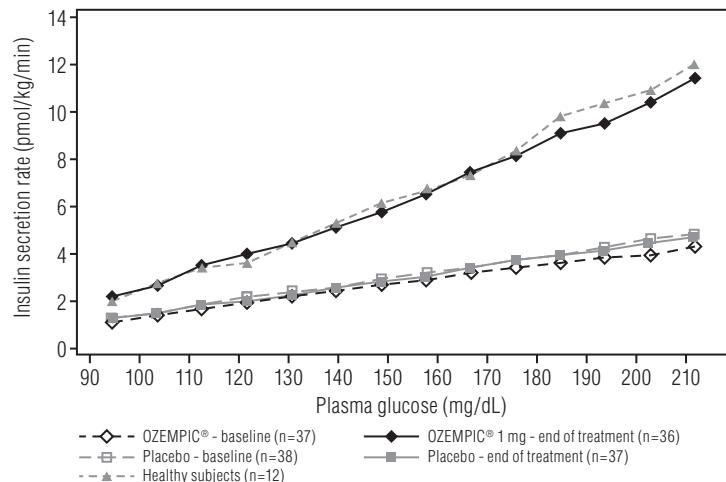
**Glucagon Secretion**

Semaglutide lowers the fasting and postprandial glucagon concentrations. In patients with type 2 diabetes, treatment with semaglutide resulted in the following relative reductions in glucagon compared to placebo, fasting glucagon (8%), postprandial glucagon response (14 to 15%), and mean 24-hour glucagon concentration (12%).

**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 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. Semaglutide does not prolong QTc intervals at doses up to 1.5 mg at steady-state.

**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, 1 mg and 2 mg. Steady-state exposure is achieved following 4 to 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 ng/mL and 123 ng/mL, respectively. In the trial comparing semaglutide 1 mg and 2 mg, the mean steady state concentrations were 111.1 ng/mL and 222.1 ng/mL, respectively.

**Distribution**

The mean apparent volume of distribution of semaglutide following subcutaneous administration in patients with type 2 diabetes is approximately 12.5L. 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**

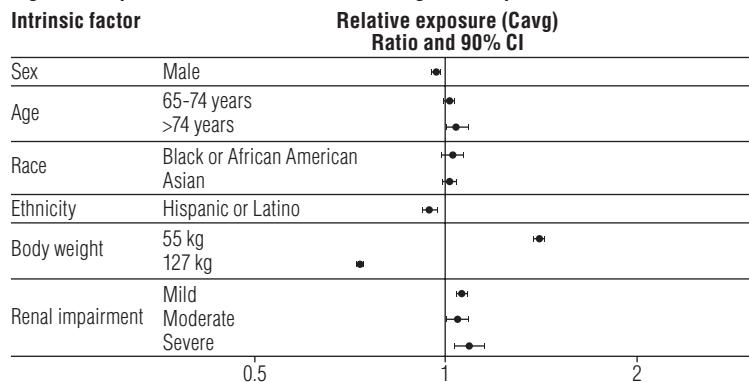
The primary route of elimination for semaglutide is metabolism following proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain.

**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 to 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**

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, or kidney failure) 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.

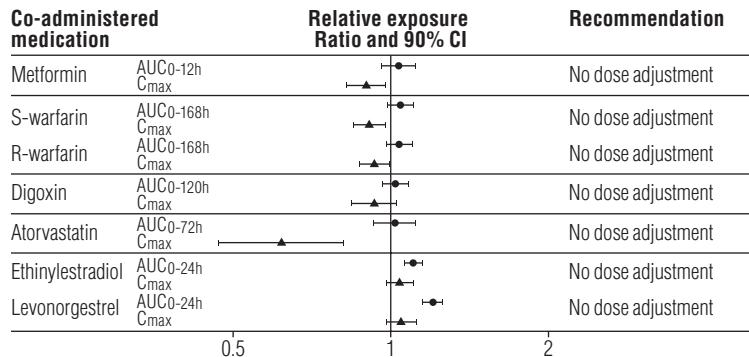
**Pediatric Patients** - Semaglutide has not been studied in pediatric patients.

**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 (see **Drug Interactions (7.2)**). 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. In a separate study, no apparent effect on the rate of gastric emptying was observed with semaglutide 2.4 mg.

**Figure 4. Impact of Semaglutide on the Exposure of Coadministered Oral Medications**

Relative exposure in terms of AUC and C<sub>max</sub> for each medication when given with semaglutide compared to without semaglutide. Metformin and oral contraceptive drug (ethinylestradiol/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. C<sub>max</sub>: maximum concentration. CI: confidence interval.

**12.6 Immunogenicity**

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies (ADAs) in the studies described below with the incidence of ADAs in other studies, including those of semaglutide or of other semaglutide products.

Across the placebo- and active-controlled glycemic control trials, 32 out of 3,150 (1%) OZEMPI®-treated patients developed ADAs to the active ingredient in OZEMPI® (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.

**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 [2-, 11-, and 30-fold the maximum recommended human dose (MRHD) of 2 mg/week, based on AUC] were administered to the males, and 0.1, 0.3 and 1 mg/kg/day (1-, 2-, and 7-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 clinically relevant exposures.

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, 0.2-, 0.5-, and 3-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  $\geq 0.01$  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, 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 (0.06-, 0.2-, and 0.6-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  $\geq 0.03$  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 Glycemic Control Trials in Adults with Type 2 Diabetes Mellitus

OZEMPI<sup>®</sup> has been studied as monotherapy and in combination with metformin, metformin and sulfonylureas, metformin and/or thiazolidinedione, and basal insulin in patients with type 2 diabetes mellitus. The efficacy of OZEMPI<sup>®</sup> was compared with placebo, sitagliptin, exenatide extended-release (ER), and insulin glargine.

Most trials evaluated the use of OZEMPI<sup>®</sup> 0.5 mg, and 1 mg, with the exception of the trial comparing OZEMPI<sup>®</sup> and exenatide ER where only the 1 mg dose was studied. One trial evaluated the use of OZEMPI<sup>®</sup> 2 mg once weekly.

In patients with type 2 diabetes mellitus, OZEMPI<sup>®</sup> produced clinically relevant reduction from baseline in HbA<sub>1c</sub> compared with placebo.

The efficacy of OZEMPI<sup>®</sup> was not impacted by age, gender, race, ethnicity, BMI at baseline, body weight (kg) at baseline, diabetes duration and level of renal function impairment.

#### Monotherapy Use of OZEMPI<sup>®</sup> in Adults 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 OZEMPI<sup>®</sup> 0.5 mg or OZEMPI<sup>®</sup> 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/m<sup>2</sup>. Overall, 64% were White, 8% were Black or African American, and 21% were Asian; 30% identified as Hispanic or Latino ethnicity.

Monotherapy with OZEMPI<sup>®</sup> 0.5 mg and 1 mg once weekly for 30 weeks resulted in a statistically significant reduction in HbA<sub>1c</sub> compared with placebo (see **Table 3**).

**Table 3. Results at Week 30 in a Trial of OZEMPI<sup>®</sup> as Monotherapy in Adult Patients with Type 2 Diabetes Mellitus Inadequately Controlled with Diet and Exercise**

	Placebo	OZEMPI <sup>®</sup> 0.5 mg	OZEMPI <sup>®</sup> 1 mg
Intent-to-Treat (ITT) Population (N) <sup>a</sup>	129	128	130
HbA <sub>1c</sub> (%)			
Baseline (mean)	8	8.1	8.1
Change at week 30 <sup>b</sup>	-0.1	-1.4	-1.6
Difference from placebo <sup>b</sup> [95% CI]		-1.2 [-1.5, -0.9] <sup>c</sup>	-1.4 [-1.7, -1.1] <sup>c</sup>
Patients (%) achieving HbA <sub>1c</sub> <7%	28	73	70
FPG (mg/dL)			
Baseline (mean)	174	174	179
Change at week 30 <sup>b</sup>	-15	-41	-44

<sup>a</sup>The intent-to-treat population includes all randomized and exposed patients. At week 30 the primary HbA<sub>1c</sub> 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, OZEMPI<sup>®</sup> 0.5 mg and OZEMPI<sup>®</sup> 1 mg, respectively. Missing data were imputed using multiple imputation based on retrieved dropouts.

<sup>b</sup>Intent-to-treat analysis using ANCOVA adjusted for baseline value and country.

<sup>c</sup>p<0.0001 (2-sided) for superiority, adjusted for multiplicity.

The mean baseline body weight was 89.1 kg, 89.8 kg, 96.9 kg in the placebo, OZEMPI<sup>®</sup> 0.5 mg, and OZEMPI<sup>®</sup> 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, OZEMPI<sup>®</sup> 0.5 mg, and OZEMPI<sup>®</sup> 1 mg arms, respectively. The difference from placebo (95% CI) for OZEMPI<sup>®</sup> 0.5 mg was -2.6 kg (-3.8, -1.5), and for OZEMPI<sup>®</sup> 1 mg was -3.5 kg (-4.8, -2.2).

#### Combination Therapy Use of OZEMPI<sup>®</sup> in Adults 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 OZEMPI<sup>®</sup> 0.5 mg once weekly, OZEMPI<sup>®</sup> 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 6.6 years, and the mean BMI was 32 kg/m<sup>2</sup>. Overall, 68% were White, 5% were Black or African American, and 25% were Asian; 17% identified as Hispanic or Latino ethnicity.

Treatment with OZEMPI<sup>®</sup> 0.5 mg and 1 mg once weekly for 56 weeks resulted in a statistically significant reduction in HbA<sub>1c</sub> compared to sitagliptin (see **Table 4** and **Figure 5**).

