The Rise of GLP-1s to Improve Metabolic Health

Clinical background and considerations for plan sponsors



The Evolution of GLP-1s

Obesity, a complex chronic disease, is becoming increasingly prevalent in the United States.

This is due to a variety of causes including metabolic factors, eating patterns, nutrition attributes within the standard American diet, and physical activity levels.²

Glucagon-like peptide 1 receptor agonists (GLP-1s) have altered the way obesity and its frequently co-occurring condition, diabetes, are treated. Both are highly prevalent; obesity affects 70 million U.S. adults, while more than 37 million have diabetes.^{3,4} The use of GLP-1s has skyrocketed over the past few years, and the upward curve shows no sign of slowing: The category could reach more than \$77 billion in global sales by 2030.⁵

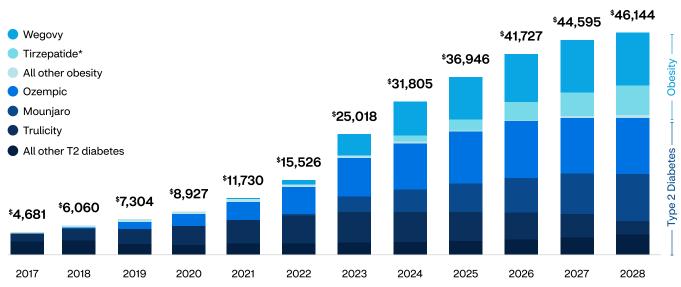
These medications can be costly and can result in significant cost increases for payors. With varying degrees of efficacy, adverse side effects, and adherence challenges, as well as potential downstream health outcomes, clients have much to consider as they weigh decisions on managing cost, coverage, and care for their plan members.



<u>Learn more about</u> <u>GLP-1s for obesity</u> >

GLP-1 pharmacy sales forecast

\$ in millions



Evaluate Pharma, September 20, 2023. *Includes current off-label use of Mounjaro for obesity and future use of tirzepatide following potential approval for obesity indication.

These estimates are supported by prescribing trends. Whereas only 230,000 scripts were written for GLP-1s in 2019, that number exceeded 9 million in 2022 and continues to grow.⁶ As GLP-1s are approved for expanded indications and new products in the category

are launched, this growth curve could continue to rise steeply.

GLP-1 medications for metabolic health

Drug	Frequency	Dosage form	Approved for	Who can take it?
Ozempic (semaglutide)	Weekly	EET	Type 2 diabetes	Adults
Rybelsus (semaglutide)	Daily	\bigcirc	Type 2 diabetes	Adults
Trulicity (dulaglutide)	Weekly	ET	Type 2 diabetes	Children 10 and up & adults
Victoza (liraglutide)	Daily	EET	Type 2 diabetes	Children 10 and up & adults
Byetta (exenatide)	Twice Daily	EET	Type 2 diabetes	Adults
Bydureon BCise (exenatide)	Weekly	EET	Type 2 diabetes	Children 10 and up & adults
Mounjaro (tirzepatide)	Weekly	EET	Type 2 diabetes	Adults
Wegovy (semaglutide)	Weekly	EET	Weight management	Children 10 and up & adults
Saxenda (liraglutide)	Daily	E	Weight management	Children 10 and up & adults

The potential cost and clinical impact of GLP-1 drugs

GLP-1s are a novel class of medications that drive weight loss by impacting brain signaling around appetite, hunger, and satiety. They are extremely effective, helping to reduce body weight on average by up to 21 percent.



Learn more about how GLP-1s work >

However, they are also expensive. Novo Nordisk's Wegovy, the branded name for semaglutide with the label indication for obesity, costs \$16,000 annually (\$1,300 per person per month) in the United States. If every U.S. adult with obesity were prescribed a GLP-1 agonist, the cost would total \$1.2 trillion.⁷

As new products are introduced, the market is likely to see downward pressure on cost when the effects of increased competition are felt. In its 2022 report, Morgan Stanley stated, "We expect the net price of GLP-1 medicines in obesity to fall to \$450/script in 2025E and \$350/script in 2030E."

The potential health impact of decreased obesity from use of GLP-1s may be significant.

