How to Manage the GLP-1 Drug Class for Obesity Management

A Point of View Resource from Aon

August 31, 2023

Executive Summary

Even with varying efficacy and adverse effects, glucagon-like peptide-1 receptor agonists, or GLP-1s, have altered the drug treatment landscape for diabetes and obesity.

Currently, two GLP-1s on the market are approved by the FDA specifically for weight loss: Wegovy (semaglutide) and Saxenda (liraglutide). Just over the obesity treatment horizon is a dual-acting GLP drug, Mounjaro (tirzepatide), currently approved for treating diabetes. With even more significant weight loss efficacy, Mounjaro is expected to be approved by the FDA for weight loss by the end of Q1 2024.

Current obesity-treatment plan coverage considerations faced by U.S. plan sponsors:

- The prevalence of obesity in the United States adult population is almost 42%.
- A high price point for GLP-1s, which are not considered "Specialty" drugs, has significantly impacted plan budgets.
- These high-cost medications have also further magnified Diversity, Equity, and Inclusion (DEI) and cultural barriers to medical care.
- Off-label prescribing and significant utilization increases from unprecedented social media influence and direct-to-consumer drug advertising.
- Unknown duration of therapy for GLP-1s. It is possible patients taking GLP-1s will need to be on them for their lifetime to maintain a healthier body mass index (BMI).
- Lack of proven long-term clinical outcomes of GLP-1s.
- Supply issues due to the utilization spikes in 2023.
- Reported adherence challenge to therapy - 68% of patients taking GLP-1s stopped treatment within a year.[12] Reasons why are still being studied.
- Unknown longer-term adverse clinical outcomes associated with GLP-1 side effects.

Aon's GLP-1 guidance:

- Included both quality and quantitative questionnaire and compiled de-identified census and demographic data.
- At a minimum, plan sponsors should implement utilization management protocols, such as step therapy and prior authorization, to ensure the appropriateness of therapy, patient drug adherence, and clinical outcomes.
- Plan coverage of GLP-1 drugs should be paired with active patient engagement in a diet/exercise/lifestyle management program to support achieving and maintaining clinically appropriate weight.
  - Patients learn and adopt long-term approaches to healthier nutrition and exercise.
  - Patients receive ongoing coaching and behavioral health support for their GLP1 treatment plan.
- Implement a narrow GLP-1 prescriber network (including virtual care providers) to ensure appropriate prescribers are prescribing.
- Patient enrollment, engagement, and compliance within a diet/exercise/nutritional coaching program for three months before a GLP-1 drug is covered.
- Add utilization management programs to GLP-1 drugs for diabetes to prevent off-label use for weight loss.

Plan sponsors should check with their PBM or health plan to determine if care appropriateness strategies will impact rebate guarantees or other contracted performance or guarantees. However, it is essential to note that cost savings associated with ensuring appropriate patient care could outweigh said rebate impact.

Overview GLP-1 Drugs – Plan Sponsor Considerations

The drug therapy class known as glucagon-like peptide-1 receptor agonists, or GLP-1 has roots that date back to 1964 and research on insulin response.[1] Insulin is a hormone that helps the body manage glucose (sugar) from food. Insulin helps to move glucose out of the bloodstream and into our cells to be used as fuel for our body. Patients with type 2 diabetes cannot make and use insulin effectively, resulting in too much glucose in the bloodstream, which can have harmful consequences. The GLP-1 drugs help stimulate insulin to keep our blood sugar in check.

Research and development continued with GLP-1s, and exenatide was approved by the FDA in 2005. Since then, five other products have come to the market, as shown in the table below.

GLP-1	Route	Frequency	Indication
Bydureon (exenatide)	Injection	Weekly	Diabetes
Byetta (exenatide)	Injection	Twice daily	Diabetes
Mounjaro (tirzepatide)	Injection	Weekly	Diabetes
Ozempic (semaglutide)	Injection	Weekly	Diabetes
Rybelsus (semaglutide)	Oral	Daily	Diabetes
Saxenda (liraglutide)	Injection	Daily	Weight Loss
Trulicity (duraglutide)	Injection	Weekly	Diabetes
Victoza (liraglutide)	Injection	Daily	Diabetes
Wegovy (semaglutide)	Injection	Weekly	Weight Loss

Since 2005, research on the GLP-1 drug class has shown that these drugs effectively control blood sugar.[2] While efficacy and adverse effects vary, they have altered the drug treatment for diabetes and obesity management.

