Comparison of GLP-1 Agonists

(full update August 2024)

This chart compares GLP-1 agonists (including the "twincretin" tirzepatide) in regard to A1c reduction, weight loss, dosing, tolerability, clinical outcomes (e.g., cardiac or kidney benefit), how supplied, cost, and storage. For a review of class **adverse effects**, see **footnote f**.

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Dulaglutide (*Trulicity*) A1c: -1.09% (mean across trials)[1] Weight loss: 0.73 kg (mean across trials)[1]	Single dose pen (autoinjector): 0.75, 1.5, 3 (US), 4.5 mg (US) US: $977.42 Canada: ~$250 (1.5 mg/week) Store at 2°C to 8°C, or room temp (≤30°C) for ≤14 days.	**Initial**: 0.75 mg once weekly. **Max**: may increase to 1.5 mg once weekly, then by 1.5 mg weekly every four weeks to a max of 4.5 mg once weekly. **Comparative dose**: see footnote g. **Missed dose**: If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.[c] If ≥3 doses are missed, consider restarting with ≤1.5 mg.[15]	• Added to standard DM treatment in patients with CV disease or risk factors, over ~5.4 years reduced the composite of nonfatal MI, nonfatal stroke, and death from CV or unknown causes (NNT = 71).[4] For individual outcomes, only nonfatal stroke was significantly reduced. • Reduced a composite of new macroalbuminuria, 30% decrease in eGFR, or need for dialysis/transplant (NNT= 40), driven by prevention of macroalbuminuria (exploratory analysis).[5] • Discontinuation due to adverse GI effects (1.5 mg): ~1 in 15 patients[3]
Exenatide (*Byetta* [US]) A1c: -0.7% (10 mcg BID monotherapy)[a,c] Weight loss: -1.5 kg (10 mcg BID monotherapy)[a,c]	Sixty (60)-dose pen: 5, 10 mcg (needles not included) US: $849.95 Store at 2°C to 8°C. In-use pens can be stored at ≤25°C for up to 30 days.	**Initial**: 5 mcg BID within 60 min before the two main meals (≥6 hours apart). **Max**: may increase to 10 mcg BID after four weeks. **Comparative dose**: see footnote g. **Missed dose**: skip missed dose **Kidney impairment**: Not recommended if CrCl <30 mL/min. Use 10 mcg BID with caution if CrCl 30 to 50 mL/min. Use caution in kidney transplant.	• Discontinuation due to adverse GI effects (10 mcg BID): ~1 in 24 patients[3]

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Exenatide (*Bydureon BCise* [US]) A1c: -0.64% (adults); -0.71% (pediatrics)[a,c] Weight loss: 0.92 kg	Single dose pen (autoinjector): 2 mg US: $827.45 Store at 2°C to 8°C, or room temp (≤30°C) for ≤4 weeks.	For patients 10 years and older: 2 mg once every seven days **Comparative dose**: see footnote g. **Kidney impairment**: Not recommended if eGFR <45 mL/min/1.73 m^2. Use caution in kidney transplant. **Missed dose**: If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.	• Once-weekly exenatide added to standard DM therapy in patients with or without CV disease had a neutral CV effect, but was associated with a reduction in death from any cause compared to placebo (NNT = 341).[6] • Discontinuation due to adverse GI effects: ~1 in 22 patients.[3] • Highest rate of injection site reactions among once-weekly GLP-1s.[3] • Required mixing immediately before injection.
Liraglutide (*Saxenda*) Indicated for weight loss. Weight loss: 3.7 to 5.2 kg (3 mg once daily x 56 weeks)[a,c]	Dial-a-dose pen: 18 mg/3 mL (pen needles not included) US: $1,349.02 Canada: ~$450 Store at 2°C to 8°C. In-use pens can be stored at room temp (≤30°C) for ≤30 days.	For patients 12 years and older: 3 mg **once daily** (start with 0.6 mg once daily, increase dose weekly by 0.6 mg to goal of 3 mg once daily). For adults, discontinue after 16 weeks if <4% (after 12 weeks if ≤5% [Canada]) weight loss achieved. **Comparative dose**: see footnote g. **Missed dose**: Skip the missed dose. If more than three days have elapsed since the last dose, retitrate starting with 0.6 mg once daily (US).	• See *Victoza*, below for information on clinical outcomes in type 2 DM. • ~44% to 62% of patients met weight loss goal (≥5%) at 56 weeks compared to 16% to 34% with placebo. • Discontinuation due to adverse effects: ~1 in 11 patients.[c]
Liraglutide[d] (*Victoza*)	Dial-a-dose pen: 18 mg/3 mL	For patients 10 years and older:	• Added to standard care in patients with type 2 DM with CV disease or at high CV risk over ~4 years reduced:[7]