**Table 4. Results at Week 56 in a Trial of OZEMPI<sup>®</sup> Compared to Sitagliptin in Adult Patients with Type 2 Diabetes Mellitus in Combination with Metformin and/or Thiazolidinediones**

	OZEMPI <sup>®</sup> 0.5 mg	OZEMPI <sup>®</sup> 1 mg	Sitagliptin
Intent-to-Treat (ITT) Population (N) <sup>a</sup>	409	409	407
HbA <sub>1c</sub> (%)			
Baseline (mean)	8	8	8.2
Change at week 56 <sup>b</sup>	-1.3	-1.5	-0.7
Difference from sitagliptin <sup>b</sup> [95% CI]	-0.6 [-0.7, -0.4] <sup>c</sup>	-0.8 [-0.9, -0.6] <sup>c</sup>	
Patients (%) achieving HbA <sub>1c</sub> <7%	66	73	40
FPG (mg/dL)			
Baseline (mean)	168	167	173
Change at week 56 <sup>b</sup>	-35	-43	-23

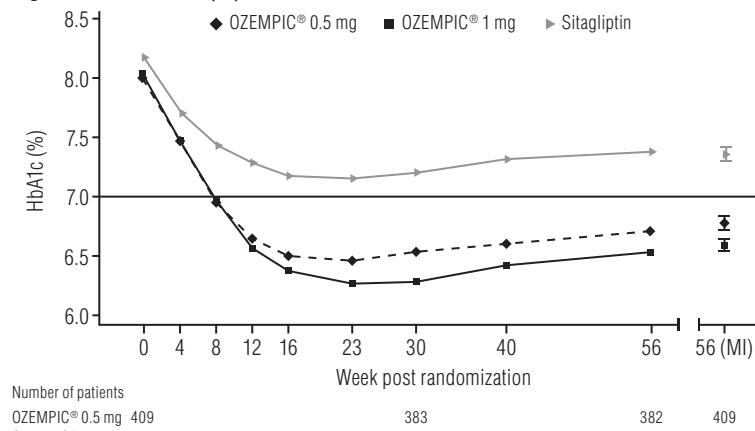
<sup>a</sup>The intent-to-treat population includes all randomized and exposed patients. At week 56 the primary HbA<sub>1c</sub> endpoint was missing for 7%, 5% and 6% of patients and during the trial rescue medication was initiated by 5%, 2% and 19% of patients randomized to OZEMPI<sup>®</sup> 0.5 mg, OZEMPI<sup>®</sup> 1 mg and sitagliptin, respectively. Missing data were imputed using multiple imputation based on retrieved dropouts.

<sup>b</sup>Intent-to-treat analysis using ANCOVA adjusted for baseline value and country.

<sup>c</sup>p<0.0001 (2-sided) for superiority, adjusted for multiplicity.

The mean baseline body weight was 89.9 kg, 89.2 kg, 89.3 kg in the OZEMPI<sup>®</sup> 0.5 mg, OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 0.5 mg, OZEMPI<sup>®</sup> 1 mg, and sitagliptin arms, respectively. The difference from sitagliptin (95% CI) for OZEMPI<sup>®</sup> 0.5 mg was -2.5 kg (-3.2, -1.8), and for OZEMPI<sup>®</sup> 1 mg was -3.8 kg (-4.5, -3.1).

**Figure 5. Mean HbA<sub>1c</sub> (%) Over Time - Baseline to Week 56**



Observed mean HbA<sub>1c</sub> at scheduled visits and retrieved dropout multiple imputation (MI) based estimate at week 56 with standard error

##### Combination with metformin or metformin with sulfonylurea

In a 56-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 OZEMPI<sup>®</sup> 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/m<sup>2</sup>. Overall, 84% were White, 7% were Black or African American, and 2% were Asian; 24% identified as Hispanic or Latino ethnicity.

Treatment with OZEMPI<sup>®</sup> 1 mg once weekly for 56 weeks resulted in a statistically significant reduction in HbA<sub>1c</sub> compared to exenatide 2 mg once weekly (see **Table 5**).

**Table 5. Results at Week 56 in a Trial of OZEMPI<sup>®</sup> Compared to Exenatide 2 mg Once Weekly in Adult Patients with Type 2 Diabetes Mellitus in Combination with Metformin or Metformin with Sulfonylurea**

	OZEMPI <sup>®</sup> 1 mg	Exenatide ER 2 mg
Intent-to-Treat (ITT) Population (N) <sup>a</sup>	404	405
HbA <sub>1c</sub> (%)		
Baseline (mean)	8.4	8.3
Change at week 56 <sup>b</sup>	-1.4	-0.9
Difference from exenatide <sup>b</sup> [95% CI]	-0.5 [-0.7, -0.3] <sup>c</sup>	
Patients (%) achieving HbA <sub>1c</sub> <7%	62	40
FPG (mg/dL)		
Baseline (mean)	191	188
Change at week 56 <sup>b</sup>	-44	-34

<sup>a</sup>The intent-to-treat population includes all randomized and exposed patients. At week 56 the primary HbA<sub>1c</sub> endpoint was missing for 9% and 11% of patients and during the trial rescue medication was initiated by 5% and 10% of patients randomized to OZEMPI<sup>®</sup> 1 mg and exenatide ER 2 mg, respectively. Missing data were imputed using multiple imputation based on retrieved dropouts.

<sup>b</sup>Intent-to-treat analysis using ANCOVA adjusted for baseline value and country.

<sup>c</sup>p<0.0001 (2-sided) for superiority, adjusted for multiplicity.

The mean baseline body weight was 96.2 kg and 95.4 kg in the OZEMPI<sup>®</sup> 1 mg and exenatide ER arms, respectively. The mean changes from baseline to week 56 were -4.8 kg and -2 kg in the OZEMPI<sup>®</sup> 1 mg and exenatide ER arms, respectively. The difference from exenatide ER (95% CI) for OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 0.5 mg once weekly, OZEMPI<sup>®</sup> 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/m<sup>2</sup>. 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 HbA<sub>1c</sub> 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 had been titrated to goal by the primary endpoint at week 30, at which time the mean daily insulin dose was 29 U per day.

Treatment with OZEMPI<sup>®</sup> 0.5 mg and 1 mg once weekly for 30 weeks resulted in a statistically significant reduction in HbA<sub>1c</sub> compared with the insulin glargine titration implemented in this study protocol (see **Table 6**).

**Table 6. Results at Week 30 in a Trial of OZEMPI<sup>®</sup> Compared to Insulin Glargine in Adult Patients with Type 2 Diabetes Mellitus in Combination with Metformin or Metformin with Sulfonylurea**

	OZEMPI <sup>®</sup> 0.5 mg	OZEMPI <sup>®</sup> 1 mg	Insulin Glargine
Intent-to-Treat (ITT) Population (N) <sup>a</sup>	362	360	360
HbA <sub>1c</sub> (%)			
Baseline (mean)	8.1	8.2	8.1
Change at week 30 <sup>b</sup>	-1.2	-1.5	-0.9
Difference from insulin glargine <sup>b</sup> [95% CI]	-0.3 [-0.5, -0.1] <sup>c</sup>	-0.6 [-0.8, -0.4] <sup>c</sup>	
Patients (%) achieving HbA <sub>1c</sub> <7%	55	66	40
FPG (mg/dL)			
Baseline (mean)	172	179	174
Change at week 30 <sup>b</sup>	-35	-46	-37

<sup>a</sup>The intent-to-treat population includes all randomized and exposed patients. At week 30 the primary HbA<sub>1c</sub> endpoint was missing for 8%, 6% and 6% of patients and during the trial rescue medication was initiated by 4%, 3% and 1% of patients randomized to OZEMPI<sup>®</sup> 0.5 mg, OZEMPI<sup>®</sup> 1 mg and insulin glargine, respectively. Missing data were imputed using multiple imputation based on retrieved dropouts.

<sup>b</sup>Intent-to-treat analysis using ANCOVA adjusted for baseline value, country and stratification factors.

<sup>c</sup>p<0.0001 (2-sided) for superiority, adjusted for multiplicity.

The mean baseline body weight was 93.7 kg, 94 kg, 92.6 kg in the OZEMPI<sup>®</sup> 0.5 mg, OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 0.5 mg, OZEMPI<sup>®</sup> 1 mg, and insulin glargine arms, respectively. The difference from insulin glargine (95% CI) for OZEMPI<sup>®</sup> 0.5 mg was -4.1 kg (-4.9, -3.3) and for OZEMPI<sup>®</sup> 1 mg was -5.6 kg (-6.4, -4.8).

**Combination with metformin or metformin with sulfonylurea**

In a 40-week, double-blind trial (NCT03989232), 961 patients with type 2 diabetes currently treated with metformin with or without sulfonylurea treatment were randomized to OZEMPI<sup>®</sup> 2 mg or OZEMPI<sup>®</sup> 1 mg once weekly. Patients had a mean age of 58 years and 58.6% were men. The mean duration of type 2 diabetes was 9.5 years and the mean BMI was 34.6 kg/m<sup>2</sup>. At randomization, 53.3% of patients were treated with sulfonylurea and metformin. Overall, 88.1% were White, 4.5% were Black or African American, and 7.2% were Asian; 11.6% identified as Hispanic or Latino ethnicity. Treatment with OZEMPI<sup>®</sup> 2 mg once weekly for 40 weeks resulted in a statistically significant reduction in HbA<sub>1c</sub> compared with OZEMPI<sup>®</sup> 1 mg (see **Table 7**). Patients were stratified by region (Japan/outside Japan) at randomization.