Social media has heavily influenced the use of GLP-1 drugs, with 1.4B views of "Ozempic" on TikTok as of July 2023, along with celebrity use and commentary. The combination of effective weight-loss drugs, the disease state of obesity that has needed innovation in drug treatment, and an unprecedented social media influence has brought plan sponsors to evaluate their options surrounding pharmacy plan coverage of GLP-1 drugs.

The management challenge stems from three distinct yet interrelated elements. These include drug treatment costs, disease prevalence, and concerns related to equity in plan coverage.

[1]https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7042958/#:~:text=The%20first%20GLP%2D1%20receptor,weight%20loss%2C%20low%20risk%20for; accessed 7/21/2023. An overview of GLP-1 agonists and recent cardiovascular outcomes trials. Postgrad Med J. 2020 Mar; 96(1133): 156-161.

[2]https://www.ncbi.nlm.nih.gov/books/NBK572151/#:~:text=The%20comparison%20of%20GLP%2D1,effects%2C%20adherence%2C%20and%20persistence; accessed 7/21/23. Compare and Contrast the Glucagon-Like Peptide-1 Receptor Agonists. StatPearls [Internet], March 27, 2023.

Cost

The GLP-1s for obesity management are expensive drugs with undiscounted list prices of around $1,330 per month and discounted, net of rebate plan costs to $700 to $900 per month. While expensive, they are not as highly priced as specialty medications or new multi-million-dollar gene therapies. Price becomes an issue when disease prevalence is considered.

Disease prevalence

The CDC reports that U.S. obesity prevalence is 41.9%, which includes all individuals with a BMI of 30 or greater.[3] As the table[4] shows, obesity and severe obesity in men and women have been trending up for decades. This combination of high cost and prevalence has led Aon to see employer health plans paying $3.85 per member per month in Q1 2023 for drugs in the obesity management category, with 99.1% comprised of Wegovy and Saxenda. This represents a 165% increase from the prior measurement period.

Plan coverage equity

There is no question that obesity is a disease, as the American Medical Association affirmed in 2013. Obesity, like other diseases, cannot be classified as a "lifestyle choice." When considering cost, prevalence rates, and the pursuit of providing fair plan coverage, even the largest plan sponsors face the harsh reality that they may not have enough plan funding to pay for all the requests for obesity management drugs. This has caused them to consider more prescriptive management strategies to balance these three elements to continue providing benefit coverage in the future.

Should drug coverage be driven by a patient's Body Mass Index (BMI)? Alternatively, should plan sponsors limit their financial exposure by setting the BMI criteria at 35 to ensure support for those at higher risk of health complications? Following this path and resetting the requirements for who gets the drug under the plan risks rebate payments from the manufacturer, further exaggerating the cost concerns. Do we say that only if you are part of a lifestyle change program that includes coaching and nutrition support can you get coverage for the drug under the plan? This sounds prescriptive and restrictive, but if we must put in some criteria to help manage the cost, then perhaps we need to see some effort put in by those who benefit from the funds. But is this fair? These are tough questions, requiring some wrestling by plan sponsors to reach a consensus.

[3]https://www.cdc.gov/obesity/data/adult.html; accessed 7/21/23. Adult Obesity Facts. Centers for Disease Control and Prevention. Overweight & Obesity, Data & Statistics.

[4]https://www.cdc.gov/nchs/data/hestat/obesity-adult-17-18/overweight-obesity-adults-H.pdf; accessed 7/21/23. Health E-Stats. Prevalence of Overweight, Obesity, and Severe Obesity Among Adults Aged 20 and Over: United States, 1960-1962 Through 2017-2018. National Center for Health Statistics, December 2020.