There is promise of reduced disease burden, as obesity is associated with 200+ conditions, including cardiovascular disease, diabetes, and cancer, and even mental health conditions. Further, reduced obesity can decrease costs to the health care system. Weight loss of only 5 percent has been shown to be associated with reduced pharmacy and medical costs. 10

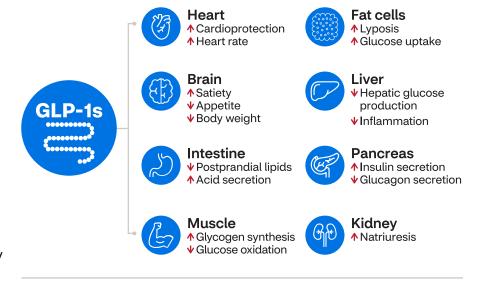
Perhaps most sobering, weight loss can prevent premature death; six of the ten leading causes of death are associated with obesity.¹¹

The link between diabetes and obesity

Being overweight increases risk for type 2 diabetes, heart disease, and stroke. In 2011, researchers warned of "the epidemic of obesity and diabetes," noting that both are risk factors for cardiovascular disease, the leading cause of death in the United States.^{12, 13}

Currently, 37.3 million Americans have diabetes, while 96 million have pre-diabetes.⁴ Approximately 90 percent of U.S. adults diagnosed with diabetes are overweight or obese.¹⁴ People with obesity are up to 80 times more likely to develop type 2 diabetes than those with a BMI of less than 22.¹⁵ However, just 7 percent of body weight loss can reduce the risk of developing diabetes by almost 60 percent.¹⁶

Both diabetes and obesity are treated with GLP-1s.



Many weight loss drugs currently on the market were originally introduced to treat type 2 diabetes; once weight loss became an evident side effect, manufacturers sought approval for new indications and developed new versions of their diabetes drugs. Wegovy is a higher-dose version of diabetes drug Ozempic (both semaglutide), while Saxenda

is a higher-dose version of Victoza (both liraglutide).

Over the past two years, off-label use of diabetes GLP-1 therapies for weight loss has become cause for national concern. This trend has been driven by high demand, which many attribute to social media, and ongoing shortages of Wegovy due to the manufacturer's inability to produce sufficient supply.¹⁷

Coming soon: Tirzepatide for weight loss

Tirzepatide is a novel agent that combines a GLP-1 agonist with a glucose-dependent insulinotropic polypeptide analogue. Approved for patients with type 2 diabetes in 2022, it is marketed under the brand name Mounjaro. The manufacturer, Eli Lilly, is seeking approval from the U.S. Food and Drug Administration for an obesity indication after a trial involving people with obesity, but not diabetes, demonstrated average weight loss of 20 percent.¹⁸

A phase III trial showed that a similar non-diabetic patient population lost up to 26.6 percent of their body weight. Market observers predict that tirzepatide will become the leading therapy in obesity and type 2 diabetes, forecasting FY2023 sales to be "significantly" higher than FY2022 sales of \$500 million.¹⁹



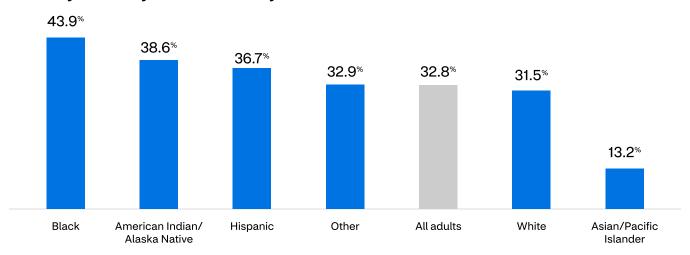
Learn more about the GLP-1 pipeline >

Health equity considerations

People of color face a disproportionate risk for obesity.²⁰ Black Americans have the highest rates of obesity and are 77 percent more likely to have diabetes.²¹ Four of five African American women are overweight or obese.²²

Additionally, 45 percent of Latinos/Hispanics struggle with obesity and are 66 percent more likely to have diabetes.²¹

Obesity rates by race/ethnicity²³



Differences in socioeconomic status, including education, employment, and income, are driven by social inequality, which affects access to resources needed to be healthy such as affordable healthy foods, safe and affordable physical activity, and others.

These social determinants impact

every aspect of health including disease burden, access to care, and health outcomes, and can represent entrenched challenges to effective disease management.

To achieve health equity in the treatment of diabetes and obesity, it's critical to deploy proven holistic and culturally relevant

models that are designed to serve this goal. In order to be maximally effective, these models must be informed by advanced data analytics and deep consumer behavior insights drawn from an integrated health care enterprise.