**Table 7. Results at Week 40 in a Trial of OZEMPI<sup>®</sup> 2 mg Compared to OZEMPI<sup>®</sup> 1 mg in Adult Patients with Type 2 Diabetes Mellitus in Combination With Metformin or Metformin with Sulfonylurea**

	OZEMPI <sup>®</sup> 1 mg	OZEMPI <sup>®</sup> 2 mg
Intent-to-Treat (ITT) Population (N) <sup>a</sup>	481	480
HbA <sub>1c</sub> (%)		
Baseline (mean)	8.8	8.9
Change at week 40 <sup>b</sup>	-1.9	-2.1
Difference from OZEMPI <sup>®</sup> 1 mg [95% CI]		-0.2 [-0.31 ; -0.04] <sup>c</sup>
Patients (%) achieving HbA <sub>1c</sub> <7% <sup>a</sup>	56	64
FPG (mg/dL)		
Baseline (mean)	196	193
Change at week 40 <sup>b</sup>	-55	-59

<sup>a</sup>The intent-to-treat population includes all randomized subjects. At week 40 the primary HbA<sub>1c</sub> endpoint was missing for 3% and 5% of patients randomized to OZEMPI<sup>®</sup> 1 mg and OZEMPI<sup>®</sup> 2 mg, respectively. Missing data were imputed using multiple imputation based on retrieved dropouts. For calculation of proportions, imputed values are dichotomized and the denominator is the number of all randomized subjects.

<sup>b</sup>Intent-to-treat analysis using ANCOVA adjusted for baseline value and stratification factor.

<sup>c</sup>p<0.01 (2-sided) for superiority, adjusted for multiplicity.

The mean baseline body weight was 98.6 kg and 100.1 kg in the OZEMPI<sup>®</sup> 1 mg and OZEMPI<sup>®</sup> 2 mg arms, respectively. The mean changes from baseline to week 40 were -5.6 kg and -6.4 kg in the OZEMPI<sup>®</sup> 1 mg and OZEMPI<sup>®</sup> 2 mg arms, respectively. The difference between treatment arms in body weight change from baseline at week 40 was not statistically significant.

**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 OZEMPI<sup>®</sup> 0.5 mg once weekly, OZEMPI<sup>®</sup> 1 mg once weekly, or placebo. Patients with HbA<sub>1c</sub> ≤8.0% at screening reduced their insulin dose by 20% at 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/m<sup>2</sup>. Overall, 78% were White, 5% were Black or African American, and 17% were Asian; 12% identified as Hispanic or Latino ethnicity.

Treatment with OZEMPI<sup>®</sup> resulted in a statistically significant reduction in HbA<sub>1c</sub> after 30 weeks of treatment compared to placebo (see **Table 8**).

**Table 8. Results at Week 30 in a Trial of OZEMPI<sup>®</sup> in Adult Patients with Type 2 Diabetes Mellitus in Combination with Basal Insulin with or without Metformin**

	Placebo	OZEMPI <sup>®</sup> 0.5 mg	OZEMPI <sup>®</sup> 1 mg
Intent-to-Treat (ITT) Population (N) <sup>a</sup>	133	132	131
HbA <sub>1c</sub> (%)			
Baseline (mean)	8.4	8.4	8.3
Change at week 30 <sup>b</sup>	-0.2	-1.3	-1.7
Difference from placebo <sup>b</sup> [95% CI]		-1.1 [-1.4, -0.8] <sup>c</sup>	-1.6 [-1.8, -1.3] <sup>c</sup>
Patients (%) achieving HbA <sub>1c</sub> <7%	13	56	73
FPG (mg/dL)			
Baseline (mean)	154	161	153
Change at week 30 <sup>b</sup>	-8	-28	-39

<sup>a</sup>The intent-to-treat population includes all randomized and exposed patients. At week 30 the primary HbA<sub>1c</sub> endpoint was missing for 7%, 5% and 5% of patients and during the trial rescue medication was initiated by 14%, 2% and 1% of patients randomized to placebo, OZEMPI<sup>®</sup> 0.5 mg and OZEMPI<sup>®</sup> 1 mg, respectively. Missing data were imputed using multiple imputation based on retrieved dropouts.

<sup>b</sup>Intent-to-treat analysis using ANCOVA adjusted for baseline value, country and stratification factors.

<sup>c</sup>p<0.0001 (2-sided) for superiority, adjusted for multiplicity.

The mean baseline body weight was 89.9 kg, 92.7 kg, and 92.5 kg in the placebo, OZEMPI<sup>®</sup> 0.5 mg, and OZEMPI<sup>®</sup> 1 mg arms, respectively. The mean changes from baseline to week 30 were -1.2 kg, -3.5 kg, and -6 kg in the placebo, OZEMPI<sup>®</sup> 0.5 mg, and OZEMPI<sup>®</sup> 1 mg arms, respectively. The difference from placebo (95% CI) for OZEMPI<sup>®</sup> 0.5 mg was -2.2 kg (-3.4, -1.1), and for OZEMPI<sup>®</sup> 1 mg was -4.7 kg (-5.8, -3.6).

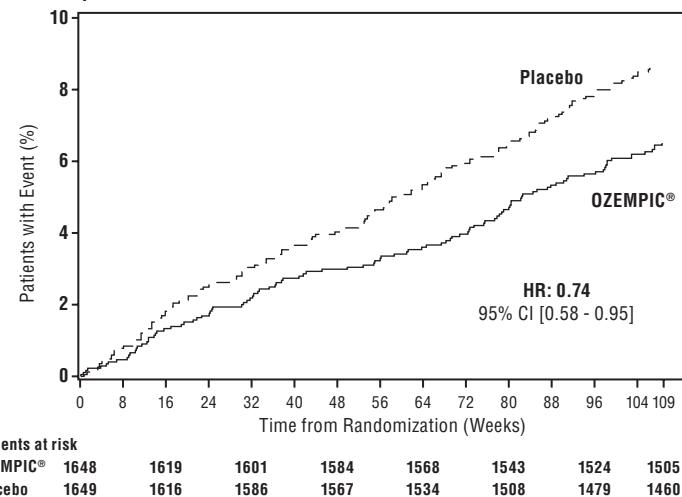
**14.2 Cardiovascular Outcomes Trial of OZEMPI<sup>®</sup> in Adults with Type 2 Diabetes Mellitus and Cardiovascular Disease**

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 OZEMPI<sup>®</sup> (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 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 duration of diabetes was 13.9 years, and mean BMI was 33 kg/m<sup>2</sup>. 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%.

For the primary analysis, a Cox proportional hazards model was used to test for non-inferiority of OZEMPI<sup>®</sup> to placebo for time to first MACE using a risk margin of 1.3. The statistical analysis plan pre-specified that the 0.5 mg and 1 mg doses would be combined. Type-1 error was controlled across multiple tests using a hierarchical testing strategy.

OZEMPI<sup>®</sup> significantly reduced the occurrence of MACE. The estimated hazard ratio for time to first MACE was 0.74 (95% CI: 0.58, 0.95). Refer to **Figure 6** and **Table 9**.

**Figure 6. Kaplan-Meier: Time to First Occurrence of a MACE in the SUSTAIN 6 Trial**



The treatment effect for the primary composite endpoint and its components in the SUSTAIN 6 trial is shown in **Table 9**.

**Table 9. Treatment Effect for MACE and its Components, Median Study Observation Time of 2.1 Years**

	Placebo N=1649 (%)	OZEMPI® N=1648 (%)	Hazard ratio vs Placebo (95% CI) <sup>a</sup>
Composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke (time to first occurrence)	146 (8.9)	108 (6.6)	0.74 (0.58, 0.95)
Non-fatal Myocardial Infarction	64 (3.9)	47 (2.9)	0.74 (0.51, 1.08)
Non-fatal Stroke	44 (2.7)	27 (1.6)	0.61 (0.38, 0.99)
Cardiovascular Death	46 (2.8)	44 (2.7)	0.98 (0.65, 1.48)
Fatal or Non-fatal Myocardial Infarction	67 (4.1)	54 (3.3)	0.81 (0.57, 1.16)
Fatal or Non-fatal Stroke	46 (2.8)	30 (1.8)	0.65 (0.41, 1.03)

<sup>a</sup>Cox-proportional hazards models with treatment as factor and stratified by evidence of cardiovascular disease, insulin treatment and renal impairment.

#### 14.3 Kidney Outcomes Trial of OZEMPI® in Adults with Type 2 Diabetes Mellitus and Chronic Kidney Disease

FLOW (NCT03819153) was a randomized, double-blind, placebo-controlled, event driven trial in adults with type 2 diabetes mellitus and chronic kidney disease (eGFR 25 to 75 mL/min/1.73 m<sup>2</sup> with urine albumin-to-creatinine ratio [UACR] >100 mg/g and <5000 mg/g). All patients needed to have an HbA1c ≤10% at screening and be receiving standard of care background therapy, including a maximum tolerated labeled dose of a renin-angiotensin-aldosterone system (RAAS) blocking agent including an angiotensin converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB), unless such treatment was contraindicated or not tolerated. The trial excluded patients with congenital or hereditary kidney diseases including polycystic kidney disease, autoimmune kidney diseases including glomerulonephritis or congenital urinary tract malformations.

A total of 3,533 patients were randomized to receive OZEMPI® 1 mg once weekly or placebo and were followed for a median of 41 months. The mean age of the study population was 67 years, and 70% of patients were male. Approximately 66% of the trial population was White, 24% Asian, and 5% Black or African American. At baseline, the mean eGFR was 47 mL/min/1.73m<sup>2</sup>, with 11% of patients having an eGFR <30 mL/min/1.73m<sup>2</sup>. Median baseline UACR was 568 mg/g with 69% of patients with a UACR >300 mg/g. At baseline, 95% of patients were treated with an ACE inhibitor or ARB, 16% were on sodium-glucose cotransporter 2 (SGLT2) inhibitors, 76% were on a statin, and 50% were on an antiplatelet agent.

