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*APPLICATION NUMBER:*

**209637Orig1s000**

**LABELING**

## HIGHLIGHTS OF PRESCRIBING INFORMATION

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

OZEMPIC (semaglutide) injection, for subcutaneous use  
Initial U.S. Approval: 2017

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

### INDICATIONS AND USAGE

OZEMPIC is a glucagon-like peptide 1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (1).

#### Limitations of Use:

- Not recommended as first-line therapy for patients inadequately controlled on diet and exercise (1, 5.1).
- Has not been studied in patients with a history of pancreatitis. Consider another antidiabetic therapy (1, 5.2).
- Not indicated for use in type 1 diabetes mellitus or treatment of diabetic ketoacidosis (1).

### DOSAGE AND ADMINISTRATION

- Start at 0.25 mg once weekly. After 4 weeks, increase the dose to 0.5 mg once weekly. If after at least 4 weeks additional glycemic control is needed, increase to 1 mg once weekly (2.1).
- Administer once weekly at any time of day, with or without meals (2.1).
- If a dose is missed administer within 5 days of missed dose (2.1).
- Inject subcutaneously in the abdomen, thigh, or upper arm (2.2).

### DOSAGE FORMS AND STRENGTHS

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

- Single-patient-use pen that delivers 0.25 mg or 0.5 mg per injection (3).
- Single-patient-use pen that delivers 1 mg per injection (3).

### CONTRAINDICATIONS

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

### WARNINGS AND PRECAUTIONS

- **Pancreatitis:** Has been reported in clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed (5.2).
- **Diabetic Retinopathy Complications:** Has been reported in a clinical trial. Patients with a history of diabetic retinopathy should be monitored (5.3).
- **Never share an OZEMPIC pen between patients,** even if the needle is changed (5.4).
- **Hypoglycemia:** When OZEMPIC is used with an insulin secretagogue or insulin, consider lowering the dose of the secretagogue or insulin to reduce the risk of hypoglycemia (5.5).
- **Acute Kidney Injury:** Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions (5.6).
- **Hypersensitivity Reactions:** Discontinue OZEMPIC if suspected and promptly seek medical advice (5.7).
- **Macrovascular outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with semaglutide (5.8).

### ADVERSE REACTIONS

The most common adverse reactions, reported in  $\geq 5\%$  of patients treated with OZEMPIC are: nausea, vomiting, diarrhea, abdominal pain and constipation (6.1).

**To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc., at 1-888-693-6742 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

### DRUG INTERACTIONS

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

### USE IN SPECIFIC POPULATIONS

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

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 12/2017

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

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## 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 OZEMPIC causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined [see *Warnings and Precautions (5.1) and Nonclinical Toxicology (13.1)*].
- OZEMPIC is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) [see *Contraindications (4)*]. Counsel patients regarding the potential risk for MTC with the use of OZEMPIC and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with OZEMPIC [see *Contraindications (4) and Warnings and Precautions (5.1)*].

## 1 INDICATIONS AND USAGE

OZEMPIC is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus [see *Clinical Studies (14.1)*].

### Limitations of Use

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

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Recommended Dosage

- Start OZEMPIC with a 0.25 mg subcutaneous injection once weekly for 4 weeks. The 0.25 mg dose is intended for treatment initiation and is not effective for glycemic control.
- After 4 weeks on the 0.25 mg dose, increase the dosage to 0.5 mg once weekly.
- If additional glycemic control is needed after at least 4 weeks on the 0.5 mg dose, the dosage may be increased to 1 mg once weekly. The maximum recommended dosage is 1 mg once weekly.
- Administer OZEMPIC once weekly, on the same day each week, at any time of the day, with or without meals.
- The day of weekly administration can be changed if necessary as long as the time between two doses is at least 2 days (>48 hours).

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

## 2.2 Important Administration Instructions

- Administer OZEMPIC subcutaneously to the abdomen, thigh, or upper arm. Instruct patients to use a different injection site each week when injecting in the same body region.
- Inspect OZEMPIC visually before use. It should appear clear and colorless. Do not use OZEMPIC if particulate matter and coloration is seen.
- When using OZEMPIC with insulin, instruct patients to administer as separate injections and to never mix the products. It is acceptable to inject OZEMPIC and insulin in the same body region but the injections should not be adjacent to each other.

## 3 DOSAGE FORMS AND STRENGTHS

Injection: 2 mg/1.5 mL (1.34 mg/mL) of semaglutide as a clear, colorless solution available in:

- Pre-filled, disposable, single-patient-use pen that delivers 0.25 mg (for treatment initiation) or 0.5 mg (for maintenance treatment) per injection
- Pre-filled, disposable, single-patient-use pen that delivers 1 mg (for maintenance treatment) per injection.

## 4 CONTRAINDICATIONS

OZEMPIC is contraindicated in patients with:

- A personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) [*see Warnings and Precautions (5.1)*].
- Known hypersensitivity to semaglutide or to any of the product components [*see Warnings and Precautions (5.7)*].

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Risk of Thyroid C-Cell Tumors

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

Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.

OZEMPIC is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of OZEMPIC and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with OZEMPIC. 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

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