

What's the Skinny on GLP-1s?

Over the past few years, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have garnered a lot of media attention with celebrities initially speaking out about "The Hollywood Weight Loss Drug" in 2022. GLP-1 RAs, aka incretin mimetics, have been around for over a decade to treat Type 2 diabetes. However, the obesity epidemic in our country has spurred increased use of GLP-1 based therapy and manufacturing of new pharmaceutical agents. So, what do we know about these medications, and how can you help your patients?

GLP-1 is a naturally occurring hormone made in the small intestines. By definition of agonist, this class of medications was manufactured to bind to GLP receptors of the GLP-1 hormone, designed to mimic the actions of the naturally occurring hormone.

What are the primary roles of GLP-1 hormone?

- Triggers insulin release from the pancreas
- Blocks glucagon secretion

- Delays gastric emptying
- Promotes satiety

It's no surprise that based on the prevalence of diabetes and obesity in the United States, pharmaceutical manufacturers have capitalized on the opportunity to bring new GLP-1 based therapy to market. The latest approval for chronic weight management came with tirzepatide (Zepbound), a dual GLP-1/ glucose-dependent insulinotropic polypeptide (GIP) receptor agonist. Expect to see additional dual receptor agonists come to market as multiple agents are already in the pipeline. Additionally, studies evaluating heart and kidney benefits beyond current FDA labeled indications are underway.

GLP-1 RAs are generally safe however, it is common for patients to experience gastrointestinal side effects, injection site reactions and elevated heart rate with initial few doses. They are contraindicated in patients with a history or at risk of pancreatitis, pregnancy and carry a black box warning about the risk of thyroid C-cell

tumors as shown in rodent studies. Human relevance of GLP-1-induced rodent thyroid C-cell tumors has not been determined. Cautionary use is recommended in renal and hepatic impairment and in the setting of hypoglycemia. While drug labels can be utilized to determine pertinent patient-specific drug interactions, it is important to note that GLP-1 RAs may slow gastric emptying and impact the absorption rate of other medications.

Affordability of GLP-1 RAs is also a factor. These agents are expensive, costing over \$1000 per month. The cost has prompted pharmacy benefit managers (PBM) and plan sponsors to deploy formulary and utilization management (UM) strategies (e.g., prior authorizations, step-edits, tiered copays, closed formularies, etc.). The PBM strategies impact patients continuing and starting GLP-1 based therapy for both diabetes and chronic weight management indications. GLP-1 RA manufacturers add another layer to the affordability factor with savings cards and patient assistance

Commercially Available GLP-1 RA Products

Generic Name	Brand Name	Frequency	FDA approved indication ¹
dulaglutide	Trulicity	Weekly	Type 2 diabetes
exenatide	Byetta	Twice a day	Type 2 diabetes
exenatide	Bydureon	Weekly	Type 2 diabetes
liraglutide	Victoza	Daily	Type 2 diabetes
liraglutide	Saxenda	Daily	Chronic Weight Mgmt
semaglutide	Ozempic	Weekly	Type 2 diabetes
semaglutide tablets ²	Rybelsus	Daily	Type 2 diabetes
semaglutide	Wegovy	Weekly	Chronic Weight Mgmt
tirzepatide ³	Mounjaro	Weekly	Type 2 diabetes
tirzepatide ³	Zepbound	Weekly	Chronic Weight Mgmt

¹FDA approved indications vary by age and select agents include an indication of reduction in risk of major adverse cardiovascular events. Refer to the package insert for full prescribing information.

²Only commercial product available in oral formulation

³Dual GLP-1/GIP receptor agonists

programs. While most programs follow the traditional model, one manufacturer with a chronic weight management indication has a unique strategy to bypass PBM restrictions. The manufacturer works directly with patients and prescribers, assisting individuals in obtaining the medication without navigating the PBM's formulary and UM criteria.

Lastly, GLP-1 RA accessibility is challenging. Demand has outpaced supply for months, with these agents allocated or backordered for most of 2023 and the first quarter of 2024. The supply issues have left patients and providers scrambling to find the medications to continue therapy and blocked many from initiating therapy. Accessibility issues have led to polypharmacy as patients' pharmacy hop or use non-FDA-approved compounded GLP-1 RA products.

Key Takeaways

- Specific glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are indicated as an adjunct in type 2 diabetes in combination with lifestyle modifications, with some having additional indications for their cardioprotective effects.
- Specific GLP-1 RAs are indicated as an adjunct for chronic weight management in combination with lifestyle modifications.
- GLP-1 RAs are generally considered safe. However, most patients experience gastrointestinal side effects. Depending on the severity, these side effects may impact therapy adherence or result in therapy abandonment.
- GLP-1 RA accessibility and affordability need to be considered. Care teams and patients should proactively plan for care interruptions while supply and cost issues persist.

Overall, GLP-1 RAs are useful to assist with combatting the national impact of obesity and diabetes. GLP-1 RAs are one tool in the toolbox and can't treat these conditions alone. Lifestyle, dietary modifications and behavioral interventions are an integral component of the conversa-

tion when developing a person-specific treatment plan. Lastly, safety, affordability, and accessibility must be assessed before GLP-1 initiation. For assistance developing GLP-1 RA strategies or workflows contact RevityRx. ■

References provided upon request

RevityRx is a boutique consulting firm bringing over thirty-five years of medication management expertise spanning the acute, ambulatory, and population health domains. For healthcare providers and solution vendors, RevityRx integrates medication management into clinical and operational workflows optimizing care delivery. For patients and caregivers, RevityRx's MedStew™ offering provides a known and trusted resource that simplifies medication use. We partner with our clients to shift from reactive to proactive healthcare. Contact Donna and John at info@RevityRx.com.



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