

# The Medical Letter<sup>®</sup>

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# The Medical Letter®

## on Drugs and Therapeutics

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### IN BRIEF

## Higher-Dose Semaglutide (*Ozempic*) for Type 2 Diabetes

The FDA has approved a higher-dose injectable formulation of the long-acting glucagon-like peptide-1 (GLP-1) receptor agonist semaglutide (*Ozempic*) for treatment of type 2 diabetes in adults. A single SC injection of the new 8 mg/3 mL formulation delivers 2 mg of semaglutide.

**SEMAGLUTIDE FORMULATIONS** – *Ozempic* has been available since 2018 in two multidose pens: one that delivers doses of 0.25 or 0.5 mg and one that delivers 1-mg doses (see Table 1). Up to 30% of patients treated with 1-mg doses of the drug do not achieve the desired A1C goal.<sup>1,2</sup> An oral formulation of semaglutide (*Rybelsus*) has been available for treatment of type 2 diabetes since 2019.<sup>3</sup> Injectable semaglutide is also available in a higher dose (2.4 mg) as *Wegovy* for chronic weight management in adults with or without type 2 diabetes who have a body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup> or a BMI  $\geq 27$  kg/m<sup>2</sup> and at least one weight-related comorbidity.<sup>4</sup>

Table 1. *Ozempic* Formulations

Strength	Dose Per Injection <sup>1</sup>	Cost <sup>2</sup>
2 mg/1.5 mL multidose pens	0.25 or 0.5 mg	\$892.00
4 mg/3 mL multidose pens	1 mg	892.00
8 mg/3 mL multidose pens	2 mg	892.00

1. Pens do not deliver doses lower than those specified.  
2. Approximate WAC for one pen WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly, April 5, 2022. Reprinted with permission by First Databank, Inc. All rights reserved. ©2022. www.fdbhealth.com/policies/drug-pricing-policy.

**CLINICAL STUDIES** – FDA approval of the new formulation was based on the results of a double-blind trial (SUSTAIN FORTE) in 961 patients with type 2 diabetes that was inadequately controlled on metformin with or without a sulfonyleurea. Patients were randomized to receive semaglutide 1 or 2 mg SC once weekly. Patients in the 2-mg group had statistically significantly greater mean changes from baseline at 40 weeks in A1C (-2.2% vs -1.9%) and weight (-6.9 kg vs -6.0 kg) compared to those in the 1-mg group.<sup>5</sup>

**ADVERSE EFFECTS** – GI adverse effects (nausea, vomiting, diarrhea, constipation) are common with semaglutide. In SUSTAIN FORTE, GI adverse effects occurred in 34% of patients in the 2-mg group and in 31% of those in the 1-mg group. Acute pancreatitis and cholelithiasis have been reported with use of injectable and oral semaglutide. The labels of all semaglutide formulations include a boxed warning about a risk of thyroid C-cell tumors (based on animal data, no corroborating human data); the drug is contraindicated for use in patients with a personal or family history of medullary thyroid carcinoma and in those with multiple endocrine neoplasia syndrome type 2.

**DOSAGE AND ADMINISTRATION** – The starting dosage of *Ozempic* for treatment of type 2 diabetes is 0.25 mg injected SC once weekly in the abdomen, thigh, or upper arm. After 4 weeks, if tolerated, the dose should be increased to 0.5 mg. If additional glycemic control is needed, the dose can be doubled every 4 weeks to a maximum of 2 mg once weekly.

Unused pens should be stored in the refrigerator; after first use, they can be kept at room temperature for up to 56 days. A new needle should be attached for each injection and injection sites should be rotated each week. *Ozempic* does not need to be reconstituted before administration.

**CONCLUSION** – A 2-mg dose of the injectable GLP-1 receptor agonist semaglutide (*Ozempic*) has been approved by the FDA for use in patients with type 2 diabetes that requires additional glycemic control. In one clinical trial, addition of semaglutide 2 mg once weekly to standard treatment reduced A1C and weight more than addition of a 1-mg dose of the drug, but the effect was modest. GI adverse effects were common with both doses. ■

1. Semaglutide (*Ozempic*) – another injectable GLP-1 receptor agonist for type 2 diabetes. *Med Lett Drugs Ther* 2018; 60:19.
2. Drugs for type 2 diabetes. *Med Lett Drugs Ther* 2019; 61:169.
3. Oral semaglutide (*Rybelsus*) for type 2 diabetes. *Med Lett Drugs Ther* 2019; 61:166.
4. Semaglutide (*Wegovy*) for weight loss. *Med Lett Drugs Ther* 2021; 63:106.
5. JP Frias et al. Efficacy and safety of once-weekly semaglutide 2.0 mg versus 1.0 mg in patients with type 2 diabetes (SUSTAIN FORTE): a double-blind, randomised, phase 3B trial. *Lancet Diabetes Endocrinol* 2021; 9:563.

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