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Global Health Brief: The rise of GLP-1 receptor agonists and their impact on health insurance

By: Dr. Steve Woh, Simon Dreyer, Raajeev Bhayana...

Much of the focus on the impact of GLP-1 receptor agonists (and combination drugs with components that target other receptors such as gastric inhibitory polypeptide – collectively termed “GLP-1s” in this article) to date has been on their potential to improve long-term health outcomes for people with type 2 diabetes, obesity, and related cardiovascular diseases.

However, when making decisions for reimbursement and setting premiums, health insurers need to balance such long-term policyholder health improvements against short- to medium-term increases in claims expenditure. In the case of GLP-1s, that means balancing the cost of treatment – approximately $1,000 wholesale per month in the US, for example – with these drugs’ proven effectiveness.

This article delves into key considerations and challenges health insurers face in the evolving landscape of approval and reimbursement for GLP-1s. It further examines actions insurers might take to benefit policyholders while maintaining a sustainable portfolio. As with most GLP-1-related topics at this early stage, insurers have more questions than answers.

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What's the exposure?

GLP-1s are primarily indicated for obesity and diabetes, two major global health challenges that continue to grow at alarming rates. Obesity rates among adults have more than doubled since 1990, from 7% to 16% in 2022, according to the World Health Organization (WHO). Similarly, diabetes has experienced a dramatic increase. The WHO reports worldwide diabetes rates steadily increasing over the past three decades, growing most rapidly in low- and middle-income countries.

While the prevalence of these conditions is expected to be lower in fully underwritten insured populations compared to the general population, no population – including countries in Asia with lower prevalence – is immune to these global trends. Obesity, diabetes, and associated comorbidities have emerged as a modern health crisis and a priority area of concern for health insurers. GLP-1s offer a new hope for helping to address this crisis. Furthermore, GLP-1s also have been shown to reduce cardiovascular risks, as well as potentially providing a range of other health benefits for patients with chronic kidney disease, gastrointestinal disorders, neurodegenerative diseases and psychiatric disorders.1

Are GLP-1s reimbursed?

In many markets, GLP-1s are reimbursed for the indications for which they are approved by the relevant authorities, such as the Food and Drug Administration (FDA) in the US. In other markets, insurers may include general exclusion wordings for all treatment costs related to weight management or obesity and will not reimburse the costs of these drugs.

Reimbursement also would depend on the benefits available under a policy. For example, policies with in-patient-only benefits would be expected to have limited exposure to GLP-1 utilization because these drugs are mainly prescribed in the outpatient setting.

While the exclusion of weight management treatment may limit reimbursement of GLP-1s, non-obesity/overweight diseases such as diabetes mellitus and certain cardiovascular conditions may be eligible for reimbursement because these indications are not excluded. In addition, signs of abusive practices have surfaced in which non-approved indications are masqueraded as approved ones to secure reimbursement or circumvent policy exclusions.

Insurers in some markets are facing mounting market pressure to remove the exclusion on weight management to promote inclusivity, resulting in the imminent exposure of insurers in these markets to reimbursement of this class of drugs.

How do insurers account for market demand and take-up rates?

Take-up rates for medications can vary widely depending on several factors, from the type of medication and potential side effects to patient demographics and treatment costs. Important factors affecting GLP-1 market demand and take-up include:

- The need for better long-term data on the safety and efficacy of use for the designated indications
- The rapidly expanding list of potential new indications for the drugs, including chronic kidney disease, broader cardiovascular risk reduction, metabolic liver disease, and Alzheimer's disease
- The number of similar drugs in the development pipeline

- Price point versus competition, which affects affordability and insurance coverage
- Marketing efforts of the manufacturers, supply and distribution constraints.
- Clinical practices and adoption rates among providers
- Patient compliance and adherence

Mixed sentiments abound in both the healthcare and insurance industries about actual take-up rates, with some bullish about the outlook given the hype generated both in the clinical setting and commercially. Others are more conservative due to concerns about the high costs, access issues, side effects, and lack of longitudinal data on long-term outcomes.

