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No Added Benefit from Concomitant Use of GLP-1 Receptor Agonists or Dual GIP/GLP-1 Receptor Agonists with DPP-4 Inhibitors

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 RA, and dipeptidyl peptidase-4 (DPP-4) inhibitors are novel medications used in the treatment of type 2 diabetes mellitus (T2DM). These classes target the incretin system and increase the action of the endogenous hormones GLP-1 and GIP, which regulate blood sugar levels by simulating 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 RAs or the dual GIP/GLP-1 RA with DPP-4 inhibitors, as no additional benefit is provided beyond that of a GLP-1 RA alone. In addition to not seeing additional clinical benefit, concurrent therapy may increase the risks of side effects, pill burden, and other negative outcomes associated with polypharmacy. The table below lists current DPP-4 inhibitors, GLP-1 RAs, and the dual GIP/GLP-1 RA. Note; this table only lists individual agents. Some agents may be found in combination products which are not listed in the table (e.g. alogliptin + metformin or liraglutide + insulin degludec).

For patients currently taking a DPP-4 inhibitor and a GLP-1 receptor agonist or dual GIP/GLP-1 RA, the ADA and AACE recommend discontinuing the DPP-4 inhibitor and continuing the GLP-1 receptor agonist or dual GIP/GLP-1 RA, when possible. Comparative trials show important differences between these agents with respect to glycemic lowering, weight effects, effects on cardiovascular disease (MACE and HF), and effects on chronic kidney disease. In contrast with GLP-1 RAs and dual GIP/GLP-1 RA, DPP-4 inhibitors have not been shown to reduce the occurrence of major cardiovascular events or improve kidney disease and are neutral in terms of weight loss. 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- 2025](#) and the [American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update](#).

DPP-4 Inhibitors	GLP-1 Receptor Agonists	Dual GIP and GLP-1 RA
<ul style="list-style-type: none"> • Alogliptin • Linagliptin • Saxagliptin • Sitagliptin 	<ul style="list-style-type: none"> • Dulaglutide • Exenatide • Exenatide (ER) • Liraglutide • Semaglutide 	<ul style="list-style-type: none"> • Tirzepatide

Section 9. Pharmacologic Approaches to Glycemic Treatment for Adults with Type 2 Diabetes; ADA Standards of Care in Diabetes – 2025 Key Updates

Recommendation 9.8 A person-centered shared decision-making approach should guide the choice of glucose-lowering medications for adults with type 2 diabetes. Use medications that provide sufficient effectiveness to achieve and maintain intended treatment goals with consideration of the effects on cardiovascular, kidney, weight, and other relevant comorbidities, hypoglycemia risk, cost and access, risk for adverse reactions and tolerability, and individual preferences.

Recommendation 9.10 In adults with type 2 diabetes and established or high risk of atherosclerotic cardiovascular disease, the treatment plan should include medications with demonstrated benefits to reduce cardiovascular events (e.g., glucagon-like peptide 1 receptor agonist [GLP-1 RA] and/or sodium–glucose cotransporter 2 [SGLT2] inhibitor) for glycemic management and comprehensive cardiovascular risk reduction (irrespective of A1C).

Recommendation 9.11 In adults with type 2 diabetes who have heart failure (HF) (with either reduced or preserved ejection fraction), an SGLT2 inhibitor is recommended for both glycemic management and prevention of HF hospitalizations (irrespective of A1C).

Recommendation 9.12 In adults with type 2 diabetes and symptomatic heart failure with preserved ejection fraction (HFpEF) and obesity, a GLP-1 RA with demonstrated benefits for both glycemic management and reduction of HF-related symptoms (irrespective of A1C) is recommended.

Recommendation 9.15 In adults with type 2 diabetes, metabolic dysfunction–associated steatotic liver disease (MASLD), and overweight or obesity, consider using a GLP-1 RA or a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA with potential benefits in metabolic dysfunction–associated steatohepatitis (MASH) for glycemic management and as an adjunctive to healthy interventions for weight loss.

Recommendation 16a In adults with type 2 diabetes and biopsy-proven MASH or those at high risk for liver fibrosis (based on noninvasive tests), pioglitazone, a GLP-1 RA, or a dual GIP and GLP-1 RA is preferred for glycemic management due to potential beneficial effects on MASH.

Recommendation 16b Combination therapy with pioglitazone plus a GLP-1 RA can be considered for the treatment of hyperglycemia in adults with type 2 diabetes with biopsy-proven MASH or those at high risk of liver fibrosis (identified with noninvasive tests) due to potential beneficial effects on MASH.

**Medicaid Statistics for Prescription Claims
March through May 2025**

	FFS	Wellpoint	Iowa Total Care	Molina Healthcare
Total \$ Paid	\$3,017,844	\$104,898,653	\$81,632,091	\$57,684,601
# Paid Claims	23,257	807,765	660,847	479,338
Unique Users	3,565	101,950	93,568	76,692
Avg Cost/Rx	\$129.76	\$129.86	\$123.53	\$120.34
Top 5 Therapeutic Class by RX Count <small>Therapeutic class taxonomy may differ among each plan</small>	Antidepressants	Antidepressants	Antidepressants	Antidepressants
	Anticonvulsants	Anticonvulsants	Anticonvulsants	ADHD/Anti-Narcolepsy
	ADHD/Anti-Narcolepsy	ADHD/Anti-Narcolepsy	ADHD/Anti-Narcolepsy	Anticonvulsants
	Antiasthmatic and Bronchodilator Agents	Antiasthmatic and Bronchodilator Agents	Antiasthmatic and Bronchodilator Agents	Antiasthmatic and Bronchodilator Agents
	Antihypertensives	Ulcer Drugs / Antispasmodics / Anticholinergics	Antidiabetics	Antidiabetics
Top 5 Therapeutic Class by \$ Amount <small>(pre-rebate) Therapeutic class taxonomy may differ among each plan</small>	Antidiabetics	Antidiabetics	Antidiabetics	Antidiabetics
	Dermatologicals	Dermatologicals	Dermatologicals	Dermatologicals
	Antipsychotics/Antimanic Agents	Antipsychotics/Antimanic Agents	Antipsychotic/Antimanic Agents	Antipsychotic/Antimanic Agents
	Analgesics – Anti-Inflammatory	Analgesics – Anti-Inflammatory	Analgesics – Anti-Inflammatory	Analgesics – Anti-Inflammatory
	Neuromuscular Agents	ADHD / Anti-Narcolepsy	Antiasthmatic and Bronchodilator Agents	Antivirals
Top 5 Drugs by Prescription Count	Albuterol	Omeprazole	Albuterol	Omeprazole
	Trazodone	Trazodone	Omeprazole	Amoxicillin
	Sertraline	Sertraline	Sertraline	Sertraline
	Fluoxetine	Levothyroxine	Trazodone	Albuterol HFA
	Cetirizine	Bupropion XL	Bupropion	Trazodone
Top 5 Drugs by Paid Amount <small>(pre-rebate)</small>	Evrysdi	Ozempic	Humira Pen	Ozempic
	Ozempic	Humira (CF) Pen	Ozempic	Dupixent
	Vraylar	Vraylar	Trikafta	Humira (2 pen)
	Humira Pen	Dupixent Pen	Dupixent	Vraylar
	Biktarvy	Jardiance	Vraylar	Biktarvy