NCHS Health E-Stats, December 2020

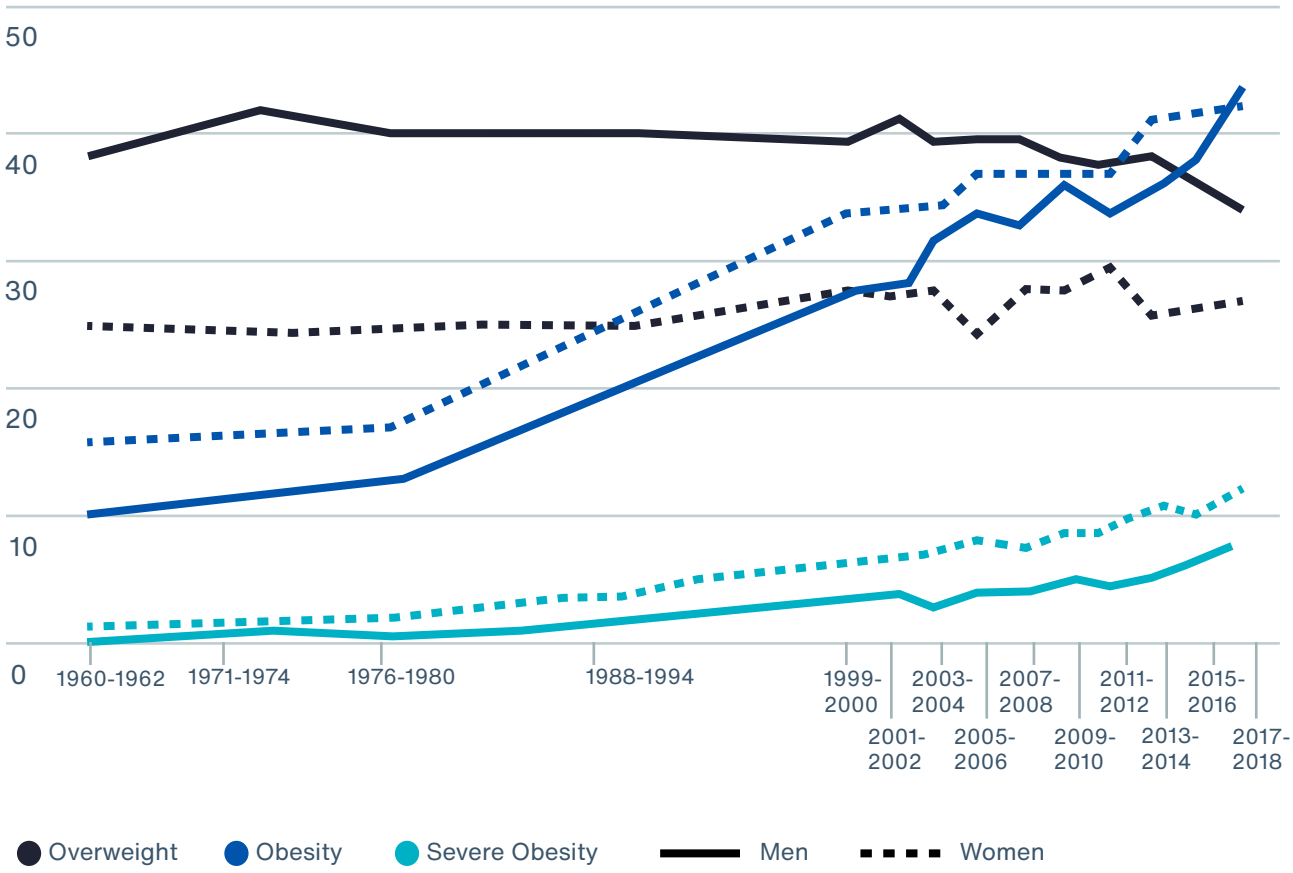


Figure. Age-adjusted trends in overweight, obesity, and severe obesity among men and women aged 20–74: United States, 1960–1962 through 2017–2018.

NOTES: Data are age adjusted by the direct method to U.S. Census 2000 estimates using age groups 20–39, 40–59, and 60–74. Overweight is body mass index (BMI) of 25.0–29.9 kg/m². Obesity is BMI at or above 30.0 kg/m². Severe obesity is BMI at or above 40.0kg/m². Pregnant women are excluded from the analysis.

SOURCES: National Center for Health Statistics, National Health Examination Survey and National Health and Nutrition Examination Surveys.

GLP-1 Drugs for Weight Loss

The market currently has two FDA-approved products for obesity management, Wegovy and Saxenda. Wegovy's efficacy has been reported up to 17% in the WSJ, which outpaces the 9% noted for Saxenda.[5] This reduced effectiveness and the once-daily injections make it a less favorable alternative. One of the GLP-1 drugs, Mounjaro (tirzepatide), is indicated for diabetes and is being studied for obesity management labeling. This newly labeled tirzepatide is expected as early as Q4 2023 or Q1 2024. As shown below, its weight loss results are even more significant.

	Ozempic	Wegovy	Mounjaro
Average Percentage Body Weight Loss	Studies not de-signed to assess weight loss	Up to 17%	Up to 22.5%
Approved Use	Type 2 diabetes	Obesity	Type 2 diabetes
Year Introduced in the U.S.	2017	2021	2022
Most Common Side Effects	Nausea, vomiting, diarrhea, abdominal pain	Nausea, diarrhea, vomiting, constipation	Nausea, diarrhea, decreased appetite, vomiting
Generic Name	semaglutide	semaglutide	tirzepatide
Manufacturer	Novo Nordisk	Novo Nordisk	Eli Lily

Figures are from separate studies that tested different dose levels for varying durations.

Source: The companies and the New England Journal of Medicine.