OZEMPI® was superior to placebo in reducing the incidence of the primary composite endpoint of a sustained decline in eGFR of ≥50%, sustained eGFR <15 mL/min/1.73 m<sup>2</sup>, chronic renal replacement therapy, renal death, CV death (HR 0.76 [95% CI 0.66, 0.88], p=0.0003) as shown in **Table 10** and **Figure 7**. The treatment effect reflected a reduction in a sustained decline in eGFR of ≥50%, progression to kidney failure and CV death. There were few renal deaths during the trial.

OZEMPI® also reduced the annual rate of change in eGFR (**Figure 9**), the incidence of a composite cardiovascular endpoint, consisting of non-fatal myocardial infarction (MI), non-fatal stroke, and cardiovascular death, and the incidence of all-cause death (**Table 10** and **Figure 8**).

The treatment effect on the primary composite endpoint was generally consistent across the pre-specified subgroups examined, including age, biological sex, eGFR and UACR. The treatment benefit on the primary composite endpoint was not evident in patients taking SGLT2 inhibitors at baseline, but there were few events in these patients.

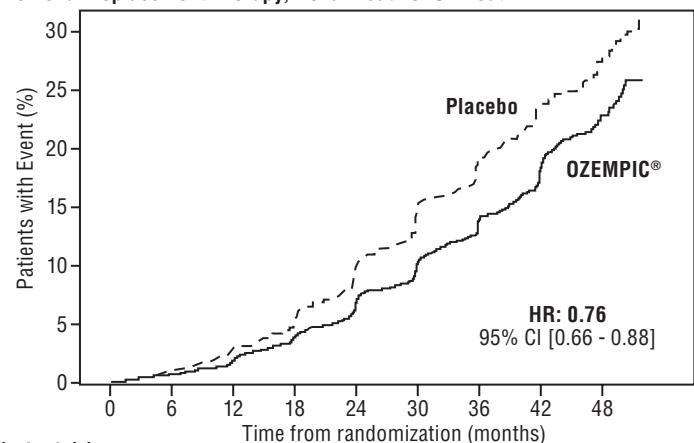
**Table 10: Analyses of the Primary and Secondary Endpoints and their Individual Components in FLOW Trial**

	Placebo N=1766 (%)	OZEMPI® 1 mg N=1767 (%)	Hazard ratio vs placebo (95% CI) <sup>1</sup>	p-value <sup>2</sup>
	Number of Patients (%)			
Composite Endpoint (≥50% sustained eGFR decline, sustained eGFR <15 mL/min/1.73 m <sup>2</sup> , chronic renal replacement therapy, or renal or cardiovascular death (time to first occurrence) <sup>3</sup> )	410 (23.2)	331 (18.7)	0.76 (0.66, 0.88)	0.0003
≥50% sustained eGFR decline <sup>3</sup>	213 (12.1)	165 (9.3)	0.73 (0.59, 0.89)	
Sustained eGFR <15mL/min/1.73 m <sup>2</sup> <sup>3</sup>	110 (6.2)	92 (5.2)	0.8 (0.61, 1.06)	
Chronic renal replacement therapy	100 (5.7)	87 (4.9)	0.84 (0.63, 1.12)	
Renal death	5 (0.3)	5 (0.3)	0.97 (0.27, 3.49)	
Cardiovascular death	169 (9.6)	123 (7)	0.71 (0.56, 0.89)	
Composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke (time to first occurrence)	254 (14.4)	212 (12)	0.82 (0.68, 0.98)	0.0289
All-cause death	279 (15.8)	227 (12.8)	0.8 (0.67, 0.95)	0.0104

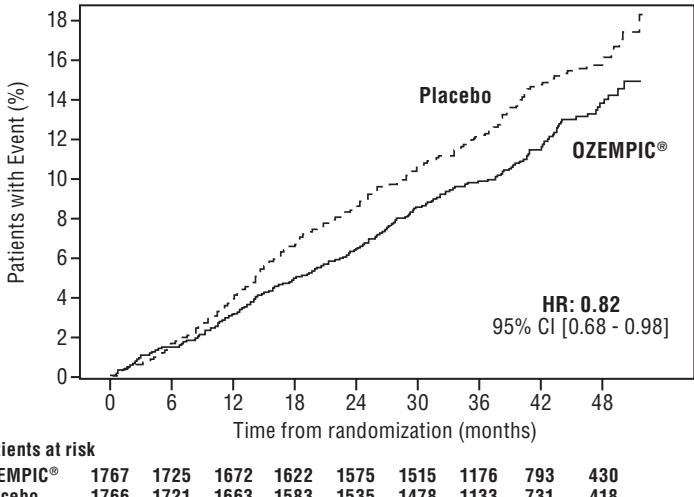
<sup>1</sup>Cox proportional hazards model with treatment as factor and stratified by baseline use of SGLT2-inhibitor at baseline (yes or no).

<sup>2</sup>Two-sided p-value for the test of no difference. The significance level was 0.03224.

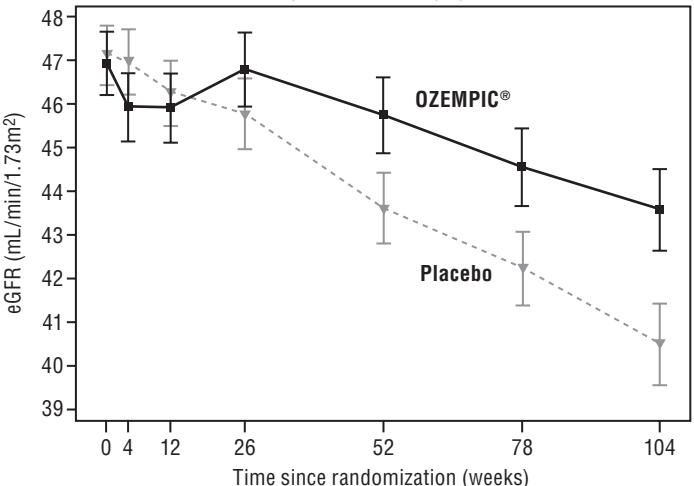
<sup>3</sup>Sustained was defined as having 2 consecutive measurements ≥28 days apart fulfilling the criteria.

**Figure 7. Cumulative Incidence: Time to First Occurrence of the Primary Composite Endpoint - Sustained Decline in eGFR ≥50%, Sustained eGFR<15 mL/min/1.73m<sup>2</sup>, Chronic Renal Replacement Therapy, Renal Death or CV Death**

Cumulative incidence estimates are based on time from randomization to first composite renal event with non-CV and non-renal death modelled as competing risk. The x-axis is truncated at 52 months where approximately 5% of the population was in the trial. Sustained was defined as having 2 consecutive measurements ≥28 days apart fulfilling the criteria.

**Figure 8. Cumulative incidence: Time to First Occurrence of MACE in FLOW Trial**

Cumulative incidence estimates are based on time from randomization to first EAC-confirmed MACE with non-CV death modelled as competing risk. The x-axis is truncated at 52 months where approximately 5% of the population was in the trial.

**Figure 9. Observed Mean Plot: eGFR (mL/min/1.73m<sup>2</sup>) by Week in FLOW Trial**

Observed data from the in-trial period until week 104. Error bars are +/- 1.96 \*standard error of the mean eGFR, which was calculated using the CKD-EPI 2009 formula.

CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration, eGFR: estimated glomerular filtration rate.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### How Supplied

Injection: clear, colorless solution of 0.68 mg/mL, 1.34 mg/mL or 2.68 mg/mL of semaglutide available in prefilled, disposable, single-patient-use pens in the following packaging configurations:

Dose per Injection	Use For	Total Strength per Total Volume	Doses per Pen	Carton Contents	NDC
0.25 mg	Initiation	2 mg/3 mL	4 doses of 0.25 mg and 2 doses of 0.5 mg or 4 doses of 0.5 mg	1 pen 6 NovoFine® Plus needles	0169-4181-13
0.5 mg	Maintenance				
1 mg	Maintenance	4 mg/3 mL	4 doses of 1 mg	1 pen 4 NovoFine® Plus needles	0169-4130-13
2 mg	Maintenance	8 mg/3 mL	4 doses of 2 mg	1 pen 4 NovoFine® Plus needles	0169-4772-12

The 2 mg/1.5 mL (1.34 mg/mL) strength (NDC 0169-4132-12) is not currently marketed by Novo Nordisk Inc.

Each OZEMPI® pen is for use by a single patient. An OZEMPI® 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, OZEMPI® should be stored in a refrigerator between 36°F to 46°F (2°C to 8°C). Do not store in the freezer or directly adjacent to the refrigerator cooling element. Do not freeze OZEMPI® and do not use OZEMPI® if it has been frozen.

After first use of the OZEMPI® 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. OZEMPI® should be protected from excessive heat and sunlight.

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

### Recommended Storage Conditions for the OZEMPI® Pen

Prior to first use	After first use	
Refrigerated 36°F to 46°F (2°C to 8°C)	Room Temperature 59°F to 86°F (15°C to 30°C)	Refrigerated 36°F to 46°F (2°C to 8°C)
Until expiration date	56 days	

## 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, Warnings and Precautions* (5.1)].

### Acute Pancreatitis

Inform patients of the potential risk for acute pancreatitis and its symptoms: severe abdominal pain that may radiate to the back, and which may or may not be accompanied by nausea or vomiting. Instruct patients to discontinue OZEMPI® promptly and contact their physician if pancreatitis is suspected [see *Warnings and Precautions* (5.2)].

