

Shed Light on Oral Semaglutide for Cardiovascular Protection

Top Takeaways

- Oral semaglutide shows CV benefits in high-risk type 2 diabetes.
- It's another option alongside certain GLP-1 agonists and SGLT2 inhibitors.
- Daily dosing while fasting is crucial, and switching between products needs careful timing.

Oral semaglutide (Rybelsus) is now approved to prevent major adverse CV events in certain high-risk adults with type 2 diabetes.

We know that some injectable GLP-1 agonists (dulaglutide, etc) and oral SGLT2 inhibitors (canagliflozin, etc) reduce major CV events in patients with type 2 diabetes and high CV risk...and are recommended in Canadian guidelines.

Now evidence shows that oral semaglutide 14 mg/day prevents one CV death, nonfatal MI, or nonfatal stroke for every 56 type 2 diabetes patients with CV disease and/or CKD treated for about 4 years...versus placebo.

But there are no head-to-head trials to say if one GLP-1 agonist is better than another or better than SGLT2 inhibitors at reducing major CV events.

For adults with type 2 diabetes who have CV disease or are at high CV risk, consider oral semaglutide as another option.

Choose a med based on cost, comorbidities, patient preference, etc.

For example, GLP-1 agonists cost at least \$240/month versus about \$90/month for SGLT2 inhibitors.

Emphasize “starting low and going slow” with GLP-1 agonists...to improve GI tolerability. And consider risks, such as gallbladder disease, rare pancreatitis, etc.

Be aware that oral semaglutide must be taken DAILY with no more than half a cup or 120 mL of water...at least 30 minutes before the first food, other beverage, or oral meds of the day. Not doing so reduces efficacy.

Point out that injectable semaglutide and dulaglutide are given SC WEEKLY...but liraglutide is given SC DAILY...at any time of day, regardless of meals.

Help patients switch between semaglutide injectable and oral.

For example, patients on semaglutide 0.5 mg SC weekly can start oral semaglutide 7 or 14 mg/day up to 7 days after the last injection.

On the other hand, suggest semaglutide 0.5 mg SC weekly for patients switching from semaglutide 14 mg po daily, starting the day after the last oral semaglutide dose.

Recommend more frequent blood glucose checks during either switch.

Discuss risks with SGLT2 inhibitors...since they're linked to volume depletion, genital yeast infections, etc.

Be aware, these meds can cause euglycemic ketoacidosis...and may need to be held around surgery, during vomiting or severe diarrhea, etc.

For more guidance on selecting treatment based on comorbidities, see our *Stepwise Treatment of Type 2 Diabetes and Diabetes Medications: Cardiovascular and Kidney Impact*.

Cite this document as follows: Article, Shed Light on Oral Semaglutide for Cardiovascular Protection, Pharmacists' Letter Canada, March 2026

The content of this article is provided for educational and informational purposes only, and is not a substitute for the advice, opinion or diagnosis of a trained medical professional. If your organization is interested in an enterprise subscription, email sales@trchealthcare.com.

© 2026 Therapeutic Research Center (TRC). TRC and Pharmacists' Letter Canada and the associated logo(s) are trademarks of Therapeutic Research Center. All Rights Reserved.

Key References:

- McGuire DK, Marx N, Mulvagh SL, et al. Oral semaglutide and cardiovascular outcomes in high-risk type 2 diabetes. N Engl J Med 2025;392:2001-12.
 - Diabetes Canada. <https://guidelines.diabetes.ca/home> (Accessed February 4, 2026).
- Pharmacist's Letter Canada. March 2026, No. 420325

Cite this document as follows: Article, Shed Light on Oral Semaglutide for Cardiovascular Protection, Pharmacist's Letter Canada, March 2026

The content of this article is provided for educational and informational purposes only, and is not a substitute for the advice, opinion or diagnosis of a trained medical professional. If your organization is interested in an enterprise subscription, email sales@trchealthcare.com.

© 2026 Therapeutic Research Center (TRC). TRC and Pharmacist's Letter Canada and the associated logo(s) are trademarks of Therapeutic Research Center. All Rights Reserved.