The pipeline of new drugs for obesity management runs deep. In addition to tirzepatide mentioned above, the pipeline includes:

- An oral form of semaglutide from Novo Nordisk is currently in phase 3 research.[6]
- Eli Lilly's GLP-1 product (orforglipron) is in phase 2 research[7] (further from launch). Weight reduction of up to 14.7% was seen at 36 weeks with orforglipron.[8]
- Eli Lilly's retatrutide (also phase 2) has demonstrated up to 17.5% mean weight reduction at 24 weeks and up to 24.2% at 48 weeks.[9]

More than a dozen products are being studied in Phase 2, and more than two dozen in Phase 1, the earliest research phase. While most of these products will not reach the market, the pipeline will continue to grow.

Generic availability of the less effective products will happen sooner than the more effective products. This does not create a favorable financial situation for plan sponsors as it is unlikely that prescribers will switch patients to less effective drugs for obesity management. Saxenda is expected to go generic in 2026, while a generic for Wegovy is not expected until 2032. The products coming to market, which appear likely to be more effective than Wegovy, will have patent expiration dates that push further out.

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9063254/; accessed 7/22/23. Efficacy of GLP-1 RA Approved for Weight Management in Patients With or Without Diabetes: A Narrrative Review. Adv Ther, 2022; 39(6): 2452-2467.

[6] https://www.novonordisk.com/news-and-media/news-and-ir-materials/news-details.html?id=166110; accessed 7/21/23. Company Announcement. Novo Nordisk A/S: Oral semaglutide 50mg achieved 15.1% weight loss (17.4% if all people adhered to treatment) in adults with obesity or overweight in the OASIS 1 Trial. Novo Nordisk, May 22, 2023.

[7] https://www.medscape.com/viewarticle/993667?form=fpf; accessed 7/21/23. New Oral GLP-1 Agonisit for Obesity, Type 2 Diabetes. Medscape, Miriam Tucker, June 24, 2023.

[8] https://www.nejm.org/doi/full/10.1056/NEJMoa2302392; accessed 7/21/23. Daily Oral GLP-1 Receptor Agonist Orforglipron for Adults with Obesity. NEJM, DOI: 10.1056/NEJMoa2302392, June 23, 2023.

[9] https://investor.lilly.com/news-releases/news-release-details/lillys-phase-2-retatrutide-results-published-new-england-journal; accessed 7/21/23. Lilly Investors. News Release. Lilly's phase 2 retatrutide results published in the New England Journal of Medicine show the investigational molecule achieved up to 17.5% mean weight reduction at 24 weeks in adults with obesity and overweight. June 26, 2023.

Managing the GLP-1s

Aon's recommended approach to managing the GLP-1s for obesity management is anchored in attending to the elements mentioned above: prevalence, cost, and equity. A review of the tactics shown below follows. Thoughtful action in each component begins with a data review.

Drug Data Overivew

Prevalence

- Third-party (or PBM) solution for diet, exercise, and coaching
- Prescriber focus
- Increase member accountability

Cost

- Incoporate utilization management
- Consider the use of step therapy
- Rebate analysis for potential changes
- Coverage on-ramp and off-ramp

Equity

- Cover under the plan
- Plan design
- Cultural competency
- Account for body type variations

Addressing Prevalence of Utilizers

We know the universe of potential utilizers is significant, and the utilization trend is accelerating, so tactics that address prevalence are key. Plan sponsor goals should be two-fold: ensure that those who need a GLP-1 for weight loss can access the drug and take advantage of this opportunity for patients to create lifelong changes toward healthier outcomes.

The FDA label for both Wegovy and Saxenda describes the drug as an "adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adult patients...."[10] This adjunct should be an organization that provides complete oversight of enrollment and engagement of the patient seeking coverage of a weight loss GLP-1 under the plan. A third-party point solution, a PBM, or a health plan carrier could provide these services.

Enrollment comes with questions that plans must answer in the design phase. For example, how much time should be spent on weight loss-related activities before GLP-1 coverage under the program is allowed? Should design consistency in medical management or step therapy align with the medical plan's bariatric surgery requirements?

If so, how? A goal is creating sustainable change, so perhaps one to three months is adequate to display a commitment to diet and exercise changes. Some may see this as disruptive and want the start of drug coverage and the program enrollment to be concurrent. In either scenario, collaborate with your PBM or health plan to ensure interfaces allow for data collection, which will be a step in the prior authorization process. Use of third-party solutions should not be an issue or impact any contractual rebate and pricing arrangements as long as the PBM/health plan prior authorization criteria for the obesity management GLP-1s, specifically the BMI ranges, are not adjusted beyond the FDA product labeling.