### Diabetic Retinopathy Complications

Inform patients to contact their physician if changes in vision are experienced during treatment with OZEMPI® [see *Warnings and Precautions* (5.3)].

### Never Share an OZEMPI® Pen Between Patients

Advise patients that they must never share an OZEMPI® 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 OZEMPI® 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)].

### Acute Kidney Injury Due to Volume Depletion

Inform patients of the potential risk of acute kidney injury due to dehydration associated with gastrointestinal adverse reactions. Advise patients to take precautions to avoid fluid depletion. Inform patients of the signs and symptoms of acute kidney injury and instruct them to promptly report any of these signs or symptoms or persistent (or extended) nausea, vomiting, and diarrhea to their healthcare provider [see *Warnings and Precautions* (5.6)].

### Severe Gastrointestinal Adverse Reactions

Inform patients of the potential risk of severe gastrointestinal adverse reactions. Instruct patients to contact their healthcare provider if they have severe or persistent gastrointestinal symptoms [see *Warnings and Precautions* (5.7)].

### Hypersensitivity Reactions

Inform patients that serious hypersensitivity reactions have been reported during postmarketing use of OZEMPI®. Advise patients on the symptoms of hypersensitivity reactions and instruct them to stop taking OZEMPI® and seek medical advice promptly if such symptoms occur [see *Warnings and Precautions* (5.8)].

### Acute Gallbladder Disease

Inform patients of the potential risk for cholelithiasis or cholecystitis. Instruct patients to contact their physician if cholelithiasis or cholecystitis is suspected for appropriate clinical follow-up [see *Warnings and Precautions* (5.9)].

### Pulmonary Aspiration During General Anesthesia or Deep Sedation

Inform patients that OZEMPI® may cause their stomach to empty more slowly which may lead to complications with anesthesia or deep sedation during planned surgeries or procedures. Instruct patients to inform healthcare providers prior to any planned surgeries or procedures if they are taking OZEMPI® [see *Warnings and Precautions* (5.10)].

### 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)].

### Missed doses

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)].

### Manufactured by:

Novo Nordisk A/S  
DK-2880 Bagsvaerd  
Denmark

For information about OZEMPI® contact:

Novo Nordisk Inc.  
800 Scudders Mill Road  
Plainsboro, NJ 08536  
1-888-693-6742

OZEMPI® and NovoFine® are registered trademarks of Novo Nordisk A/S.

### PATENT INFORMATION:

<http://www.novonordisk-us.com/products/product-patents.html>

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US250ZM01123 October 2025



<p><b>Medication Guide</b> <b>OZEMPI® (oh-ZEM-pick)</b> (semaglutide) injection, for subcutaneous use</p> <p><b>Do not share your OZEMPI® 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.</b></p> <p>Read this Medication Guide before you start using OZEMPI® 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.</p> <p><b>What is the most important information I should know about OZEMPI®?</b></p> <p><b>OZEMPI® may cause serious side effects, including:</b></p> <ul style="list-style-type: none"> <li>• <b>Possible thyroid tumors, including cancer.</b> 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, OZEMPI® and medicines that work like OZEMPI® caused thyroid tumors, including thyroid cancer. It is not known if OZEMPI® will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people.</li> <li>• Do not use OZEMPI® 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).</li> </ul> <p><b>What is OZEMPI®?</b></p> <p>OZEMPI® is an injectable prescription medicine used:</p> <ul style="list-style-type: none"> <li>• along with diet and exercise to improve blood sugar (glucose) in adults with type 2 diabetes mellitus.</li> <li>• 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.</li> <li>• to reduce the risk of kidney disease worsening, kidney failure (end-stage kidney disease), and death due to cardiovascular disease in adults with type 2 diabetes mellitus and chronic kidney disease.</li> </ul> <p>It is not known if OZEMPI® is safe and effective for use in children.</p> <p><b>Do not use OZEMPI® if:</b></p> <ul style="list-style-type: none"> <li>• 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).</li> <li>• you have had a serious allergic reaction to semaglutide or any of the ingredients in OZEMPI®. See the end of this Medication Guide for a complete list of ingredients in OZEMPI®. See “<b>What are the possible side effects of OZEMPI®?</b>” for symptoms of a serious allergic reaction.</li> </ul> <p><b>Before using OZEMPI®, tell your healthcare provider if you have any other medical conditions, including if you:</b></p> <ul style="list-style-type: none"> <li>• have or have had problems with your pancreas.</li> <li>• have a history of diabetic retinopathy.</li> <li>• have severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems with digesting food.</li> <li>• are scheduled to have surgery or other procedures that use anesthesia or deep sleepiness (deep sedation).</li> <li>• are pregnant or plan to become pregnant. It is not known if OZEMPI® will harm your unborn baby. You should stop using OZEMPI® at least 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.</li> <li>• are breastfeeding or plan to breastfeed. It is not known if OZEMPI® passes into your breast milk. You should talk with your healthcare provider about the best way to feed your baby while using OZEMPI®.</li> </ul> <p><b>Tell your healthcare provider about all the medicines you take,</b> including prescription and over-the-counter medicines, vitamins, and herbal supplements. OZEMPI® may affect the way some medicines work and some medicines may affect the way OZEMPI® works.</p> <p><b>Before using OZEMPI®, talk to your healthcare provider about low blood sugar and how to manage it.</b> Tell your healthcare provider if you are taking other medicines to treat diabetes, including insulin or sulfonylureas.</p> <p>Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.</p>	<p>This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 01/2025</p> <p>For more information, go to OZEMPI.com or call 1-888-693-6742. © 2025 Novo Nordisk All rights reserved. US250ZM01123 October 2025</p> 
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**INSTRUCTIONS FOR USE****OZEMPI<sup>®</sup> [oh-ZEM-pick]**

(semaglutide) injection, for subcutaneous use

0.25 mg or 0.5 mg doses

(pen delivers doses in 0.25 mg or 0.5 mg increments only)

- **Read these instructions carefully before using your OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> pen.

• Start by checking your pen to make sure that it contains OZEMPI<sup>®</sup>, 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 select doses of 0.25 mg or 0.5 mg. Each prefilled pen contains 4 doses of 0.25 mg and 2 doses of 0.5 mg or contains 4 doses of 0.5 mg.

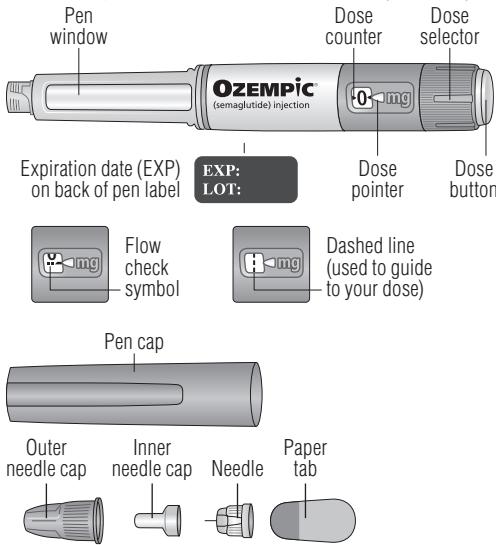
• Your pen is made to be used with NovoFine<sup>®</sup> Plus or NovoFine<sup>®</sup> disposable needles up to a length of 8 mm.

• NovoFine<sup>®</sup> Plus 32G 4 mm disposable needles are included with your OZEMPI<sup>®</sup> pen.

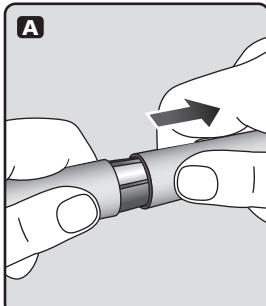
• **Always use a new needle for each injection.**

Supplies you will need to give your OZEMPI<sup>®</sup> injection:

- OZEMPI<sup>®</sup> pen
- a new NovoFine<sup>®</sup> Plus or NovoFine<sup>®</sup> needle
- 1 alcohol swab
- 1 gauze pad or cotton ball
- 1 sharps disposal container for throwing away used OZEMPI<sup>®</sup> pens and needles. See "Disposing of used OZEMPI<sup>®</sup> pens and needles" at the end of these instructions.

**OZEMPI<sup>®</sup> pen and NovoFine<sup>®</sup> Plus needle (example)****Step 1.****Prepare your pen with a new needle**

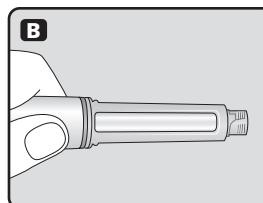
- Wash your hands with soap and water.
- Check the name and colored label of your pen, to make sure that it contains OZEMPI<sup>®</sup>. This is especially important if you take more than 1 type of medicine.
- Pull off the pen cap.



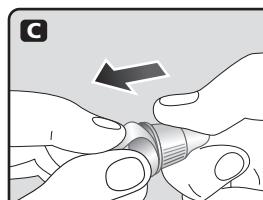
- Check that the OZEMPI<sup>®</sup> medicine in your pen is clear and colorless.

Look through the pen window. If OZEMPI<sup>®</sup> looks cloudy or contains particles, do not use the pen.

- Take a new needle, and tear off the paper tab. Do not attach a new needle to your pen until you are ready to give your injection.

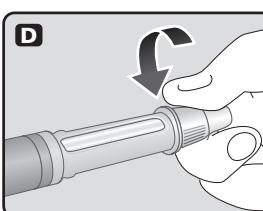


- Push the needle straight onto the pen. Turn until it is on tight.

