# **The Medical Letter**<sup>®</sup>

on Drugs and Therapeutics

GLP-1 and GIP/GLP-1 RECEPTOR AGONISTS FOR TYPE 2 DIABETES

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### GLP-1 and GIP/GLP-1 RECEPTOR AGONISTS FOR TYPE 2 DIABETES

Drug	Diabetes-Related Indications	Usual Dosage	Other Information
GLP-1 Receptor Agonists			
<b>Dulaglutide – <i>Trulicity</i></b> (Lilly) 0.75, 1.5, 3, 4.5 mg/0.5 mL single- dose pens	<ul> <li>Treatment of type 2 diabetes in patients <a>10</a> years old</li> <li>Reduce the risk of MACE in adults with type 2 diabetes and established CV disease or multiple CV risk factors</li> </ul>	<ul> <li>10-17 years old: 0.75-1.5 mg SC once/week</li> <li>Adults: 1.5-4.5 mg SC once/week</li> <li>Titration: 0.75 mg once/week x 4 weeks; increase to 1.5 mg once/week and, in adult patients, increase in 1.5-mg increments every 4 weeks as needed (max 4.5 mg/week in adults)</li> </ul>	<ul> <li>Mean reduction in A1C at 52 weeks with 4.5-mg dose: 1.8%</li> </ul>
Exenatide – <i>Byetta</i> (AstraZeneca) 250 mcg/mL (1.2, 2.4 mL) prefilled pens	Treatment of type 2 diabetes in adults	5-10 mcg SC bid 60 minutes before meals <b>Titration:</b> 5 mcg bid; increase to 10 mcg bid after 1 month if needed	<ul> <li>Not recommended in patients with severe renal impairment or ESRD</li> </ul>
<b>Bydureon BCise (</b> AstraZeneca) 2 mg/0.85 mL autoinjectors	Treatment of type 2 diabetes in patients <a>10</a> years old	2 mg SC once/week	Not recommended in patients with an eGFR <45 mL/min/1.73 m <sup>2</sup>
<b>Liraglutide – <i>Victoza</i> (Novo Nordisk)</b> 18 mg/3 mL pens	<ul> <li>Treatment of type 2 diabetes in patients <a>10</a> years old</li> <li>Reduce the risk of MACE in adults with type 2 diabetes and established CV disease</li> </ul>	<ul> <li>Adults: 1.2-1.8 mg SC once/day</li> <li>10-18 years old: 0.6-1.8 mg once/day</li> <li>Titration: 0.6 mg SC once/day x 7 days, then 1.2 mg once/day; can increase to 1.8 mg once/day after 1 week if needed</li> </ul>	<ul> <li>Mean reduction in A1C at 52 weeks with 1.8-mg dose: 1.14%</li> <li>Liraglutide is also available as <i>Saxenda</i> (SC injection) for chronic weight management in patients ≥12 years old</li> </ul>
<b>Semaglutide – Ozempic</b> (Novo Nordisk) 0.68, 1.34, 2.68 mg/mL (3 mL) prefilled pens	<ul> <li>Treatment of type 2 diabetes in adults</li> <li>Reduce the risk of MACE in adults with type 2 diabetes and established CV disease</li> </ul>	0.5-2 mg SC once/week <b>Titration:</b> 0.25 mg SC once/week x 4 weeks, then 0.5 mg once/week; if needed, increase every 4 weeks to 1 mg once/week and then to 2 mg once/week (max 2 mg/week)	<ul> <li>Mean reduction in A1C at 40 weeks with 2-mg dose: 2.2%</li> <li>Semaglutide is also available as Wegovy (SC injection) for chronic weight management in patients ≥12 years old</li> </ul>
<b>Rybelsus</b> (Novo Nordisk) 3, 7, 14 mg tabs	Treatment of type 2 diabetes in adults	7-14 mg PO once/day 30 min before food with ≥4 ounces of plain water <b>Titration:</b> 3 mg PO once/day x 30 days, then 7 mg once/day; increase to 14 mg once/day after 30 days if needed	<ul> <li>Taking two 7-mg tablets to achieve 14-mg dose is not recommended</li> </ul>
GIP/GLP-1 Receptor Agonist			
<b>Tirzepatide – <i>Mounjaro</i></b> (Lilly) 2.5, 5, 7.5, 10, 12.5, 15 mg/0.5 mL single-dose pens or vials	Treatment of type 2 diabetes in adults	5-15 mg SC once/week <b>Titration:</b> 2.5 mg SC once/week x 4 weeks, then 5 mg once/week; increase in 2.5-mg increments every 4 weeks as needed (max 15 mg once/week)	<ul> <li>Mean reduction in A1C at 40 weeks with 15-mg dose: 2.1%</li> <li>Tirzepatide is also available as <i>Zepbound</i> (SC injection) for chronic weight management in adults</li> </ul>

**MACE =** major adverse cardiovascular effects; **CV =** cardiovascular; **ESRD** = end-stage renal disease



#### Missed Dose Instructions for

#### GLP-1 and GIP/GLP-1 Agonists for Type 2 Diabetes

#### Dulaglutide (Trulicity)

Administer as soon as possible if there is at least 72 hours until the next scheduled dose.

#### Exenatide (Byetta)

• Resume as prescribed with the next scheduled dose.

#### Exenatide (Bydureon BCise)

- Administer as soon as possible, if the next scheduled dose is due at least 3 days later.
- If the next scheduled dose is due 1 or 2 days later, do not administer the missed dose and instead resume with the next scheduled dose.

#### Liraglutide (Victoza)

- Resume with the next scheduled dose.
- If more than 3 days have elapsed since the last dose, reinitiate at 0.6 mg once daily to mitigate any gastrointestinal symptoms associated with reinitiation of treatment.

#### Semaglutide (Ozempic)

• Administer as soon as possible within 5 days after the missed dose. If more than 5 days have elapsed, skip the missed dose and administer the next dose on the regularly scheduled day.

#### Semaglutide (Rybelsus)

• The missed dose should be skipped and the next dose should be taken the following day.

#### Tirzepatide (Mounjaro)

• Administer as soon as possible within 4 days after the missed dose. If more than 4 days have elapsed, skip the missed dose and administer the next dose on the regularly scheduled day.

#### **POSSIBLE ADVERSE EFFECTS**

- Nausea, vomiting, diarrhea, abdominal pain
- Injection-site reactions
- Increased heart rate
- ▶ Renal impairment and acute renal failure
- Possible pancreatitis and acute gall bladder disease
- Thyroid C-cell tumors reported in animals; contraindicated for use in patients with a personal or family history of medullary thyroid carcinoma and in patients with multiple endocrine neoplasia syndrome type 2.

#### **DRUG INTERACTIONS**

► GLP-1 and GIP/GLP-1 receptor agonists delay gastric emptying and may reduce the rate and extent of absorption of oral drugs, including oral contraceptives

#### **USE IN PREGNANCY AND LACTATION**

► Data are lacking on the safety of GLP-1 and GIP/GLP-1 receptor agonists in pregnant and lactating women