As for the patient base, a recent report found that 75% of patients stop taking the medications within two years, although the report did not elaborate on the causes of this decline in use, which may be partially attributable to factors such as high costs and self-funding requirements. Regardless of cause, sustainability of outcomes remains unclear because adherence to treatment, as with many other drugs, may be an issue. That said, continuous use is likely needed to maintain the positive effects of GLP-1s. A randomized trial assessing the effect of tirzepatide (Mounjaro/Zepbound) found that withdrawing tirzepatide led to substantial regain of lost weight in less than two years.

Despite unanswered questions, health insurers should prepare for increasing interest in and demand for GLP-1s. The extraordinary case of the cancer drug Keytruda® may offer insight into the potential road ahead for GLP-1s. The global Keytruda market is expected to achieve a CAGR of 8.9% from 2023 to 2032, with the valuation anticipated to reach $54 billion.

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Initially approved for the treatment of advanced or unresectable melanoma, Keytruda received its 40th FDA indication approval on June 17, 2024, with the most recent approval covering endometrial cancer.3 This notable milestone adds to a growing list of indications as more clinical trials demonstrate Keytruda's efficacy and safety across different types and stages of cancer.

Could GLP-1s follow similar approval trajectory and commercial growth? Figure 1 shows shows the dramatic increase in prescription volume following the launch of Wegovy and Mounjaro. A recent report suggests the global GLP-1 market is likely to grow from $49.3 billion in 2024 to $157.5 billion by 2035 – a CAGR of 11.1%.

Will improved outcomes offset the cost of treatment?

Drug prices vary significantly by market, and in general tend to be higher in the US than in other countries. This is no different for GLP-1s. In the US, the monthly cost of treatment with GLP-1s is approximately $1,000, and in other advanced markets it is $100-$500.4 While the introduction of generics promises to reduce costs, this remains several years off, and a strong pipeline of original drugs could keep prices high for some time.

Given the relatively high monthly cost of GLP-1s in the US, as well as the prevalence of obesity in that market, GLP-1s have attracted particular attention. While costs in other markets may appear lower, the drugs' cost relative to existing treatments and potential health expenditure savings from improved health outcomes will determine how health insurers are affected by their increasing use.

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Published evidence comparing drug costs to outcome measures for health insurers/systems remains sparse, but one study compared the treatment of type 2 diabetes with insulin versus treatment with GLP-1s and found that the higher drug and outpatient costs associated with GLP-1 treatment were offset by a reduction in healthcare costs from emergency visits and inpatient admissions.5 For diabetes at least, GLP-1s may therefore be cost-neutral to health funders. Further evidence is needed to accurately assess other applications of the drug class. The long-term data on health outcomes for patients with obesity, in particular, is being watched very closely for potential downstream effects of treating the condition.

What actions can health insurers take now?

In the absence of any negative findings from the research and utilization of GLP-1s, the demand for this class of drugs will likely continue to increase, potentially resulting in a significant cost burden for the economy. Health insurers will be well served to begin quantifying GLP-1s' cost impact on the portfolio for the short and long term, which will vary by market and product, to determine any necessary premium adjustments or changes to underwriting philosophy.

Insurers should also review their product coverage. If a health product covers GLP-1s, the insurer should consider means to ensure proper utilization by clearly outlining coverage and, where applicable, prior-authorization criteria. This will help to control the off-label use of the drug, which is a significant cost driver.

Health insurers can also proactively engage with patients to provide counselling on treatment, administration, and possible side effects. and support them in their journey. This active case management strategy will help to ensure a high compliance rate and thereby reduce waste.

Lastly, in markets where appropriate, insurers can also engage with pharmaceutical companies or pharmacy supply chains to ensure optimal pricing and value for the drug.

Conclusion

Health insurers are likely to be or have already been exposed to the rise of GLP-1s, and the exposure is expected to expand with approvals for new indications in the pipeline, as well as a projected increase in take-up rates. While the theoretical long-term benefits to health outcomes are welcomed, the short-term cost impact to health insurers must be considered. As an important stakeholder in healthcare, health insurers should play their part in ensuring that GLP-1s, like all other treatments, are being utilized responsibly and at prices that enable financially sustainable treatment plans for the ongoing benefit of all.

