WISCONSIN DRUG UTILIZATION REVIEW

Clinical Update

January 2026

Opportunity to Reduce and Optimize Prescribing for Patients with Type 2 Diabetes: GLP-1 RAs and DPP-4 Inhibitors

The State of Wisconsin Drug Utilization Review (DUR) program is required to retrospectively monitor drug use by Medicaid, BadgerCare Plus, and SeniorCare programs. The goal of this program is to improve patient outcomes and, when appropriate, lower health care costs. Recent updates to diabetes treatment guidelines prompted a review of concurrent use of glucagon-like peptide 1 receptor agonists (GLP-1 RAs) and dipeptidyl peptidase 4 inhibitors (DPP-4) that resulted in intervention letters being sent to prescribers with members identified on both medications.

Current guidelines from the American Diabetes Association (ADA) and the American Association of Clinical Endocrinology (AACE) do not support concurrent use of GLP-1 RAs and DPP-4 due to lack of added clinical benefit. The 2025 ADA guidelines state that concurrent use of DPP-4 inhibitors with a GLP-1 RA or a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA is not recommended due to lack of additional glucose lowering beyond that of a GLP-1 RA alone. Guidelines suggest that GLP-1 RAs are preferred over DPP4 inhibitors based on their more potent glucose-lowering effects and additional proven renal, cardiovascular, and weight loss benefits.[1] [2]

The mechanism of action by which GLP-1 RAs and DPP-4 inhibitor medications control blood glucose is by targeting the body's incretin system. Incretin system hormones (glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) help maintain glucose homeostasis by increasing insulin secretion and decreasing glucagon secretion. In patients with Type 2 diabetes, the effects of the incretin system may be blunted. The GLP-1 RAs act as "incretin mimetics" by stimulating the GLP-1 receptors to

[1] American Diabetes Association. (2025). Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes –2025. *Diabetes Care*. 48 (Suppl 1).
[2] Samson, Susan L. et al. (2023) American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update. *Endocrine Practice*. 29,5 (305 – 340)

augment insulin secretion. The DPP-4 inhibitors prevent the breakdown of endogenous incretin hormones to help elevate hormone concentrations thus improving response.[3] [4]

In clinical practice clinicians work hard with patients to establish glycemic control. After patients achieve improved control, clinicians do not always move quickly to discontinue medication, which is understandable. This might also seem reasonable given the mechanism of action of these medications, and it is common to think that concurrent use would result in improved glycemic control. However, this is not the case. Unlike endogenous GLP-1, pharmacological GLP-1 is not broken down by the DPP-4 enzyme. Therefore, using these medications concurrently yields no additional benefit.[4] [5] Prescribers should consider discontinuation of one of the medications due to lack of added clinical benefit, possible increased risk of side effects, and increased cost without enhanced glycemic control. They also should avoid starting new GLP-1 medications without considering simultaneous discontinuation of DPP-4 medications, when starting them. Periodic review of this clinical issue will continue as part of the retrospective DUR program.

[3] Gallwitz, Baptist. (2019). Clinical Use of DPP-4 Inhibitors. *Frontiers in Endocrinology* 10. doi: 10.3389/fendo.2019.00389.

[4] Gilbert, Matthew P., Pratley, Richard E. (2020). GLP-1 Analogs and DPP-4 Inhibitors in Type 2 Diabetes Therapy: Review of Head-to-Head Clinical Trials. *Frontiers in Endocrinology* 11. doi: 10.3389/fendo.2020.00178.

[5] Brunton S. GLP-1 receptor agonists vs. DPP-4 inhibitors for type 2 diabetes: is one approach more successful or preferable than the other? Int J Clin Pract. 2014 May;68(5):557-67. doi: 10.1111/ijcp.12361. Epub 2014 Feb 6. PMID: 24499291; PMCID: PMC4238422.