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Review Article

A review on the impact of the worldwide shortage of glucagon-like peptide-1 medications on control of diabetic patients

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ABSTRACT

Glucagon-like peptide 1 receptor agonists (GLP-1 RA) have shown promising benefits in improving outcomes for patients with type 2 diabetes, particularly those affected by obesity-related complications such as cardiovascular disease, cardiometabolic disorders, and heightened cancer risks, posing significant public health challenges. Notably, GLP-1 RA have been recognized for their potential to achieve up to a 15% weight reduction over a span of two years, making them a preferred choice in specific conditions for diabetic patients with a body mass index (BMI) above 27. However, widespread public interest, particularly amplified through social media, has intensified the demand for GLP-1 RA due to their weight loss properties, thereby straining global supplies and fostering a black market among non-diabetic individuals seeking these effects. This heightened attention has prompted various medical regulatory bodies worldwide to enact strategies and policies aimed at alleviating shortages. Measures include minimizing new prescriptions of GLP-1 RA, exploring alternative medications within the GLP-1 RA category, carefully transitioning patients to other anti-diabetic treatments and managing patient expectations. These efforts appear effective in managing overall outcomes amid ongoing supply challenges. This narrative review provides a focused evaluation of how these GLP-1 RA medication shortages have impacted type 2 diabetic patients around the world and their overall diabetic outcomes.

Keywords: GLP-1 RA, Shortage, Diabetes, Worldwide, Semaglutide, Ozempic®

INTRODUCTION

Obesity, recognized as a chronic disease, has emerged as a significant public health concern in recent times due to its adverse effects on health, leading to heightened morbidity and mortality rates. Within the European Region, which ranks second in adult obesity prevalence among all world health organisation (WHO) regions, obesity and overweight have reached epidemic proportions. Notably, prevalence rates are higher among men (63%) compared to women (54%).[1] Adults exhibiting a BMI between 25.0 and 29.9 kg/m^2 are categorized as overweight, while those with a BMI of 30 kg/m^2 or above are classified as obese. Elevated BMI levels have been linked with escalated mortality rates, with a notable 29% increase in overall mortality, a 41% increase in vascular mortality, and a striking 21% increase in diabetes-related mortality for each 5-unit rise in BMI over 25 kg/m^2.[1] Complications associated with obesity mirror those of other chronic ailments, contributing to heightened rates of morbidity and mortality. Biomechanical complications, such as osteoarthritis and obstructive sleep apnoea, stem from surplus adipose tissue, while adipose tissue dysfunction exacerbates cardiometabolic complications. Cardiometabolic diseases manifest initially as insulin resistance, progressing stealthily to metabolic syndrome, prediabetes, elevated blood pressure, dyslipidaemia, and hepatic steatosis. Cardiovascular complications encompass hypertension, atherosclerosis, heart failure, and atrial fibrillation, while

metabolic ramifications include type 2 diabetes mellitus, dyslipidaemias, hyperuricemia, and metabolic syndrome.[2-7] Respiratory challenges like mixed ventilatory dysfunction, Pickwick syndrome, and asthma, alongside digestive issues including gastroesophageal reflux, hiatal hernia, gallstones, and non-alcoholic fatty liver, are frequently observed in obese individuals.[8-12] Projections suggest that in forthcoming years, obesity will supersede smoking as the primary preventable risk factor for cancer in select countries. Furthermore, it underscores that obesity necessitates specific treatment and management, transcending its mere classification as a risk factor.[1]

GLP-1 is an endogenous hormone primarily synthesized in the gastrointestinal tract, particularly in the L cells located in the ileum and colon. Its principal function is the regulation of blood glucose levels following food intake. Upon secretion, GLP-1 binds to receptors on pancreatic beta cells, eliciting a glucose-dependent increase in insulin secretion, thereby aiding in the reduction of blood sugar levels. Furthermore, GLP-1 suppresses glucagon secretion from pancreatic alpha cells, thereby decreasing hepatic glucose production. Additionally, it modulates gastric emptying, regulating the rate of nutrient absorption into the bloodstream and mitigating postprandial blood sugar spikes. Notably, GLP-1 exerts effects on the central nervous system, influencing appetite regulation and satiety, resulting in decreased food intake and body weight regulation. GLP-1-based medications replicate the actions of endogenous GLP-1 by activating receptors and eliciting similar effects on insulin secretion, glucagon suppression, and appetite modulation.