Significant Drug Updates

By: Debbie Hoffer

Upstaza (Gene Therapy)

Eladocagene exuoarvovec, Aromatic l-amino acid decarboxylase deficiency, Intracranial infusion, PDUFA date is 11/13/2024, TBD on price but anticipate $2M+.

The UK name for this gene therapy is Upstaza. It was named Kebilidi and was approved in November as anticipated. We don’t know the cost but the price in the UK 3M pounds which equal about 3.75 M US dollars. It is rare condition. The therapy should be available for administration Q12025.

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NIH findings shed light on risks and benefits of integrating AI into medical decision-making

By: Qiao Jin

AI model scored well on medical diagnostic quiz, but made mistakes explaining answers.

Researchers at the National Institutes of Health (NIH) found that an artificial intelligence (AI) model solved medical quiz questions—designed to test health professionals' ability to diagnose patients based on clinical images and a brief text summary—with high accuracy. However, physician-graders found the AI model made mistakes when describing images and explaining how its decision-making led to the correct answer. The findings, which shed light on AI's potential in the clinical setting, were published in npj Digital Medicine(link is external). The study was led by researchers from NIH's National Library of Medicine (NLM) and Weill Cornell Medicine, New York City.

"Integration of AI into health care holds great promise as a tool to help medical professionals diagnose patients faster, allowing them to start treatment sooner," said NLM Acting Director, Stephen Sherry, Ph.D. "However, as this study shows, AI is not advanced enough yet to replace human experience, which is crucial for accurate diagnosis."

The AI model and human physicians answered questions from the New England Journal of Medicine (NEJM)'s Image Challenge. The challenge is an online quiz that provides real clinical images and a short text description that includes details about the patient's symptoms and presentation, then asks users to choose the correct diagnosis from multiple-choice answers.

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The researchers tasked the AI model to answer 207 image challenge questions and provide a written rationale to justify each answer. The prompt specified that the rationale should include a description of the image, a summary of relevant medical knowledge, and provide step-by-step reasoning for how the model chose the answer.

Nine physicians from various institutions were recruited, each with a different medical specialty, and answered their assigned questions first in a “closed-book” setting, (without referring to any external materials such as online resources) and then in an “open-book” setting (using external resources). The researchers then provided the physicians with the correct answer, along with the AI model’s answer and corresponding rationale. Finally, the physicians were asked to score the AI model’s ability to describe the image, summarize relevant medical knowledge, and provide its step-by-step reasoning.

The researchers found that the AI model and physicians scored highly in selecting the correct diagnosis. Interestingly, the AI model selected the correct diagnosis more often than physicians in closed-book settings, while physicians with open-book tools performed better than the AI model, especially when answering the questions ranked most difficult.

Importantly, based on physician evaluations, the AI model often made mistakes when describing the medical image and explaining its reasoning behind the diagnosis — even in cases where it made the correct final choice. In one example, the AI model was provided with a photo of a patient’s arm with two lesions. A physician would easily recognize that both lesions were caused by the same condition.

However, because the lesions were presented at different angles — causing the illusion of different colors and shapes — the AI model failed to recognize that both lesions could be related to the same diagnosis.

The researchers argue that these findings underpin the importance of evaluating multi-modal AI technology further before introducing it into the clinical setting.

“This technology has the potential to help clinicians augment their capabilities with data-driven insights that may lead to improved clinical decision-making,” said NLM Senior Investigator and corresponding author of the study, Zhiyong Lu, Ph.D. “Understanding the risks and limitations of this technology is essential to harnessing its potential in medicine.”

The study used an AI model known as GPT-4V (Generative Pre-trained Transformer 4 with Vision), which is a ‘multimodal AI model’ that can process combinations of multiple types of data, including text and images. The researchers note that while this is a small study, it sheds light on multi-modal AI’s potential to aid physicians’ medical decision-making. More research is needed to understand how such models compare to physicians’ ability to diagnose patients.

The study was co-authored by collaborators from NIH’s National Eye Institute and the NIH Clinical Center; the University of Pittsburgh; UT Southwestern Medical Center, Dallas; New York University Grossman School of Medicine, New York City; Harvard Medical School and Massachusetts General Hospital, Boston; Case Western Reserve University School of Medicine, Cleveland; University of California San Diego, La Jolla; and the University of Arkansas, Little Rock.

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