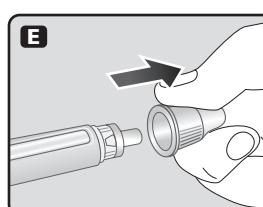


- The needle is covered by 2 caps. You must remove both caps. If you forget to remove both caps, you will not inject any medicine.

- Pull off the outer needle cap. Do not throw it away.



- Pull off the inner needle cap and throw it away. A drop of OZEMPI<sup>®</sup> may appear at the needle tip. This is normal, but you must still check the OZEMPI<sup>®</sup> flow if you use a new pen for the first time.



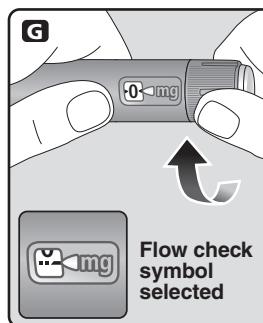
- ⚠ Always use a new needle for each injection. This will reduce the risk of contamination, infection, leakage of OZEMPI<sup>®</sup>, and blocked needles leading to the wrong dose.

**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.

**Step 2.****First Time Use for Each New Pen: Check the OZEMPI<sup>®</sup> flow**

- Check the OZEMPI<sup>®</sup> flow before the first injection with each new pen only. If your OZEMPI<sup>®</sup> 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 (---).

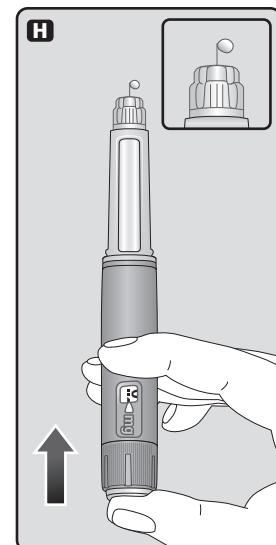


Flow check symbol selected

- 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> flows.

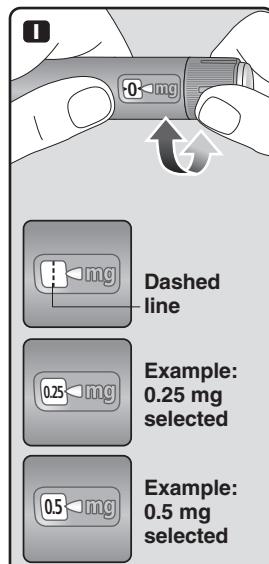
If no drop appears, you will not inject any OZEMPI<sup>®</sup>, even though the dose counter may move. **This may mean that there is a blocked or damaged needle.**

A small drop may remain at the needle tip, but it will not be injected. Only check the OZEMPI<sup>®</sup> flow before your first injection with each new pen.

**Step 3.**  
**Select your dose**

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

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



⚠ 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.**

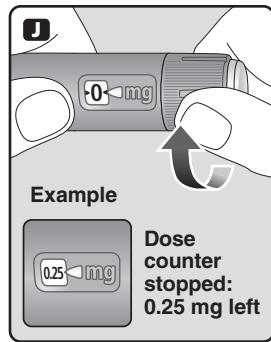
**Only doses of 0.25 mg or 0.5 mg can be selected with the dose selector.** The selected dose must line up exactly with the dose pointer to make sure that you get a correct dose. The dose selector changes the dose. **Only the dose counter and dose pointer will show how many mg you select for each dose.**

You can select 0.25 mg or 0.5 mg for each dose. When your pen contains less than 0.5 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 OZEMPI® is left?**

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



▲ Always watch the dose counter to make sure you have injected your complete dose. Hold the dose button down until the dose counter shows 0.

**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 OZEMPI® even though the dose counter has moved from the original dose that you have set.

**How to handle a blocked needle?**

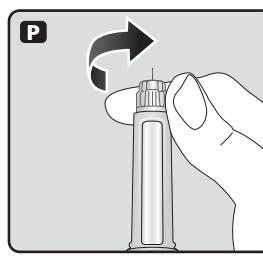
Change the needle as described in Step 5, and repeat all steps starting with Step 1: "Prepare your pen with a new needle".

**Never touch the dose counter when you inject.** This can stop the injection.

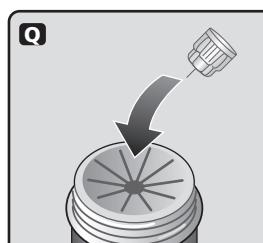
You may see a drop of OZEMPI® at the needle tip after injecting. This is normal and does not affect your dose.

**Step 5.****After your injection**

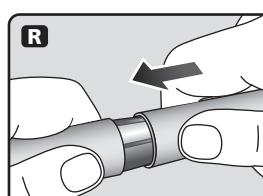
- Carefully remove the needle from the pen. Do not put the needle caps back on the needle to avoid needle sticks.



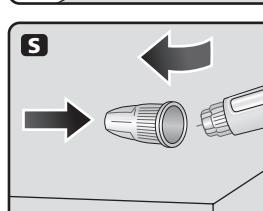
- Place the needle in a sharps disposal container right away to reduce the risk of needle sticks. See "Disposing of used OZEMPI® pens and needles" below for more information about how to dispose of used pens and needles the right way.



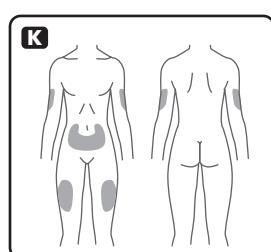
- Put the pen cap on your pen after each use to protect OZEMPI® from light.



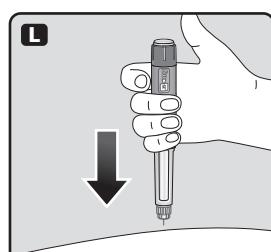
- If you do not have a sharps disposal container, follow a 1-handed needle recapping method. Carefully slip the needle into the outer needle cap. Dispose of the needle in a sharps disposal container as soon as possible.

**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.

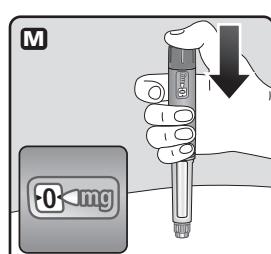


- Press and hold down the dose button until the dose counter shows 0.

The 0 must line up with the dose pointer. You may then hear or feel a click. Continue pressing the dose button while keeping the needle in your skin.

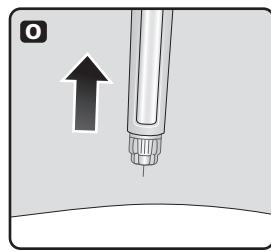
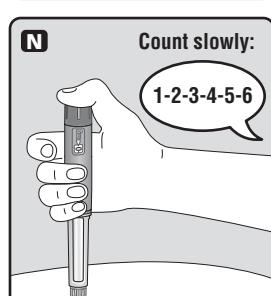
- Count 6 seconds while keeping the dose button pressed.

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



- Remove the needle from your skin. You can then release the dose button.

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 OZEMPI®, and blocked needles leading to the wrong dose. If the needle is blocked, you will not inject any OZEMPI®.

**Always dispose of the needle after each injection.****Disposing of used OZEMPI® pens and needles:**

- Put your used OZEMPI® 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 OZEMPI® 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 OZEMPI® 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 OZEMPI® 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 OZEMPI® pen?**

- Store your new, unused OZEMPI® 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 OZEMPI® pen you are using should be disposed of (thrown away) after 56 days, even if it still has OZEMPI® left in it. Write the disposal date on your calendar.
- Do not freeze OZEMPI®. Do not use OZEMPI® if it has been frozen.
- Unused OZEMPI® 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 OZEMPI® pens directly next to the cooling element.
- Keep OZEMPI® away from heat and out of the light.
- Keep the pen cap on when not in use.
- Keep OZEMPI® and all medicines out of the reach of children.



For more information go to [www.OZEMPI.com](http://www.OZEMPI.com)

**Manufactured by:**

Novo Nordisk A/S  
DK-2880 Bagsvaerd  
Denmark

**For information about OZEMPI® contact:**

Novo Nordisk Inc.  
800 Scudders Mill Road  
Plainsboro, NJ 08536  
1-888-693-6742

Version: 2

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**PATENT Information:** <http://novonordisk-us.com/patents/products/product-patents.html>

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Revised: September/2023

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US250ZM01123 October 2025



**INSTRUCTIONS FOR USE****OZEMPI<sup>®</sup> [oh-ZEM-pick]  
(semaglutide) injection, for subcutaneous use**

1 mg dose

(pen delivers doses in 1 mg increments only)

- Read these instructions carefully before using your OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> pen.

**Start by checking your pen to make sure that it contains OZEMPI<sup>®</sup>, 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. Each prefilled pen contains 4 doses of 1 mg.

