

REPORT AT A GLANCE: OBESITY

KEY FINDINGS

Intervention	Comparators	Evidence Rating	US Price	Health-Benefit Price Benchmark
Injectable semaglutide	Lifestyle modification	A	Injectable semaglutide: \$6,829	Injectable semaglutide: \$9,100-\$12,500
Oral semaglutide	Lifestyle modification	A		
Tirzepatide	Lifestyle modification	A		
Tirzepatide	Injectable semaglutide	P/I	Tirzepatide: \$7,973	Tirzepatide: \$\$11,700-\$16,100
Tirzepatide	Oral semaglutide	P/I		
Oral semaglutide	Injectable semaglutide	C-	Oral semaglutide: Not yet approved	Oral semaglutide: \$8,300-\$11,400

“Semaglutide and tirzepatide have revolutionized the management of obesity. In addition to typically producing meaningful weight loss, these therapies reduce cardiovascular risk and improve multiple other aspects of the metabolic syndrome as well as additional obesity-related conditions. On average, these drugs are highly cost-effective, but the population in need of treatment is so great that even at these prices the US healthcare system will be strained to provide them to most people who need them in an affordable manner.”

– ICER’s Chief Medical Officer, David Rind, MD, MSc

THEMES AND RECOMMENDATIONS

- Existing GLP-1 manufacturers should extend the same ability offered to CMS to narrow the eligible patient population to other payers and purchasers without reducing the rebate or discount available.
- Large employers and other entities tasked with providing health benefits to patients should consider some of the innovative direct-to-business options being tried to expand access to comprehensive obesity care.
- Existing GLP-1 manufacturers, and those with products in the pipeline, should consider steep discounts to prices in exchange for higher volume.

Clinical Analyses

KEY CLINICAL BENEFITS STUDIED IN CLINICAL TRIALS

Obesity is a complex, chronic, and costly disease that affects physical and mental health and can result in an increased risk for other conditions such as diabetes, hypertension, liver disease, sleep apnea, cancer, and cardiovascular disease. Around 40% of the US population is currently living with obesity; there are racial and ethnic differences in obesity prevalence, with Black and Hispanic adults having higher rates of obesity. Adults living with obesity often have comorbidities – more than half have hypertension and nearly one-quarter have diabetes. Thus, the consequences of obesity are costly to both patients and to the health care system.

Obesity can start in childhood and thus can have lifelong effects on an individual's education, work, and social interactions. People living with obesity face substantial social stigma from the disease, with discrimination in workplace, education, and health care settings resulting in high rates of depression and anxiety. Additionally, individuals living with obesity shared that the health care system is ill-equipped to treat obesity, particularly as a lifelong, chronic disease. We heard that weight bias leads to delays in diagnosis and treatment and contributes to poorer health outcomes. Historically marginalized populations may have particular difficulty obtaining treatment for obesity and its complications. Finally, variable insurance coverage and high out-of-pocket costs substantially limit access to semaglutide and tirzepatide.

Comprehensive care for obesity includes lifestyle modifications (e.g., nutrition therapy, physical activity, behavioral modifications), medications, and bariatric surgery, alone or in combination. The emergence of GLP-1 receptor agonists (GLP-1 RA) like semaglutide and dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) RA like tirzepatide

have dramatically altered the landscape of obesity treatment. We evaluated the net health benefits of injectable semaglutide 2.4 mg, oral semaglutide 25 mg, and tirzepatide 15 mg in individuals with obesity and without diabetes. Treatment with all three drugs resulted in substantial weight loss compared with placebo, with a mean difference in weight loss compared with placebo of -17.8% with tirzepatide treatment, -13.1% with injectable semaglutide treatment, and -11.4% with oral semaglutide treatment. Greater weight loss with tirzepatide than injectable semaglutide was also seen in a head-to-head trial (-20.2% vs. -13.7%).

In patients with obesity and established cardiovascular (CV) disease, injectable semaglutide has been shown to reduce the risk of major cardiovascular events (MACE) (HR 0.80; 95% CI: 0.72, 0.90) and all-cause mortality (HR 0.81; 95% CI: 0.71, 0.93). Whether this CV risk reduction extends to oral semaglutide 25 mg is not clear, as this dose results in less weight loss than the injectable form, and a lower dose (14 mg) resulted in smaller CV risk reduction in a diabetes population. For tirzepatide, reported results from a CV outcomes trial in patients with diabetes showed an 8% reduction in MACE and a 16% reduction in all-cause mortality compared with dulaglutide, a GLP-1 RA, although full trial results have yet to be published.

All three drugs generally improved health-related quality of life, as well as metabolic risk factors such as blood pressure, blood glucose, and lipids. However, stopping semaglutide or tirzepatide appears to result in weight regain and regression of improvement in metabolic risk factors.