GLP-1 RA, administered via once-weekly subcutaneous injection, have demonstrated notable efficacy in lowering glucose levels and reducing weight.[13] GLP-1 RA include semaglutide, (Ozempic®, Wegovy®, Rybelsus®) liraglutide (Victoza®, Saxenda®), tirzapeptide (Mounjaro®) and dulaglutide (Trulicity®). This heralds a promising advancement in peptide-based therapy for type 2 diabetes and particularly in obesity.[14] GLP-1 RA are indicated for patients with a body mass index (BMI) of ≥30 or those with a BMI of ≥27 accompanied by a weight-related condition such as diabetes or hypertension. Several studies have demonstrated that these medications are correlated with an approximate 15% reduction in weight over a span of 1-2 years.[1]

LITERATURE REVIEW

To construct this narrative review, the authors searched PubMed, Medline, Google Scholar and articles using a combination of keywords “GLP-1 receptor agonists”, “diabetes” “worldwide”, “shortage”, “semaglutide” OR “Ozempic® OR “Wegovy®”, “liraglutide” OR “Saxenda®”. The search was conducted from databases beginning from July 2023. Pubmed yielded over 575 articles. Whilst google scholar yielded 2330 results. Authors evaluated case reports and series, retrospective and prospective studies and randomized control trials, systematic reviews and meta-analyses and others.

THE SHORTAGE DILEMMA

Given their established clinical efficacy, evidenced by their capacity to induce weight loss comparable to that achieved through bariatric surgery, GLP-1 RAs have garnered significant attention.[15-18] Notably, endorsement by various public celebrities has propelled their popularity, resulting in widespread interest in medications such as Ozempic® and GLP-1 RAs across social media platforms and academic forums.[19,20] Consequently, challenges emerged concerning their distribution and availability through conventional channels and regular prescription protocols.[21,22]

Unforeseen shortages of dulaglutide, semaglutide, and tirzepatide emerged in late 2022 and persisted through the first quarter of 2023.[23] The increase in semaglutide consumption is thought to be associated with “off-label” prescribing of semaglutide (Ozempic®) for weight loss in people without type 2 diabetes, fuelled by social media interest (which some have dubbed “Ozempic® craze”).[24] Notably, these shortages have impacted the availability of different product doses disparately.[25] The primary cause of these shortages stems from an unanticipated surge in demand for GLP-1 RA, outpacing production capacity adjustments.[26] Consequently, patients reliant on or seeking to initiate these medications for glycaemic control, weight management, and/or cardiovascular risk reduction have encountered new challenges in accessing treatment.[21]

Disruptions within the supply chain pose significant challenges for both patients and healthcare providers, necessitating the exploration of alternative strategies to navigate what is ideally a temporary setback. Numerous social media platforms and online clinics purport to provide commercially available GLP-1 RA, or even compounded versions, at discounted rates.[21] Due to the prevailing scarcity and high cost of these medications, numerous patients have resorted to acquiring them from non-licensed and unregulated sources, thereby heightening the potential for serious complications. Long et al.'s review of these associated complications delineated a spectrum of adverse events, encompassing gastrointestinal complications, pancreatitis, biliary diseases, hypersensitivity reactions, renal complications linked with gastrointestinal loss, and concurrent hypoglycaemia when concomitantly administered with sulfonylureas and insulin. Additionally, ambulatory patients may opt to self-ration their supply to prolong the availability of their GLP-1 RA product. This may involve deliberately extending the interval between doses and seeking guidance on the duration for which they can safely postpone their next dose without compromising efficacy.[27]