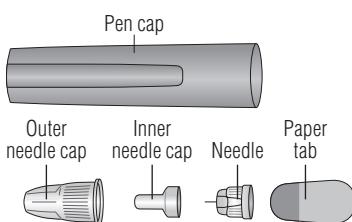
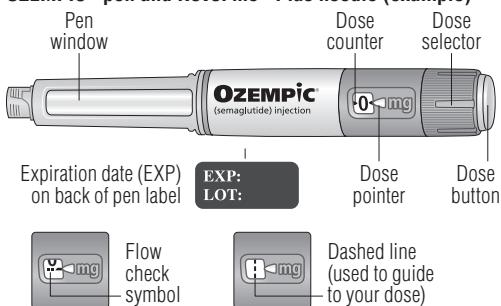
**Your pen is made to be used with NovoFine<sup>®</sup> Plus or NovoFine<sup>®</sup> disposable needles up to a length of 8 mm.**

**NovoFine<sup>®</sup> Plus 32G 4 mm disposable needles are included with your OZEMPI<sup>®</sup> pen.**

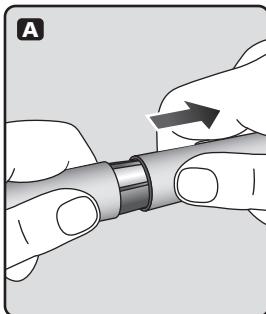
**Always use a new needle for each injection.**

Supplies you will need to give your OZEMPI<sup>®</sup> injection:

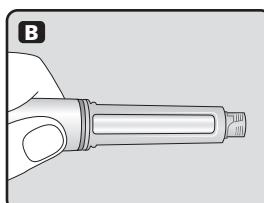
- OZEMPI<sup>®</sup> pen 1 mg dose
- a new NovoFine<sup>®</sup> Plus or NovoFine<sup>®</sup> needle
- 1 alcohol swab
- 1 gauze pad or cotton ball
- 1 sharps disposal container for throwing away used OZEMPI<sup>®</sup> pens and needles. See "Disposing of used OZEMPI<sup>®</sup> pens and needles" at the end of these instructions.

**OZEMPI<sup>®</sup> pen and NovoFine<sup>®</sup> Plus needle (example)****Step 1.****Prepare your pen with a new needle**

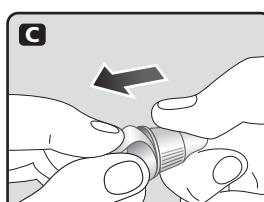
- Wash your hands with soap and water.**
- Check the name and colored label** of your pen, to make sure that it contains OZEMPI<sup>®</sup>. This is especially important if you take more than 1 type of medicine.
- Pull off the pen cap.**



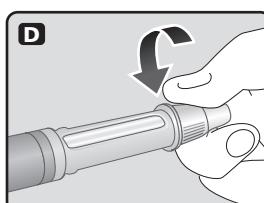
- Check that the OZEMPI<sup>®</sup> medicine in your pen is clear and colorless.** Look through the pen window. If OZEMPI<sup>®</sup> looks cloudy or contains particles, do not use the pen.



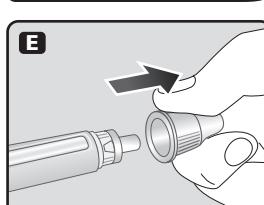
- Take a new needle,** and tear off the paper tab. **Do not attach a new needle** to your pen until you are ready to give your injection.



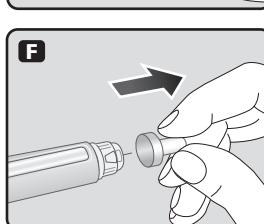
- Push the needle straight onto the pen.** Turn until it is on tight.



- The needle is covered by 2 caps. You must remove both caps.** If you forget to remove both caps, you will not inject any medicine.



- Pull off the outer needle cap.** Do not throw it away.

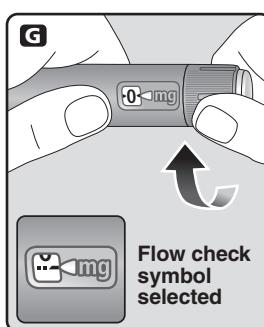


- Pull off the inner needle cap** and throw it away. A drop of OZEMPI<sup>®</sup> may appear at the needle tip. This is normal, but you must still check the OZEMPI<sup>®</sup> flow if you use a new pen for the first time.

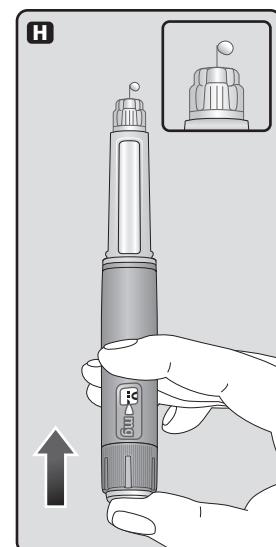
- Always use a new needle for each injection.** This will reduce the risk of contamination, infection, leakage of OZEMPI<sup>®</sup>, and blocked needles leading to the wrong dose. **Do not reuse or share your needles with other people. You may give other people a serious infection, or get a serious infection from them.** Never use a bent or damaged needle.

**Step 2.****First Time Use for Each New Pen: Check the OZEMPI<sup>®</sup> flow**

- Check the OZEMPI<sup>®</sup> flow before the first injection with each new pen only.** If your OZEMPI<sup>®</sup> 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 (—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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> still does not appear. Contact Novo Nordisk at 1-888-693-6742.

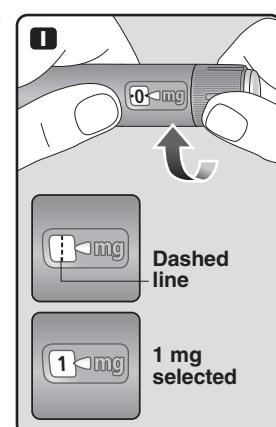
**Always make sure that a drop appears** at the needle tip before you use a new pen for the first time. This makes sure that OZEMPI<sup>®</sup> flows.

If no drop appears, you will **not** inject any OZEMPI<sup>®</sup>, 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 OZEMPI<sup>®</sup> flow before your first injection with each new pen.**

**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.



**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 OZEMPI<sup>®</sup> is left?**

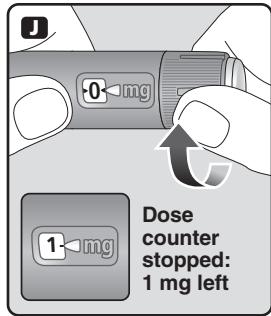
- To see how much OZEMPI<sup>®</sup> is left in your pen, use the dose counter. Turn the dose selector until the dose counter stops.

- 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 OZEMPI<sup>®</sup> left for a full dose of 1 mg.

If there is not enough OZEMPI<sup>®</sup> left in your pen for a full dose, do not use it. Use a new OZEMPI<sup>®</sup> 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 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 OZEMPI<sup>®</sup> 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".

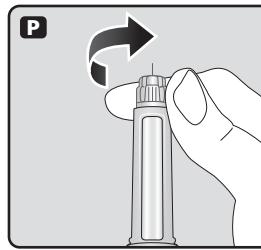
**Never touch the dose counter when you inject.** This can stop the injection.

You may see a drop of OZEMPI<sup>®</sup> 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.

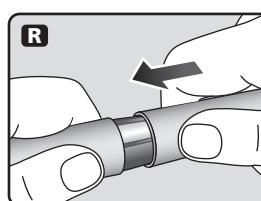
Do not put the needle caps back on the needle to avoid needle sticks.



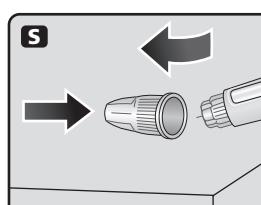
- Place the needle in a sharps disposal container right away to reduce the risk of needle sticks. See "Disposing of used OZEMPI<sup>®</sup> pens and needles" below for more information about how to dispose of used pens and needles the right way.



- Put the pen cap on your pen after each use to protect OZEMPI<sup>®</sup> from light.



- If you do not have a sharps disposal container, follow a 1-handed needle recapping method. Carefully slip the needle into the outer needle cap. Dispose of the needle in a sharps disposal 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 OZEMPI<sup>®</sup>, and blocked needles leading to the wrong dose. If the needle is blocked, you will not inject any OZEMPI<sup>®</sup>.

**Always dispose of the needle after each injection.****Disposing of used OZEMPI<sup>®</sup> pens and needles:**

- Put your used OZEMPI<sup>®</sup> 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>

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- 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> pen?**

- Store your new, unused OZEMPI<sup>®</sup> 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).
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- Do not freeze OZEMPI<sup>®</sup>. Do not use OZEMPI<sup>®</sup> if it has been frozen.
- Unused OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> pens directly next to the cooling element.
- Keep OZEMPI<sup>®</sup> away from heat and out of the light.
- Keep the pen cap on when not in use.
- Keep OZEMPI<sup>®</sup> and all medicines out of the reach of children.



For more information go to [www.OZEMPI.com](http://www.OZEMPI.com)

**Manufactured by:**

Novo Nordisk A/S  
DK-2880 Bagsvaerd  
Denmark

**For information about OZEMPI<sup>®</sup> contact:**

Novo Nordisk Inc.  
800 Scudders Mill Road  
Plainsboro, NJ 08536  
1-888-693-6742

Version: 4

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**PATENT Information:** <http://novonordisk-us.com/patents/products/product-patents.html>

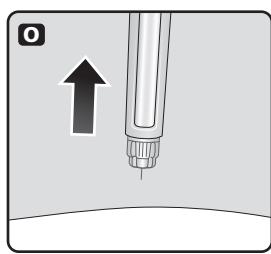
This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Revised: September/2023

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US250ZM01123 October 2025

- Remove the needle from your skin. You can then release the dose button.

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



**Always watch the dose counter to make sure you have injected your complete dose.** Hold the dose button down until the dose counter shows 0.



**INSTRUCTIONS FOR USE****OZEMPI<sup>®</sup> [oh-ZEM-pick]  
(semaglutide) injection, for subcutaneous use**

2 mg dose

(pen delivers doses in 2 mg increments only)

- **Read these instructions carefully before using your OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> pen.

**Start by checking your pen to make sure that it contains OZEMPI<sup>®</sup>, 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 8 mg of semaglutide, and you can only select doses of 2 mg. Each prefilled pen contains 4 doses of 2 mg.