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
A1c: -1.04% (adults); -1.06 (pediatrics)[1,a,c] Weight loss: 1.33 kg[1]	(needles not included) US: $815.27 Canada: $336.10 Store at 2°C to 8°C. In-use pens can be stored at room temp (≤30°C) for ≤30 days.	**Initial**: 0.6 mg once daily for one week, then 1.2 mg once daily. (Pediatric patients may achieve control with 0.6 mg once daily.) **Max**: may increase to 1.8 mg once daily after one week. **Comparative dose**: see footnote g. **Missed dose**: Skip the missed dose. If more than three days have elapsed since the last dose, retitrate starting with 0.6 mg once daily (US).	○ death from CV causes, nonfatal MI, or nonfatal stroke, NNT = 53; death from CV causes, NNT = 77; death from any cause, NNT = 71. ○ new macroalbuminuria or doubling of SCr plus eGFR ≤45 mL/min/1.73 m^2, need for dialysis/transplant, or death from kidney causes (NNT =67), driven by prevention of macroalbuminuria (NNT = 83). ○ Did not reduce the individual rates of MI, nonfatal stroke, or HF-related hospitalizations. • Discontinuation due to adverse GI effects (1.8 mg): ~1 in 18 patients[3]
Semaglutide (*Ozempic*) A1c: -1.4% (1 mg weekly as monotherapy)[a,c] Weight loss (1 mg): 3.5 kg[a,c] *Continued… Ozempic*, continued	Multi-dose pen: 0.25 or 0.5 mg (four 0.25 mg doses or two 0.5 mg doses), 1 mg (4 doses), 2 mg (4 doses [US]) (includes needles) US: $1,291.36 Canada: ~$235 (1 mg/week) Store at 2°C to 8°C. In-use pens can be stored at room temp (≤30°C) for ≤56 days.	**Initial**: 0.25 mg once weekly for four weeks, then 0.5 mg once weekly, **Max**: may increase to 1 mg once weekly after four weeks. After four weeks on the 1 mg dose, may increase to 2 mg once weekly. **Comparative dose**: see footnote g. **Missed dose**: if <48 hours remain until the next scheduled dose, skip the missed dose. If >48 remain, administer the missed dose. If two or more consecutive doses are missed, consider starting with 0.25 mg once weekly.[c] Some experts would restart with 1 mg if one or two doses are missed, 0.5 mg if three or four doses are missed, or 0.25 mg if ≥5 doses are missed.[15]	• In type 2 DM patients with CV disease, CKD, or CV risk factors, reduced the combined endpoint of CV death, nonfatal MI, or nonfatal stroke (NNT = 44 for ~ 2 years). For individual outcomes, only nonfatal stroke was significant. A composite of new onset macroalbuminuria or doubling of SCr plus eGFR ≤45 mL/min/1.73 m^2, need for dialysis/transplant, or death from kidney causes was reduced (NNT = 44), driven by prevention of macroalbuminuria.[8] • In type 2 DM with CKD, reduced a composite of major kidney events (kidney failure, ≥50% reduction in eGFR, kidney or CV death) (NNT = 20 over 3 years). Kidney function declined more slowly, and the risks of major CV events and all-cause mortality were reduced.[21] • Discontinuation due to adverse GI effects (1 mg): ~1 in 10 patients[3]

