



Incretins and Pharmacologic Management of Obesity and Associated Comorbidities

1st Generation

2nd Generation

Generic (Brand)	Liraglutide (Saxenda)	Semaglutide (Wegovy)	Tirzepatide (Zepbound)
Indication	Chronic Obesity Management	Chronic Obesity Management Mitigate CV risk	Chronic Obesity Management
MOA	GLP-1 RA	GLP-1 RA	Dual GIP/GLP-1 RA
Effect	↓ appetite	↓ appetite	↓ appetite
How taken	SQ, once daily	SQ, once weekly	SQ, once weekly
Weight loss	~5-7%	~10-16%	~15-21%
A1C Benefit	-0.8 to -1.5%	-1.5 to -2%	-2 to -2.5%
Cardiac Benefits ASCVD/HF/CV Mortality	Benefit/Neutral/Benefit	Benefit/Neutral/Benefit	Unknown
MASLD Benefits	Improves steatosis, no proven impact on fibrosis	Improves steatosis, activity, and MASH resolution, no proven benefit on fibrosis, but may slow fibrosis progression	Reduces steatosis on imaging
OSA Benefits	Significant improvements in OSA outcomes vs diet and exercise alone	Unknown	Ph 3 results showed a significant reduction in AHI vs placebo
CKD Benefits	Ph 3 results showed lower rates of the development and progression of diabetic kidney disease than placebo	Ph 3 results showed a reduced risk of clinically important kidney outcomes and death from CV causes vs placebo	Unknown

AHI, apnea-hypopnea index; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cardiovascular; GLP-1, glucagon-like peptide-1; HF, heart failure; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MOA, mechanism of action; OSA, obstructive sleep apnea; PO, oral; SQ, subcutaneous injection.

Blonde L, et al. *Endocr Pract.* 2022;28(10):923-1049; Chakhtoura M, et al. *EClinicalMedicine.* 2023;58:101882; Dugan K, DeSantis A. Glucagon-like peptide 1-based therapies for the treatment of type 2 diabetes mellitus. In: Post TW, ed. *UpToDate.* 2024. Accessed July 18, 2024. <https://www.uptodate.com/contents/glucagon-like-peptide-1-based-therapies-for-the-treatment-of-type-2-diabetes-mellitus>; Grunvald E, et al. *Gastroenterology.* 2022;163(5):1198-1225; FDA Prescribing Information; Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216; Mann JFE. *N Engl J Med.* 2017;377(9):839-848; Enright C, et al. *J Endocr Soc.* 2023;7(3):bvac195; Wadden TA, et al. *Nat Med.* 2023;29(11):2909-2918; Perkovic V, et al. *N Engl J Med.* 2024;391(2):109-121.