Whitely et al study delineated several strategies aimed at mitigating the global shortage of GLP-1 RAs. These strategies encompassed recommencing treatment at a lower dose of an alternative GLP-1 RA to alleviate gastrointestinal side effects, considering the utilization of a more readily accessible higher-strength product while adjusting the dosage to a safe and appropriate level, taking into account the product's shelf life. However, it is crucial to acknowledge that the administration of alternative doses carries a heightened risk of confusion and dosing errors.[21]

Whitely et al. also emphasized the significance of open communication to assist prescribers in identifying available GLP-1 RAs, which may prompt community pharmacists to promptly process prior authorization requests. Moreover, clear and comprehensive documentation in the medical record elucidating the rationale, significance, and necessity of transitioning between GLP-1 RAs can expedite patient access. Assigning a dedicated staff member to manage prior authorizations can further streamline the process.[21,28]

In due course, findings from numerous studies will inform equivalent dosing substitutions within the class of GLP-1 RAs.[29,30] Trujillo et al conducted exhaustive analyses of investigations involving GLP-1 RAs with active comparative treatment arms.[31] Subsequent to the publication of these analyses, higher therapeutic doses of GLP-1 RAs have garnered approval from the U.S. food and drug administration (FDA), and novel products like the dual GLP-1 RA tirzepatide have entered the market helping with alleviating shortages.

The authors reviewed the literature on how these shortages have impacted different countries around the world.

NORTH AMERICA AND CANADA

The most commonly utilized GLP-1 RAs in the United States (US) are semaglutide (Ozempic®, Wegovy®, Rybelsus®), liraglutide (Saxenda®, Victoza®), and tirzepatide (Mounjaro®).[27] The increased demand of GLP-1 RA experienced in the US, was perpetuated by the added benefits of weight loss, especially as the American gastroenterological association recommended guidance in November 2022 informing that semaglutide 2.4 mg could be used for the treatment of obesity.[1] As the rising demands continued, American healthcare professionals struggled to maintain adequate levels of the prescriptions of GLP-1 RA. According to the FDA drug shortages webpage, the shortage of Wegovy® began in March 2022 while the shortage of dulaglutide (Trulicity®) was first posted in December 2022.[32] The FDA on 27th April 2023 wrote to the national association of boards of pharmacy expressing the agency's concerns with use of the salt forms in compounded products and its safety. It was reported that compounders may be using salt form of semaglutide. The basis of this was based on the GLP-1 RA shortages and patient access to similar products due to their availability. The FDA was aware of fraudulent and unapproved products for the distribution of illegally marketed semaglutide and advised that only a prescription from a licenced health care provider should be offered.[33] In May 2023, Novo Nordisk US, the pharmaceutical entity responsible for semaglutide production and distribution, noted only being able to supply limited quantities of 0.25 mg, 0.5 mg, and 1 mg dose strengths to wholesalers for distribution to retail pharmacies, which resulted in many patients having difficulty filling prescriptions at those doses through September 2023. In an attempt to quell further demand, the company paused promotional efforts and planned to work with wholesalers to create a steadier level of inventory.[32]

Equally shortages were also experienced in Canada. ministry of health of Canada anticipated shortages from as early as 2022. Particularly, as many Americans who were experiencing shortages within their own country would fulfil their prescription requests in certain parts of Canada. Deemed with the very prospect of spending considerable dollars in the US, many Americans sought out using insurance in places like British Columbia to offset large differences in GLP-1 RA prescription. This led to in early 2023, the ministry of health cracking down on prescription requests from American citizens for the purpose of weight loss.[34] Repeated recommendations were advised to reduce initiation whilst Novo Nordisk Canada Inc increased their long-term capital investments to increase manufacturing capacity.[35,36]

EUROPE AND UK

Shortages were apparent from as early as September 2022 when the department of health and social care (DHSC) in the UK issued a medicine supply notification for Ozempic® and Trulicity®. At this time promises were made that stock would be available in January 2023. Advice was sought instructing family physicians to avoid initiation and consider alternative GLP-1 RA. Though it was not anticipated about the further surge of demand which led to further action.[26] In July 2023, Novo Nordisk UK, in collaboration with the medicine and healthcare products regulatory agency (MHRA) and the DHSC issued a statement addressing the shortage of semaglutide and liraglutide. This announcement prompted the DHSC to issue a national patient safety alert on July 18th, 2023 (NatPSA/2023/008/DHSC). The guidance advised healthcare providers to refrain from prescribing medications experiencing shortages to patients who have not previously used them. In cases where comparable GLP-1 RAs are also unavailable, clinicians were advised to explore alternative antihyperglycemic treatments to maintain glycaemic control instead of initiating treatment with a new GLP-1 RA. Additionally patient education and setting expectations were considerations that many authors and regulatory health bodies introduced to address patient concerns with the drug shortages.