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Semaglutide (*Rybelsus*) A1c: -1.1% (as monotherapy, 14 mg/day)[a,c] Weight loss (14 mg): 3.8 kg[a,c]	3 mg, 7 mg, or 14 mg tablets. US: 968.52 Canada: 233.38	**Initial**: 3 mg once daily at least 30 minutes before the first food, beverage, or other oral medications of the day, with ≤120 mL of water (~half a glass). After 30 days, increase the dose to 7 mg once daily. **Max**: After 30 days on the 7 mg dose, may increase to 14 mg once daily. **Comparative dose**: patients taking *Rybelsus* 14 mg may switch to *Ozempic* 0.5 mg. Patients on *Ozempic* 0.5 mg can be switched to *Rybelsus* 7 mg or 14 mg (US). Also see footnote g. **Missed dose**: skip the missed dose	• ORAL semaglutide in patients with type 2 DM and CV disease, CKD, or CV risk factors had a neutral CV effect.[9] • Discontinuation due to adverse GI effects: ~1 in 15 patients[c]
Semaglutide (*Wegovy*) Indicated for weight loss. Weight loss: ~10.6 to 12.7 kg (2.4 mg once weekly at one year)[13,14]	Single-dose pen (autoinjector): 0.25, 0.5, 1, 1.7, 2.4 mg. US: $1,349.02 Canada: $419.73 Store at 2°C to 8°C. Can be stored at room temp (≤30°C) for ≤28 days.	For patients 12 years and older: 0.25 mg once weekly, increased every four weeks to 0.5 mg, 1 mg, 1.7 mg, then 2.4 mg once weekly. Canada: consider stopping if the patient is not showing progress after 12 weeks on the maintenance dose. **Comparative dose**: see footnote g. **Missed dose**: if <48 hours remain until the next scheduled dose, skip the missed dose. If >48 hours remain, administer the missed dose. If two or more consecutive doses are missed, consider restarting with 0.25 mg once weekly.[c] Some experts would restart with 1 mg if one or two doses are missed, 0.5 mg if three or four doses are missed, and 0.25 mg if ≥5doses are missed.[15]	• Reduces CV risk (prevents 1 event for every 67 patients treated for ~ 3 years.[10] • 67% to 85% of patients met weight loss goal (≥5%) at 52 weeks compared to 30% to 48% with placebo.[13,14] • Discontinuation due to adverse effects: ~ 1 in 15 patients[c]
Tirzepatide[e] (*Mounjaro*) A1c: -2.1%[1,a]	Single-dose vial or pen (autoinjector [US]): 2.5, 5, 7.5, 10, 12.5 (US), 15 mg (US)	**Initial**: 2.5 mg once weekly for four weeks, then 5 mg once weekly. **Max**: may increase by 2.5 mg/week every four weeks to a max of 15 mg once weekly.	• May delay oral contraceptive absorption. Advise switching to a non-oral contraceptive or adding a barrier contraceptive for four weeks after initiation or a dosage increase.[c]

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Weight loss: 6.18 kg (as monotherapy, 15 mg/week).[a,c]	(vial does not includes needles or syringe) US: $1,069.08 Canada: ~$97 (10 mg vial) Store at 2°C to 8°C. Can be stored at room temp (≤30°C) for ≤21 days.	**Comparative dose**: see footnote g. **Missed dose:** If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.[c] If ≥3 doses are missed, consider restarting with ≤5 mg once weekly.[15]	• Discontinuation due to adverse GI effects (15 mg): ~1 in 16 patients.[c]
Tirzepatide[e] (*Zepbound* [US]) Indicated for weight loss. Weight loss: ~18.8 kg (15 mg once weekly at week 72)[12,a]	Single-dose vial or pen: 2.5, 5, 7.5, 10, 12.5, 15 mg (vials do not include syringe or needle) US: $1,059.87 Store at 2°C to 8°C. Can be stored at room temp (≤30°C) for ≤21 days.	Start with 2.5 mg once weekly, increase dose every 4 weeks to 5 mg, 7.5 mg, 10 mg, 12.5 mg, then 15 mg. **Comparative dose**: see footnote g. **Missed dose**: If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.[c] If ≥3 doses are missed, consider restarting with ≤5 mg once weekly.[15]	• May delay oral contraceptive absorption. Advise switching to a non-oral contraceptive or adding a barrier contraceptive for four weeks after initiation or a dosage increase.[c] • Discontinuation due to adverse effects: ~ 1 in 15 patients • Though no specific guidance is available, stopping after 12 weeks if <5% weight loss achieved is reasonable based on guidelines.[11] • 85% to 91% of patients met weight loss goal (≥5%) at 72 weeks compared to 35% with placebo.[12]