Clinical Analyses

Treatment with injectable semaglutide and tirzepatide have also been associated with improvements in obesity-related complications. Injectable semaglutide has been shown to improve outcomes in knee osteoarthritis (OA), metabolic-associated steatohepatitis (MASH), and heart failure with preserved ejection fraction (HFpEF), as well as reduce the risk of diabetes and chronic kidney disease (CKD). Tirzepatide has been shown to reduce the risk of diabetes and improve symptoms of obstructive sleep apnea.

The most common harms of both semaglutide and tirzepatide are gastrointestinal (GI) side effects, with around three-quarters of participants taking either injectable or oral semaglutide reporting GI side effects. For tirzepatide, 20-40% of participants reported nausea, diarrhea, or constipation in clinical trials. However, serious adverse events were uncommon, occurring in 3-10% of participants in the semaglutide trials and 4-6% in the tirzepatide trials.

Finally, discontinuation due to adverse events was also less than 10% for all three drugs.

Because treatment with all three drugs results in substantial weight loss and improvement in metabolic risk factors, we have high certainty that all three drugs have substantial net health benefit over lifestyle modifications alone (**A**). There is less certainty about the relative effects of the drugs to each other, particularly for outcomes beyond weight loss (e.g., CV outcomes), and thus we have judged the comparison between tirzepatide and semaglutide as “promising but inconclusive” (**P/I**). Treatment with oral semaglutide results in slightly lower amounts of weight loss compared with injectable semaglutide, with uncertainty about the degree of CV benefit, and thus we judged oral semaglutide to be “comparable or worse” than injectable semaglutide (**C-**).

Economic Analyses

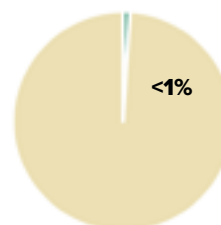
LONG-TERM COST EFFECTIVENESS

In cost-effectiveness analyses, we used estimated net prices from SSR Health of \$6,830 for injectable semaglutide and \$7,973 for tirzepatide; we assumed the price of oral semaglutide was the same as injectable semaglutide. Treatment with injectable semaglutide, oral semaglutide, and tirzepatide resulted in increased quality-adjusted life years (QALYs), equal-value life-years (evLYs) and life-years and fewer CV events compared with treatment with lifestyle modifications alone, with tirzepatide treatment resulting in the greatest gains. All drugs were cost-effective at the \$100,000 per QALY and evLY gained thresholds.

POTENTIAL BUDGET IMPACT

Despite these therapies being highly cost-effective, their potential budget impact is large. We estimate that fewer than 1% of eligible patients could be treated at current and assumed net prices before crossing the ICER budget impact threshold of \$880,000,000 annually. This raises serious concerns about affordability.

semaglutide (injectable/oral) and tirzepatide



Percent of eligible patients with obesity that could be treated in a given year before crossing the ICER potential budget impact threshold

Public Meeting Deliberations

VOTING RESULTS

ICER's Virtual Public Meeting: Voting Results on Clinical Effectiveness and Contextual Considerations .

ICER assessed, and the independent appraisal committee voted on the evidence for the net health benefit of injectable semaglutide, oral semaglutide, and tirzepatide. Some of the voting results on clinical effectiveness and benefits beyond health include the following:

- The panelists unanimously (**14-0**) found that current evidence is adequate to demonstrate a net health benefit of each of the three treatments (injectable semaglutide, oral semaglutide, and tirzepatide) as an add-on therapy to lifestyle modification in comparison to lifestyle modification alone.
- The majority of panelists (**13-1**) found that current evidence is not adequate to distinguish the net health benefit between tirzepatide and injectable semaglutide.
- The majority of panelists (**9-5**) found that the current evidence is not adequate to distinguish between the net health benefit between oral semaglutide and injectable semaglutide.

ICER's Virtual Public Meeting: Voting Results on Long-Term Value for Money

After reviewing the clinical evidence and considering the treatments' benefits beyond health noted above, the New England CEPAC evaluated the long-term value of injectable semaglutide, oral semaglutide, and tirzepatide at their current pricing:

- The majority of panelists (**12**) found that at their current pricing, both injectable semaglutide and oral semaglutide as add-on therapies to lifestyle modification represent "high" long-term value for money.
- The majority of panelists (**13**) found that at its current pricing, tirzepatide as an add-on therapy to lifestyle modification represents "high" long-term value for money.

About ICER

The Institute for Clinical and Economic Review ([ICER](https://www.icer.org)) is an independent, non-profit research institute that conducts evidence-based reviews of health care interventions, including prescription drugs, other treatments, and diagnostic tests. In collaboration with patients, clinical experts, and other key stakeholders, ICER analyzes the available evidence on the benefits and risks of these interventions to measure their value and suggest fair prices. ICER also regularly reports on the barriers to care for patients and recommends solutions to ensure fair access to prescription drugs. For more information about ICER, please visit www.icer.org.