



Pharmacy Pearls

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New medication class for the treatment of adults with Type 2 Diabetes Mellitus

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New dual-targeted treatment for Type 2 Diabetes: tirzepatide (Mounjaro®)

- **Novel mechanism of action:** dual GLP-1 and GIP (glucose-dependent insulinotropic polypeptide) agonist that increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, and slows gastric emptying.
- **Formulation:** Once-weekly subQ injection given via single-use auto-injector pen (volume per injection = 0.5 mL).
- **Dosing:** Starting dose = 2.5 mg once weekly x 4 weeks, Maintenance dose = 5-15 mg once weekly
 - Can increase dose by 2.5 mg weekly every 4 weeks, up to a max of 15 mg weekly
- **Contraindications:** Personal or family history of medullary thyroid cancer or multiple endocrine neoplasia syndrome type 2
- Evaluated in multiple clinical trials (SURPASS for diabetes and SURMOUNT for weight loss)
 - Most frequent adverse events reported with tirzepatide were nausea, diarrhea, vomiting, and decreased appetite.

Tirzepatide Published Studies:

Study	Comparator	Patient Population	Duration	Change in A1c (%)*	Change in weight (kg)*
SURPASS-1	Placebo	T2DM, drug naïve	40 weeks	Tirzepatide: -2.07 Placebo: +0.04	Tirzepatide: -9.5 Placebo: -0.7
SURPASS-2 [^]	Semaglutide SubQ 1 mg	T2DM, metformin monotherapy	40 weeks	Tirzepatide: -2.3 Semaglutide: -1.86	Tirzepatide: -11.2 Semaglutide: -5.7
SURPASS-3	Insulin degludec	T2DM, metformin +/- SGLT2i	52 weeks	Tirzepatide: -2.37 Degludec: -1.34	Tirzepatide: -7.5 to -12.9 Degludec: +2.3
SURPASS-4	Insulin glargine	T2DM, metformin +/- SFU or SGLT2i	104 weeks	Tirzepatide: -2.58 Glargine: -1.44	Tirzepatide: -7.1 to -11.7 Glargine: +1.9
SURPASS-5	Placebo	T2DM, insulin glargine +/- metformin	40 weeks	Tirzepatide: -2.59 Placebo: -0.93	Tirzepatide: -10.9 Placebo: -1.7
SURMOUNT-1	Placebo	BMI > 30 kg/m ² OR > 27 kg/m ² w/ ≥1 weight-related complication	72 weeks	N/A	Tirzepatide: -23.6 Placebo: -2.4

Tirzepatide Ongoing Studies:

Study	Comparator	Patient Population	Duration	Outcomes	Expected Completion
SURPASS-AP-Combo	Insulin glargine	T2DM, metformin +/- SFU	40 weeks	Mean change in HbA1c from baseline	March 2022, not published as of 6/13/22
SURMOUNT-2	Placebo	T2DM and overweight/obese	79 weeks	% change in weight and A1c from baseline	March 2023
SURPASS-CVOT	Dulaglutide 1.5 mg weekly	T2DM, overweight, confirmed ASCVD	54 months	Composite of MI, stroke, and CV death	October 2024

*Based on maximum dose (15 mg weekly) of tirzepatide, ^Rates of adverse effects were similar across all tirzepatide and semaglutide treatment groups

Tirzepatide recommended place in therapy is not well-established and insurance coverage/PA requirements vary widely. Manufacturer co-pay savings cards available for commercially-insured patients.

Comparison of available GLP-1 agonists:

Drug	Route	Frequency	Approved Indication(s)	Average HbA1c reduction (%)*	Average weight reduction (kg)*	CV benefits?
Exenatide ER (Byetta)	SubQ	Twice daily	T2DM	-0.9	-2.9	No
Exenatide (Bydureon)	SubQ	Once weekly	T2DM	-1.6	-2.3	No
Dulaglutide (Trulicity)	SubQ	Once weekly	T2DM	-1.8	-5.0	Yes
Liraglutide (Victoza, Saxenda)	SubQ	Once daily	T2DM (Victoza), weight loss (Saxenda)	-1.5	-12.2	Yes
Semaglutide SubQ (Ozempic, Wegovy) [#]	SubQ	Once weekly	T2DM (Ozempic), weight loss (Wegovy)	-1.8	-15.0	Yes (Ozempic)
Semaglutide PO (Rybelsus)	PO	Once daily	T2DM	-1.4	-2.0	No

*Based on maximum dose of GLP-1 agonists; [#]Certain doses of semaglutide continue to experience intermittent shortages, patients may have difficulty obtaining these products