Program components that can serve health equity goals include:

- A virtual program that improves access regardless of location
- A diet-agnostic nutrition plan that incorporates geographic and cultural preferences
- An enrollment assessment that includes filters for social determinants of health
- Local resources to help address factors that contribute to health disparities

Treatment in practice



Estimates of the addressable market for GLP-1s for obesity vary widely.

Currently, 70 million U.S. adults have obesity, which is defined as a body mass index (BMI) of 30 or above.⁷ Experts estimate that fully half of the American population will be obese by 2030.²⁴

For the many Americans with a comorbid condition such as hypertension or hyperlipidemia, GLP-1s are approved for weight loss with a BMI of 27. This could increase the size of the addressable market, which may currently be underestimated.

Updated clinical guidelines include evaluation of GLP-1s for

use in adolescents; Wegovy is approved for use in people ages 12-17, so the potential patient population may be even larger.

33.5M+
Americans have diabetes and are overweight or obese

Driving sustainable behavior change

This class of drugs is most effective when dosed appropriately and paired with lifestyle changes including diet and exercise.

Comprehensive care management programs can accelerate savings on GLP-1s and promote better health outcomes for members.

Providing a care management program not only can help to control costs, but also ensure that weight loss is sustainable. Further, these approaches may help to prevent members from developing costly comorbid conditions.

GLP-1s for weight loss come with

notable adherence and persistence challenges. One study showed that 68 percent of commercial plan members were no longer taking their medications at the end of the first year.25 Additional adherence challenges may include insufficient supply, unpleasant side effects such as nausea and vomiting, and discomfort with the means of administration (eight of nine of these drugs are given by injection). Recent studies have demonstrated severe gastrointestinal adverse events, underscoring the importance of monitoring real-world evidence and being aware of risks associated with this drug class.26

Further, there is the success paradox that makes sustained results challenging: A person's declining BMI affects their coverage eligibility; once their BMI dips below 30 (or 27 with comorbidities), they may no longer be eligible for coverage. Studies show that Wegovy is "only effective as long as it's used." 18,27



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Considerations for plan sponsors



\$271**-**\$542

estimated annual productivity loss per employee with obesity²⁸

Each commercial plan sponsor will want to craft an approach to GLP-1s that combines coverage, cost, and care. Within the CVS Caremark employer book of business, approximately 70 percent of current plan members have coverage for weight loss medications.

Coverage decisions will depend on each client's benefit philosophy:
Whereas some would prefer to focus coverage on addressing existing health conditions, others may prefer to provide coverage for weight loss medications that may reduce downstream pharmacy and

medical spend. Another element of philosophy is whether the plan sponsor views pharmacy benefits as an important talent attraction and retention tool in today's competitive labor market. And many clients may assess their coverage options depending on the nature of their employee population. For example, those in industries that experience high turnover may opt for a more restrictive approach, while health plans that value the health outcomes and total cost of care impact that weight management can have in preventing chronic condition onset or progression may opt for thoughtful coverage paired with a care management program.

Within coverage, a number of utilization management options exists, ranging from less to more restrictive. These include quantity limits, step therapy, and prior authorization.

To drive to low net cost, clients can choose the plan design and formulary levers that work best for their plan goals, including a 100 percent member copay option and plan benefit design with category exclusion.

These approaches can be paired with care management to make weight loss success more likely for covered plan members.

Confidence in selecting these options will depend on each plan sponsor's comfort with the unknowns as the market continues to evolve.

How CVS Caremark views GLP-1s

To efficiently manage the dynamic GLP-1 category, CVS Caremark recommends an evidence-based approach in which plan sponsors evaluate the health needs of their respective covered populations.

If the decision is made to provide coverage of this class, we advise leveraging care management in a holistic approach that results in evidence-based, judicious use of GLP-1s and makes drug therapy more effective once initiated.

We are committed to providing support for plan sponsors in thoughtful, data-driven coverage decisions, by providing a comprehensive continuum of options and available modeling to inform coverage decisions, including medical cost avoidance and pharmacy spend savings.



Learn more about our strategies to maximize GLP-1 savings >



Looking ahead

Every plan sponsor should consider articulating a long-term approach that combines coverage, cost, and care to manage this category whose growth shows no signs of slowing.



Contact your account team to request an opportunity analysis.

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