The plan should consider engagement for the patient, explicitly defining the activities required and frequency for patients to be considered "engaged." The goal is long-term diet and exercise changes, so engagement is critical. Patient engagement activities could include coaching, a food log, weight reporting, and exercise logs.

There are characteristics that Aon believes a point solution should offer, which are summarized below, that will best help plan sponsors, coach, and monitor patients taking GLP-1s for weight loss. Aon used these criteria to evaluate several point solutions and summarized four key provider offerings below. There are other vendors in the market, but we look at these four for their commitment to obesity management and cardiometabolic health.

	Calibrate	Wonder Health	Vida	Teladoc
Able to Prescribe Anti-Obesity Medications	Yes	Yes	Yes	Yes, Will even treat and prescribe for co-morbid conditions
Connect with PBM for Claim Processing	Yes	Yes	Yes	Yes
Digital Connect	Yes	Yes	Yes	Yes
Cultural Awareness/ Address SDOH	Yes, and Yes	Yes and, Yes	Yes, and Yes	Yes
ROI Guarantee	Yes	Yes	Yes	Yes
Utilize Lower Cost Therapies First	No	Yes	Yes	Yes
On-Ramp	Open to an on-ramp idea.	Yes. Recommend patients be engaged for one month before prescribing medication.	Yes. Patients must be engaged for a minimum of three months before prescribing.	Yes

[10]https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215256s000lbl.pdf; accessed 7/23/23. FDA Label for Wegovy (semaglutide).

Cost

Utilization management criteria are essential for managing the GLP-1 drugs for obesity as they will help ensure that plan funds are used appropriately. Aon believes that prior authorization criteria should require documentation of Body Mass Index and weight reduction efforts rather than attestation. Further, prescriber management is a crucial element that should not be dismissed. Aon's pharmacy data revealed evidence of non-specialized providers prescribing GLP-1s where the clinical rationale was not apparent. Controlling the prescriber type through a point solution and ensuring consistent application of prior authorization criteria will help to manage cost.

Step therapy is an approach to managing cost by starting patient treatment with less expensive drugs and/or behavioral therapy/diet/exercise change before moving to the more costly GLP-1s. Point solutions will vary in approach here, but evaluating this as part of your vendor selection is recommended. This is especially true as the criteria for obesity management include individuals with a BMI of 27-30 if a co-morbid condition is present, including hypertension, type 2 diabetes, or dyslipidemia.[11]

A thoughtful evaluation of an on-ramp to coverage under the plan for obesity management GLP-1s and an off-ramp to discontinuing drug treatment is encouraged. Considering an on-ramp, perhaps three months of behavioral change therapy guided by a coach can be consistent with pre-surgical requirements associated with bariatric surgery and can be viewed positively as the plan invests in the employee's health. The motivation is a successful health outcome with the recognition that when patients stop taking the medication, weight often does return. The only way to bend this curve is through diet, exercise, and long-term behavioral changes, which is the goal of the on-ramp. The weight regain when the drug is discontinued is detailed in the graph shown on the next page.