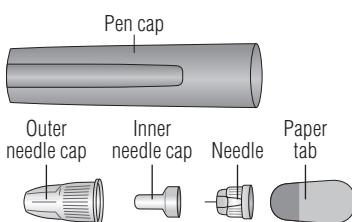
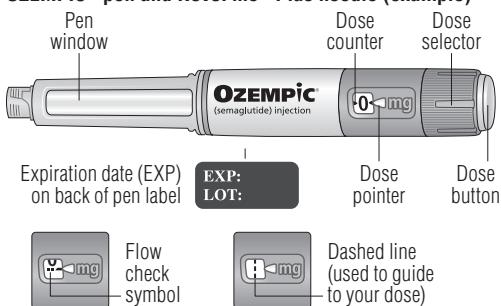
**Your pen is made to be used with NovoFine<sup>®</sup> Plus or NovoFine<sup>®</sup> disposable needles up to a length of 8 mm.**

**NovoFine<sup>®</sup> Plus 32G 4 mm disposable needles are included with your OZEMPI<sup>®</sup> pen.**

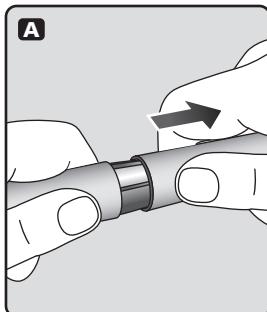
**Always use a new needle for each injection.**

Supplies you will need to give your OZEMPI<sup>®</sup> injection:

- OZEMPI<sup>®</sup> pen 2 mg dose
- a new NovoFine<sup>®</sup> Plus or NovoFine<sup>®</sup> needle
- 1 alcohol swab
- 1 gauze pad or cotton ball
- 1 sharps disposal container for throwing away used OZEMPI<sup>®</sup> pens and needles. See "Disposing of used OZEMPI<sup>®</sup> pens and needles" at the end of these instructions.

**OZEMPI<sup>®</sup> pen and NovoFine<sup>®</sup> Plus needle (example)****Step 1.****Prepare your pen with a new needle**

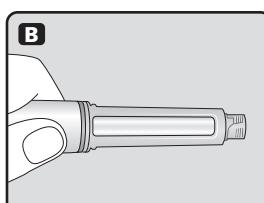
- Wash your hands with soap and water.
- Check the name and colored label of your pen, to make sure that it contains OZEMPI<sup>®</sup>. This is especially important if you take more than 1 type of medicine.
- Pull off the pen cap.



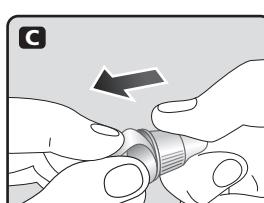
- Check that the OZEMPI<sup>®</sup> medicine in your pen is clear and colorless.

Look through the pen window. If OZEMPI<sup>®</sup> looks cloudy or contains particles, do not use the pen.

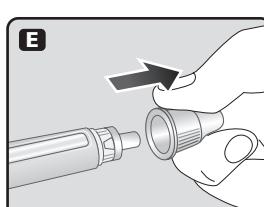
- Take a new needle, and tear off the paper tab. **Do not attach a new needle** to your pen until you are ready to give your injection.



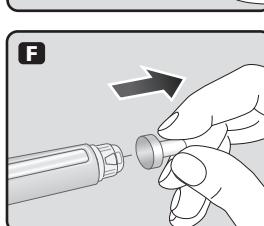
- Push the needle straight onto the pen. Turn until it is on tight.



- The needle is covered by 2 caps. You must remove both caps. If you forget to remove both caps, you will not inject any medicine.



- Pull off the outer needle cap. Do not throw it away.

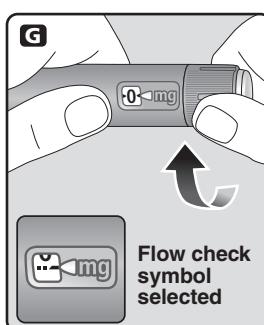


- Pull off the inner needle cap and throw it away. A drop of OZEMPI<sup>®</sup> may appear at the needle tip. This is normal, but you must still check the OZEMPI<sup>®</sup> flow if you use a new pen for the first time.

- **Always use a new needle for each injection.** This will reduce the risk of contamination, infection, leakage of OZEMPI<sup>®</sup>, 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.

**Step 2.****First Time Use for Each New Pen: Check the OZEMPI<sup>®</sup> flow**

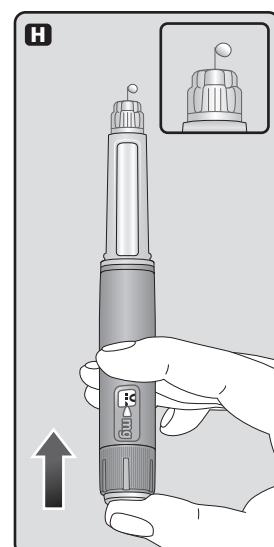
- Check the OZEMPI<sup>®</sup> flow **before the first injection with each new pen only.** If your OZEMPI<sup>®</sup> pen is already in use, go to Step 3 "Select your dose".
- Turn the dose selector **until the dose counter shows the flow check symbol (---).**



- 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> flows.

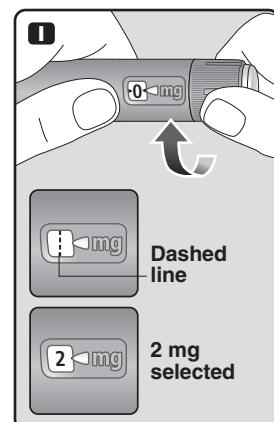
If no drop appears, you will **not** inject any OZEMPI<sup>®</sup>, even though the dose counter may move. **This may mean that there is a blocked or damaged needle.**

A small drop may remain at the needle tip, but it will not be injected. **Only check the OZEMPI<sup>®</sup> flow before your first injection with each new pen.**

**Step 3.**  
**Select your dose**

- Turn the dose selector until the dose counter stops and shows your 2 mg dose.

The dashed line in the dose counter (:) will guide you to 2 mg.



**Always use the dose counter and the dose pointer to see that 2 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 2 mg can be selected with the dose selector.** 2 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 2 mg has been selected.**

You can only select 2 mg for each dose. When your pen contains less than 2 mg, the dose counter stops before 2 mg is shown.

The dose selector clicks differently when turned forward or backward. Do not count the pen clicks.

**How much OZEMPI<sup>®</sup> is left?**

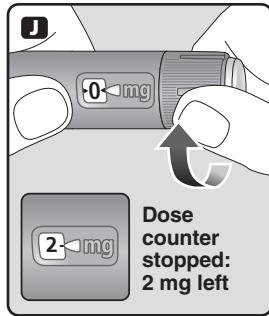
- To see how much OZEMPI<sup>®</sup> is left in your pen, use the dose counter. Turn the dose selector until the dose counter stops.

- If it shows 2, at least 2 mg is left in your pen. If the dose counter stops before 2 mg, there is not enough OZEMPI<sup>®</sup> left for a full dose of 2 mg.

If there is not enough OZEMPI<sup>®</sup> left in your pen for a full dose, do not use it. Use a new OZEMPI<sup>®</sup> 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 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 OZEMPI<sup>®</sup> 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".

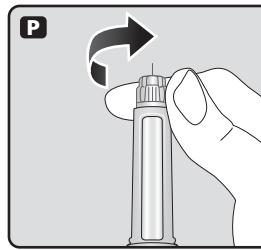
**Never touch the dose counter when you inject.** This can stop the injection.

You may see a drop of OZEMPI<sup>®</sup> 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.

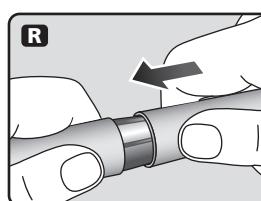
Do not put the needle caps back on the needle to avoid needle sticks.



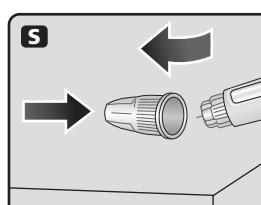
- Place the needle in a sharps disposal container right away to reduce the risk of needle sticks. See "Disposing of used OZEMPI<sup>®</sup> pens and needles" below for more information about how to dispose of used pens and needles the right way.



- Put the pen cap on your pen after each use to protect OZEMPI<sup>®</sup> from light.



- If you do not have a sharps disposal container, follow a 1-handed needle recapping method. Carefully slip the needle into the outer needle cap. Dispose of the needle in a sharps disposal 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 OZEMPI<sup>®</sup>, and blocked needles leading to the wrong dose. If the needle is blocked, you will not inject any OZEMPI<sup>®</sup>.

**Always dispose of the needle after each injection.****Disposing of used OZEMPI<sup>®</sup> pens and needles:**

- Put your used OZEMPI<sup>®</sup> 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>

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- 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> 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 OZEMPI<sup>®</sup> pen?**

- Store your new, unused OZEMPI<sup>®</sup> 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).
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**Manufactured by:**

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Denmark

**For information about OZEMPI<sup>®</sup> contact:**

Novo Nordisk Inc.  
800 Scudders Mill Road  
Plainsboro, NJ 08536  
1-888-693-6742

Version: 2

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**PATENT Information:** <http://novonordisk-us.com/patents/products/product-patents.html>

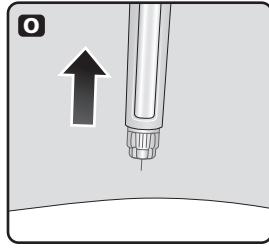
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US250ZM01123 October 2025

- Remove the needle from your skin. You can then release the dose button.

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



**Always watch the dose counter to make sure you have injected your complete dose.** Hold the dose button down until the dose counter shows 0.