The European medicine agency similarly issued a statement in December 2023 addressing the shortage of semaglutide. They delineated that heightened demands for Ozempic®, alongside capacity constraints at certain manufacturing sites, were the primary factors contributing to the shortage. The agency further prognosticated that the shortage was poised to exacerbate and persist throughout 2024, impacting all member states of the European Union (European Medicine Agency).[37,38]

Mailhac et al conducted a utilisation study in between 2008-2023 based on Denmark's entire population to evaluate current patterns of use of semaglutide. They compared trends with other frequently used GLP-1 RA and the changing trends in the profile of semaglutide. They observed a sharp increase in the use between 2021-2022 with a falling incidence in 2023. Their findings suggested that in Denmark, there was a clear increase in semaglutide off-label" use through 2022. However, of a magnitude that can explain only a minor part of the drug shortage, and with a decreasing "off-label" user trend observed in 2023. They suggested that patients were putting pressure on physicians to prescribe a reimbursed/subsidized medication such as semaglutide (Ozempic®) were expected. Though based on data from Danish health authorities, the number of users of semaglutide (Ozempic®) prescriptions who did not receive reimbursement/subsidies in Denmark in 2022 was relatively small, i.e., in the order of 15% to 20% of all users.[24,37]

AUSTRALIA

In April 2022, the therapeutic goods administration (TGA) identified a shortage of semaglutide in Australia, reflecting a broader global scarcity resulting from an unanticipated surge in demand. This shortage coincided with heightened media attention on semaglutide's potential efficacy in weight loss, suggesting a possible correlation between off-label utilization for weight management and the global deficit of this medication. In response to this shortage, The royal Australian college of general practitioners (RACGP) issued guidance to family physicians, urging cautious consideration in the off-label prescription of semaglutide to ensure prioritized treatment of patients with type 2 diabetes.[39]

Phakey et al conducted a retrospective analysis on semaglutide and dulaglutide prescriptions dispensed by primary care providers in Australia during the period spanning 2021-2022. Throughout the study duration, prescription supply patterns exhibited variability, with fluctuations in the actual number of prescriptions dispensed aligning with announcements from the TGA regarding shortages in semaglutide and dulaglutide supply in 2022. The study's predictive model outcomes underscored the possibility that the decline in semaglutide prescriptions may have been more pronounced than reflected by the observed decrease in actual semaglutide prescriptions between April and July 2022 following the TGA's April announcement of a semaglutide shortage. Concurrently, a plausible rationale for the rise in actual dulaglutide prescriptions emerged in subsequent months until August 2022, when accessing dulaglutide became challenging. Novo Nordisk Australia, notified the TGA of the commencement of limited semaglutide stock distribution in Australia, albeit initial supplies were anticipated to be insufficient to satisfy the demand from all patients with type 2 diabetes prescriptions. Correspondingly, Eli Lilly, the manufacturer of dulaglutide, informed the TGA of anticipated limited dulaglutide availability up till the conclusion of December 2023. Currently, the timeline for the full restoration of supply for both agents in Australia remains indeterminate. The findings of this investigation corroborate recent statements from the RACGP and the TGA, advocating for prescribers to prioritize semaglutide utilization for diabetic patients who are either current or prior semaglutide users, as well as those for whom alternative glucose-lowering medications, including sulfonylureas, dipeptidyl peptidase 4 inhibitors, and sodium–glucose cotransporter 2 inhibitors, may not be suitable. Where feasible, clinicians are advised to refrain from initiating new patients on semaglutide until supply stabilization occurs.[39,40]