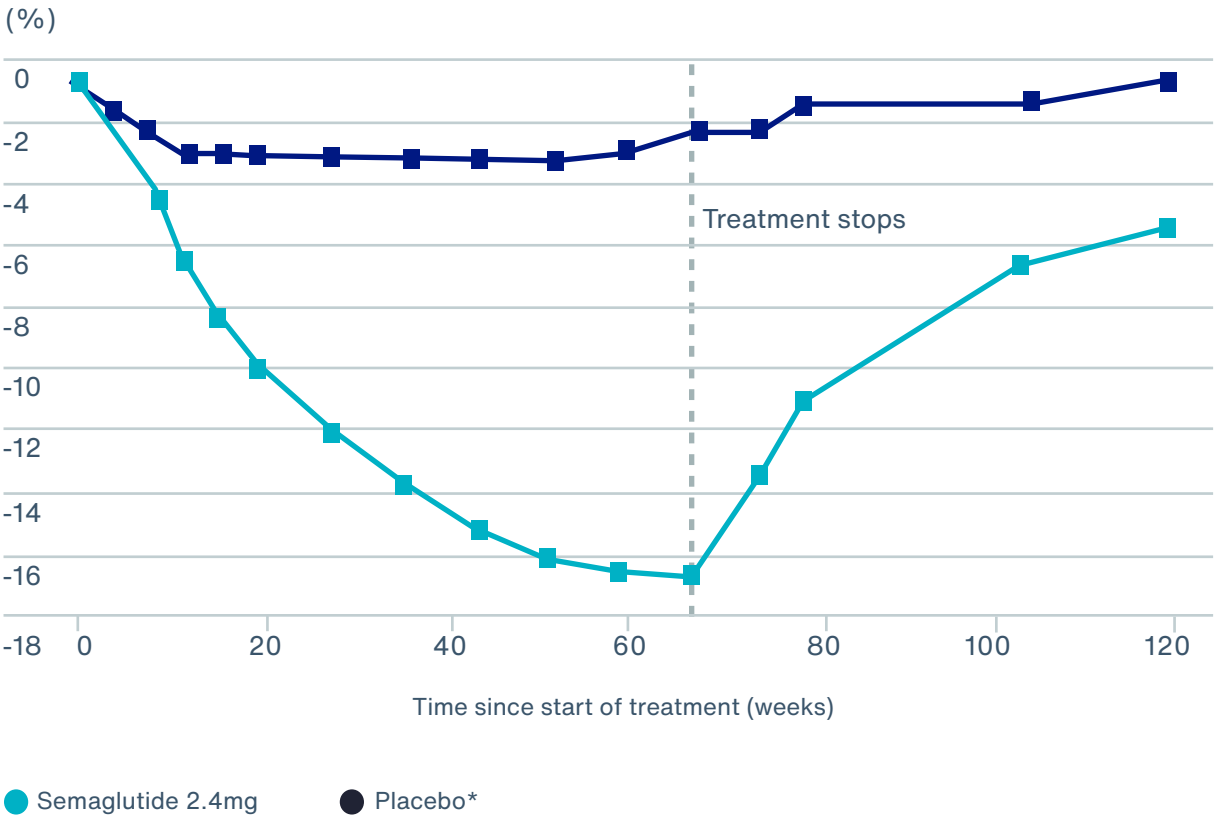
In managing cost, plan coverage equity and fairness are challenged further when considering an off-ramp for stopping coverage. Considering our prevalence element and the concern with significant cost exposure over time-based simply on the sheer number of potential utilizers, plans must consider getting individuals off these drugs to manage the entire plan funds. A lifelong drug expense with an annual list price of $15k to $16k is worrisome. Tapering patient drug treatment is not simply setting what may be viewed as an arbitrary date. There is no current research on how and when patients can stop drug treatment. In addition, we don't discuss the criteria for stopping drug therapy for other chronic conditions, which brings back the equity concern.

Patient adherence and side effects must also be considered. An initial study recently showed 68% of patients were no longer taking it at one year.[12] This suggests that the injection may not be sustainable for most, but remember that an oral form of the drug will be on the market soon. In addition, we don't discuss criteria for stopping drug therapy for other chronic conditions when considering fairness.

Cost cannot simply be reviewed at the drug level. Plan sponsors should be mindful of these patients' total cost of care. The manufacturer's economic model on ROI is set at five and ten-year marks. There is no long-term data to confirm or reject the hypothesis that investing in obesity management and helping individuals get to a healthier BMI should reduce co-morbid health conditions such as high blood pressure and/or reduce the incidence of knee or hip replacements, as an example; however, we can only speculate that this will happen. We will not know this for years.

Weight returns when treatment stops

Change in body weight (%)



*Includes diet and excercise.

Source: Diabetes, Obesity, and Metabolism, BBC.[13]

[11]https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215256s000lbl.pdf; accessed 7/23/23. FDA Label for Wegovy (semaglutide).

[12]https://www.formularywatch.com/view/real-world-study-finds-low-patient-adherence-for-weight-loss-drugs; accessed 7/23/23. Formulary Watch. Real-World Study Finds Low Patient Adherence for Weight Loss Drugs. Denise Myshko. July 14, 2023.

[13]https://www.bbc.com/news/health-64677915; accessed 7/23/23. Weight-loss: Are injections the answer to tackling obesity? James Gallagher, March 19, 2023.

