

GLP-1 Receptor Agonist Discontinuation and Reinitiation in Adults With Type 2 Diabetes: A National Claims-Based Analysis (2019-2025)

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Background: Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are established cornerstones of type 2 diabetes (T2DM) management, with proven cardiorenal and glycemic benefits. Despite their clinical importance, real-world persistence remains substantially lower than observed in randomized trials. Considering the expanding indications for GLP-1RAs, contemporary characterization of discontinuation and reinitiation patterns encompassing newer agents and diverse predictors is needed to optimize long-term therapeutic outcomes in T2DM.

Methods: We conducted a retrospective cohort study using Komodo Health U.S. claims data (January 2019–June 2025). Adults aged 18–64 with BMI ≥ 25 kg/m² and T2DM (ICD-10 codes or insulin/DPP-4 use) who initiated liraglutide, semaglutide, or tirzepatide were included, with 12 months of prior enrollment and ≥ 6 months of follow-up required. Discontinuation was defined as a ≥ 60 -day gap in GLP-1RA fills; reinitiation as a new fill following discontinuation. Cox proportional hazards models evaluated sociodemographic, clinical, and provider-level predictors.

Results: Among 60,222 T2DM patients in the discontinuation cohort, 1- and 2-year discontinuation rates were 41.5% and 58.0%, respectively. Tirzepatide (HR 0.59, 95% CI 0.56–0.63) and semaglutide (HR 0.72, 95% CI 0.69–0.76) were associated with substantially lower discontinuation hazards relative to liraglutide. Gastrointestinal adverse events were the leading driver of cessation (HR 1.37, 95% CI 1.31–1.43). Medicaid (HR 1.18, 95% CI 1.13–1.23) and Medicare (HR 1.17, 95% CI 1.13–1.20) coverage, as well as Black or African American race/ethnicity (HR 1.17, 95% CI 1.14–1.20), were associated with greater discontinuation risk. Endocrinologist-initiated prescriptions (HR 0.90, 95% CI 0.87–0.94) and $\geq 5\%$ weight loss (HR 0.91, 95% CI 0.90–0.92) were protective. Among 14,196 T2DM patients who discontinued, 53.6% reinitiated within 1 year and 65.9% within 2 years. Higher reinitiation hazards were observed in Black or African American patients (HR 1.25, 95% CI 1.18–1.32), those with $\geq 5\%$ weight gain (HR 1.10, 95% CI 1.08–1.13), and users of tirzepatide (HR 1.12, 95% CI 1.01–1.25) or semaglutide (HR 1.13, 95% CI 1.03–1.24). Medicaid (HR 0.86, 95% CI 0.79–0.95) and Medicare (HR 0.93, 95% CI 0.88–0.98) coverage

predicted lower reinitiation.

Conclusions: GLP-1RA use in T2DM follows an episodic pattern, with more than half of patients who discontinue reinitiating therapy within 1 year. Tirzepatide and semaglutide confer both greater persistence and higher reinitiation likelihood. Gastrointestinal tolerability, insurance coverage, and provider specialty represent modifiable targets to improve sustained GLP-1RA use in T2DM. Structured follow-up by endocrinologists may support improved long-term adherence.

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