DISCUSSION

GLP-1 RAs have consistently demonstrated significant efficacy in managing type 2 diabetes, with additional benefits in weight loss, signalling a promising development in obesity treatment.[14] As global obesity rates reach epidemic levels, the demand for effective treatments escalates accordingly. However, the substantial global demand for GLP-1 RAs such as liraglutide and semaglutide as anti-obesity agents has led to recent shortages, prompting prioritization of their use in type 2 diabetes therapy.[13] Heightened interest on social media platforms appears to correlate with these shortages and reports of improper self-administration among individuals without clinical indications.[21,41-43] Reduced availability and increased costs have driven patients to explore alternative sources, contributing to the emergence of a black market where compounded medications are obtained, sometimes for uses unrelated to diabetes treatment.[21] While compounded medications are generally regulated and considered safe, compounded GLP-1 RAs present unique challenges.[42] Each GLP-1 RA is proprietary to a single manufacturer, raising uncertainties regarding the source and safety of compounded versions if manufacturers fail to supply compounding pharmacies with active ingredients.[44] Instances of compounded GLP-1 RAs being sold illicitly underscore serious safety concerns, prompting calls for stricter regulatory oversight.

The academic literature offers limited guidance on addressing GLP-1 RA shortages in community or ambulatory healthcare settings. Existing resources propose several potential solutions, such as establishing

direct communication with suppliers, investigating alternative pharmacy options, switching to generic or brand-name equivalents of the medication, or considering alternative therapeutic agents altogether.[44]

Interestingly, despite the enthusiastic reception of GLP-1 RAs for weight loss, critiques and concerns have also surfaced as identified in the literature search.[36,45-47] Recent reports underscore the potential risks associated with liraglutide and semaglutide GLP-1 RAs, including the emergence of depressive symptoms, suicidal ideation, and self-harm.[46] Therefore, it is crucial that the medication continues to be regulated through established channels with appropriate monitoring, highlighting the risks associated with its availability in illicit markets.

One study identified from the literature search looked at the implication of shortages on HbA1c. This study conducted by Nanayakkara et al scrutinized data from 811 patients diagnosed with type 2 diabetes, who attended an Australian specialist diabetic clinic between 2019 and 2023. These patients were prescribed two or more GLP-1 RA medications both before and during a period of shortage. The analysis revealed a noteworthy increase in median HbA1c levels by 0.3%. Moreover, the proportion of patients achieving a HbA1c level below 7% decreased from 28.6% to 23% during the period of shortage. These findings underscore compelling evidence that the GLP-1 RA shortage experienced in Australia during 2022-2023 had a detrimental impact on glycaemic control among diabetic patients. Furthermore, the study highlights the broader implications of reduced access to these medications, extending beyond glycaemic control to encompass cardiovascular, renal, retinal, and neural health outcomes.[48]

Unfortunately, there remains limited empirical evidence regarding the impact of GLP-1 RA shortages on patients with type 2 diabetes. The available literature confirms the existence of shortages during the period under review. It is plausible that many patients facing difficulties in obtaining GLP-1 RAs resorted to diverse sources, potentially mitigating any adverse effects on their HbA1c levels and overall diabetic outcomes. Furthermore, individuals unable to access GLP-1 RAs may have been switched to alternative treatments such as insulin or oral anti-diabetic agents, thereby preserving adequate glycaemic control. This suggests that strategies advocated by global and local health authorities may have effectively alleviated the burden and upheld favourable outcomes among diabetic patients.

This review outlines the approaches taken by various countries to address the shortage, yet empirical evidence demonstrating its true impact on patients remains lacking. The authors advocate for further research to assess the effects of GLP-1 RA shortages on diabetic outcomes.