Abbreviations: BID = twice daily; CKD = chronic kidney disease; CV = cardiovascular; DM: diabetes mellitus; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; HF = heart failure; MI = myocardial infarction; NNT = number needed to treat; SCr = serum creatinine

a. Diabetes indication: mean A1c and weight reduction compared to placebo, as an add-on to other diabetes medication (unless monotherapy is specified). Weight loss indication: mean weight loss with lifestyle changes and/or diet. Weight loss is the amount above that seen with placebo. Weight loss varies based on lifestyle modification, baseline weight, etc.
b. Wholesale acquisition cost (US) per month of maximum dose (or dose specified). US medication pricing by Elsevier, accessed July 2024. Canadian cost is wholesale. Prices for products that are dosed weekly represent a 28-day supply. Prices for products that are dosed daily represent a 30-day supply.

c. **US product information used in creation of this chart**: *Trulicity* (December 2022), *Byetta* (December 2022), *Bydureon BCise* (May 2023), *Saxenda* (April 2023), *Victoza* (July 2023), *Ozempic* (September 2023), *Rybelsus* (January 2024), *Wegovy* (March 2024), *Mounjaro* (July 2023), *Zepbound* (March 2024). **Canadian product monographs used in creation of this chart**: *Trulicity* (July 2024), *Saxenda* (April 2024), *Victoza* (March 2024), *Ozempic* (March 2024), *Rybelsus* (February 2024), *Wegovy* (March 2024), *Mounjaro* (July 2024)

d. **Liraglutide** is available in combination with insulin degludec (*Xultophy*).

e. **Tirzepatide** is a GLP-1 agonist and glucose-dependent insulinotropic polypeptide (GIP) agonist (i.e., a "twincretin").

f. **Adverse effects**:[c] (Note that in the US, these medications must be dispensed with a **Medication Guide**.)

- GI side effects are common during dose escalation (e.g., nausea, vomiting, diarrhea). Resulting volume depletion may lead to acute kidney injury. GLP-1 agonists have been associated with bowel obstruction.[17] Educate patients about the potential for ileus.[20]
  - These GI side effects, and delayed gastric emptying, entail special considerations in surgical patients. See our chart, *Perioperative Management of Diabetes*.
- These drugs carry warnings about gallbladder disease (low risk) and pancreatitis (association unclear).[3,19,20,c] Stop if pancreatitis is suspected, and do not restart if pancreatitis is confirmed. There have been reports of pancreatic cancer in patients using GLP-1 agonists, but current evidence does not support causality.[19]
- These drugs are contraindicated in patients with a personal or family history of medullary thyroid cancer or patients with multiple endocrine neoplasia type 2. They cause thyroid C-cell tumors in mice.
- Rapid improvement in glycemic control is associated with diabetic retinopathy complications.
- Risk of hypoglycemia is low as monotherapy.
- Monitor for depression and suicidal ideation in patients taking these drugs for weight loss. Discontinue if symptoms develop.
- Don't combine with other GLP-1 agonists. Generally, avoid use in patients taking a dipeptidylpeptidase-4 inhibitor (e.g., saxagliptin), as combining these two classes of medications is unlikely to improve weight loss or glycemic control and is not cost-effective.[18]

g. **Comparative dosing based on glycemic efficacy**.[15] Consider a lower starting dose if GI tolerability is a priority.[16]

- exenatide 5 mcg BID ~liraglutide 0.6 mg/week ~semaglutide 3 mg orally once daily
- dulaglutide 0.75 mg/week ~ exenatide 10 mcg BID ~ liraglutide 1.2 mg/week ~ semaglutide 0.25 mg/week ~ semaglutide 7 mg orally once daily
- dulaglutide 1.5 mg/week ~ exenatide 2 mg/week ~ liraglutide 1.8 mg/week ~ semaglutide 0.5 mg/week ~ semaglutide 14 mg orally once daily ~ tirzepatide 2.5 mg/week
- dulaglutide 4.5 mg/week ~ semaglutide 1 mg/week
- semaglutide 2 mg/week ~ tirzepatide 5 mg/week

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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