Plan Coverage Equity

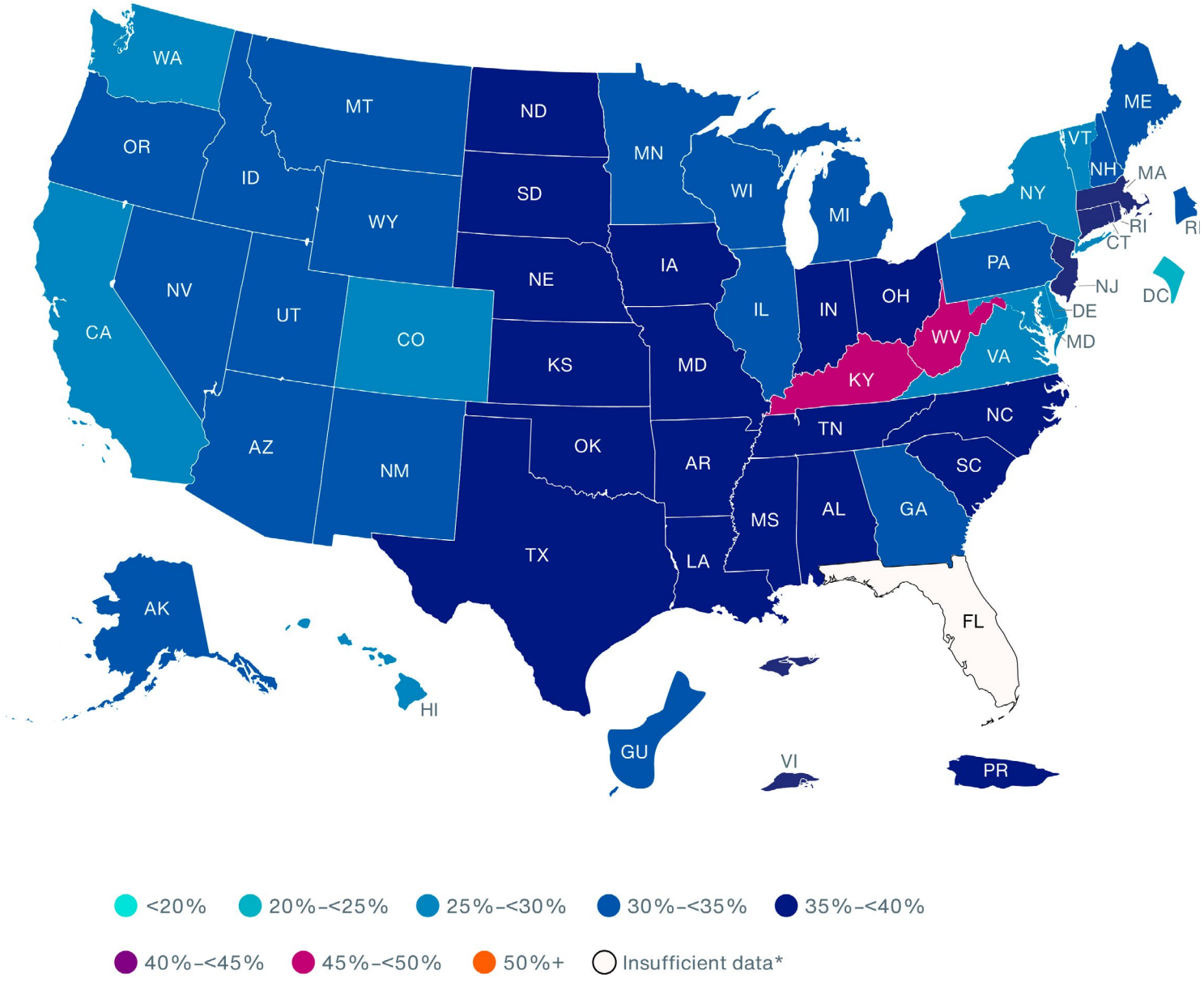
Ensuring that whatever policy or programming put into place for managing the GLP-1s for obesity management is equitable or fair is of paramount importance, as no one member should be treated in a prejudicial manner because of the disease they are managing. This is not meant to suggest that everything is at no or fractional cost, nor are additional requirements not put into place. We have cost-share methodologies in business today, and prior authorization exists for many drugs. With the GLP-1s, plan sponsors face a unique situation of extraordinary disease prevalence and high cost that they must manage while being mindful of fairness. This begins with covering these drugs under the plan. Other aspects of management, whether it be through plan design or a point solution, must be applied in a manner that is consistent and accounts for variation among members.

From a plan design perspective, plan sponsors generally should not include these drugs in the preventive drug list to ensure that cost share stays at par with other brand products treating other preventable diseases. Drug quantities can be limited to 30 days to ensure waste is managed. These drugs have side effects that can cause a patient to stop treatment; 90-day supplies can lead to wasted spending. While the Affordable Care Act requires non-grandfathered group health plans to cover in-network, at-no-cost screening for obesity and for adults with a BMI of 30 kg/m2 or higher, intensive, multicomponent behavioral interventions for weight management, it does not require the coverage of GLP-1s at this time.

Being fair is balanced against cost management, which may override fairness concerns. Concerning obesity disparities in the U.S., there are sex-based and racial and ethnic differences in biological, cultural, and socio-economic characteristics to be accounted for with management programs.[14] Aon attempted to account for this when we spoke with multiple vendors in the point solution space, and their attention to this matter varied. It is an aspect of obesity management that biological differences in body fat levels and cultural differences in body image and weight loss must be accounted for in programming deemed fair across an employee population.

