



Medi-Cal Rx

No Added Benefit from Concomitant Use of GLP-1 Agonists and DPP-4 Inhibitors

August 30, 2023

Glucagon-like peptide-1 (GLP-1) receptor agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors (Table 1) are two novel medication classes used in the treatment of type 2 diabetes mellitus (T2DM). Both classes target the incretin system and increase the action of the endogenous hormone GLP-1, which regulates blood sugar levels by stimulating insulin secretion, suppressing glucagon release, slowing gastric emptying, and promoting satiety. Although management of T2DM often requires combination therapy, the U.S. Food & Drug Administration (FDA), the American Diabetes Association (ADA), and the American Association of Clinical Endocrinology (AACE) do not recommend the concomitant use of GLP-1 agonists and DPP-4 inhibitors, as no additional benefit is provided when these agents are used together.¹⁻³ While concurrent therapy provides no clinical benefits, it may increase risks of side effects and other negative outcomes associated with polypharmacy.

What to Do if Your Patient Is Taking Both a DPP-4 Inhibitor and a GLP-1 Agonist

For patients currently taking both a DPP-4 inhibitor and a GLP-1 agonist, the ADA and AACE recommend discontinuing the DPP-4 inhibitor and continuing the GLP-1 agonist, when possible.^{1,3} Comparative trials show important differences between the two classes with respect to glycemic lowering, weight effects, and effects on systolic blood pressure and lipid profile. In contrast with GLP-1 agonists, DPP-4 inhibitors have not been shown to reduce the occurrence of major cardiovascular events and are neutral in terms of weight loss. The difference in cardiovascular efficacy may be due to improved pharmacological activation of the GLP-1 receptor with GLP-1 agonists. Discontinuation of either drug does not require tapering.

For more information regarding treatment selection for T2DM, including considerations for patient-specific factors, providers may refer to the [Standards of Care in Diabetes—2023](#) and the [American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update](#).

Table 1. GLP-1 Agonists and DPP-4 Inhibitors on the Medi-Cal Rx Contract Drugs List *

GLP-1 Agonists	DPP-4 Inhibitors	DPP-4 Inhibitor Combination Drugs
<ul style="list-style-type: none"> • Dulaglutide • Exenatide • Liraglutide • Semaglutide 	<ul style="list-style-type: none"> • Alogliptin • Linagliptin • Saxagliptin • Sitagliptin 	<ul style="list-style-type: none"> • Alogliptin/Metformin HCL • Alogliptin/Pioglitazone • Linagliptin/Empagliflozin • Linagliptin/Empagliflozin/Metformin HCL • Linagliptin/Metformin HCL • Saxagliptin/Metformin HCL ER • Sitagliptin/Metformin HCL

* For current information on covered products, check the [Medi-Cal Rx Contract Drugs List](#) page on the [Medi-Cal Rx Web Portal](#).

References

1. ElSayed NA, Aleppo G, Aroda VR, et al. 9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes—2023*. *Diabetes Care*. 2023;46(Suppl 1):S140-S157. Available at: <https://doi.org/10.2337/dc23-S009>.
2. Lajthia E, Bucheit JD, Nadpara PA, et al. Combination therapy with once-weekly glucagon like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes: a case series. *Pharm Pract (Granada)*. 2019 Oct-Dec;17(4):1588. Available at: <https://doi.org/10.18549/PharmPract.2019.4.1588>.
3. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update. *Endocr Pract*. 2023;29(5):305-340. Available at: <https://doi.org/10.1016/j.eprac.2023.02.001>.