In addition, obesity prevalence varies by geography. This should be accounted for when researching management options. See the obesity map that follows to see where your crucial population centers are and how obesity may impact your employee population.

If an employer offers a GLP-1, it should be offered and available to all plan participants on the same terms to avoid running afoul of the HIPAA nondiscrimination rules or potentially the Americans with Disabilities Act. The addition of the GLP-1 and any medical management requirements, including prior authorization, should be clearly spelled out and properly communicated by a summary of material modifications and/or updated summary plan description and reviewed by legal counsel.

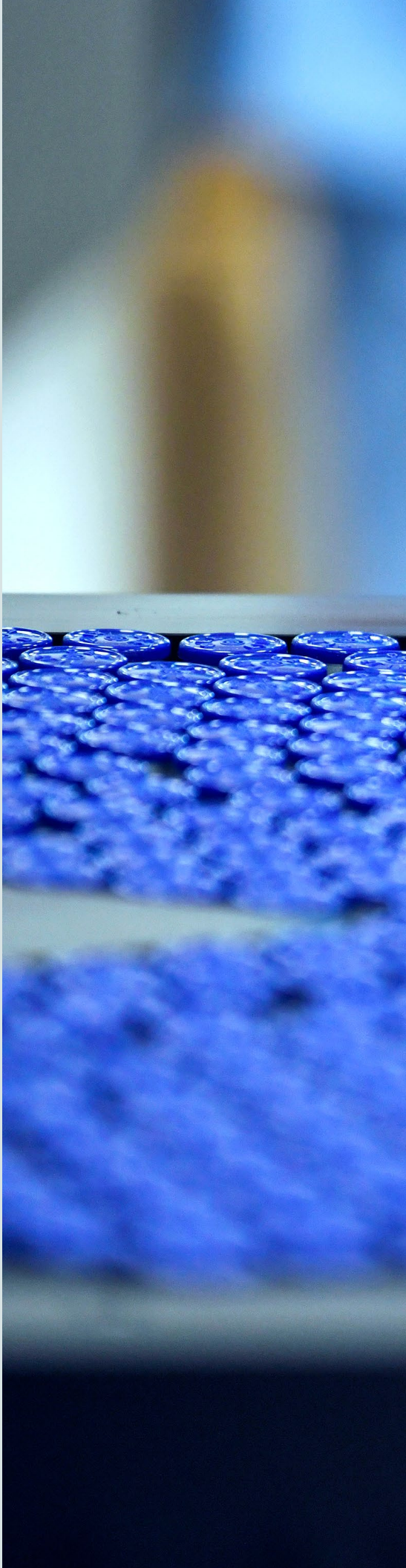


[14]https://reader.elsevier.com/reader/sd/pii/S2161831322001375?token=6880B014C7D99D473E9A001A82ED80B9E473CE770CD63BC856B661C5424C711C6F7BC771CF9FA491BB277CD6BD8F7EFF&originRegion=us-east-1&originCreation=20230516182453; accessed 7/23/23. Racial-Ethnic Disparities in Obesity and Biological, Behavioral, and Socioclutural Influences in the United States: A Systematic Review. Advances in Nutrition, Volume 12, Issue 4, July 2021, Pages 1137-48.

[15]https://www.cdc.gov/obesity/data/prevalence-maps.html; accessed 7/23/23. Adult Obesity Prevalance Maps. Center for Disease Control and Prevention; Overweight & Obesity, Data & Statistics.

Conclusion

The GLP-1 class is unique in the management challenges it presents. In contrast to gene therapies that cost millions, prevalence is so low that large market employers talk today about absorbing the gene cell therapies cost. In contrast to lipid management, in which one study noted an estimate of 53% of U.S. adults with a lipid abnormality, patients are generally not enrolled in lifestyle management programs to promote healthy eating for this disease state.[16] In part, this is because these drugs are very inexpensive. The GLP-1 class of drugs for managing obesity is different. Prevalence and cost are significant elements to consider, but fairness is also important. Ensuring that benefit coverage attends to these elements, that UM is in place and reviewed often, and that a thoughtful weight-loss solution vendor is present to guide our patients through their weight-loss journey are all essential.



[16] https://pubmed.ncbi.nlm.nih.gov/22836069/; accessed 7/23/23. Prevalence of lipid abnormalities in the United States: the National Health and Nutrition Examination Survey 2003-2006. J Clin Lipidol, 2012 Jul-Aug;6(4):325-30.

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