CONCLUSION

There is global evidence indicating an impact on the availability of GLP-1 RA. However, there remains insufficient evidence regarding the effects of these shortages on the lives and outcomes of type 2 diabetic patients. Globally implemented strategies aimed at addressing the increasing demand and diminishing supply appear to have potentially mitigated the overall disease burden of diabetes through timely interventions. Additionally, the management of type 2 diabetes often involves multiple available agents such as oral anti-diabetic medications and insulin, which may have mitigated the documentation of restrictive outcomes. Nevertheless, the growing trend of weight loss desire to combat obesity is expected to persist, prompting governmental and local health boards to regulate the prescription of GLP-1 RA to ensure safe practices and reduce overall burdensome outcomes.

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REFERENCES

1. Elmaleh-Sachs A, Schwartz J, Bramante C, Nicklas J, Gudzune K, Jay M. Obesity Management in Adults: A Review. J Am Med Assoc. 2023;330(20):2000-15.
2. Mechanick J, Farkouh M, Newman J, Garvey W. Cardiometabolic-based chronic disease, adiposity and dysglycemia drivers JACC state-of-the-art review. J Am College Cardiol. 2020;75(5):525-38.
3. Garvey W, New Horizons. A New Paradigm for Treating to Target with Second-Generation Obesity Medications. J Clin Endocrinol Metabol. 2022;107(4):1339-47.
4. Sjostrom C, Lissner L, Wedel H, Sjostrom L. Reduction in incidence of diabetes, hypertension and lipid disturbances after interventional weight loss induced by bariatric surgery: The SOS Intervention Study. Obesity Res.1999;7(5):477-84.
5. Wilson P, D'Agostino R, Sullivan L, Parise H, Kannel W. Overweight and obesity as determinants of cardiovascular risk: The Framingham experience. Arch Internal Med. 2002;162(16):1867-72.
6. Benjamin E, Levy D, Vaziri S, D'Agostino R, Belanger A, Wolf P. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. J Am Med Assoc. 1994;271(11):840-4.
7. Colditz G, Willett W, Rotnitzky A, Manson J. Weight Gain as a Risk Factor for Clinical Diabetes Mellitus in Women. Ann Internal Med. 1995;122(7):481-6.
8. Tirosh A, Shai I, Tekes-Manova D, Israeli E, Pereg D, Shochat T, et al. Normal Fasting Plasma Glucose Levels and Type 2 Diabetes in Young Men. N Eng J Med. 2005;353(14):1454-62.

9. Grundy S, Barnett J. Metabolic and health complications of obesity. Disease A Month. 1990;36(12):641-731
10. Grundy S, Cleeman J, Daniels S, Donato K, Eckel R, Franklin B, et al. Diagnosis and management of the metabolic syndrome. An American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation. 2005;112(17)2735-52.
11. Shetty S, Parthasarathy S. Obesity hypoventilation syndrome. Curr Pulmonary Rep. 2015;4(1):42-55.
12. Canargo C, Jr, Weiss S, Zhang S, Willett W, Speizer F. Prospective study of body mass index, weight change and risk of adult-onset asthma in women. Arch Internal Med. 1999;159(21):2582-8.
13. Bailey C, Flatt P, Conlon J. An update on peptide-based therapies for type 2 diabetes and obesity. Peptides. 2023;161(1):170939.
14. Camilleri M, Malhi H, Acosta A. Gastrointestinal Complications of Obesity. Gastroenterology. 2017;152(7):1656-70.
15. Azuri J, Hammerman A, Aboalhasan E, Sluckis B, Arbel R. Tirzepatide versus semaglutide for weight loss in patients with type 2 diabetes mellitus: A value for money analysis. Diabetes Obesity Metabol. 2023;25(4):961-4.
16. Han S, Safeek R, Ockerman K, Trieu N, Mars P, Klenke A, Furnas H, Sorice-Virk S. Public Interest in the Off-Label Use of Glucagon-Like Peptide 1 Agonists (Ozempic®) for Cosmetic Weight Loss: A Google Trends Analysis. Aesthetic Surg J. 2023:44(1):60-7.
17. Bonner L. GLP-1 Receptor Agonists: Breaking down the Hype and Demand. American Pharmacists Association. 2023. Available at: https://pharmacist.com/Publications/Pharmacy-Today/Article/glp-1-receptor-agonists-breaking-down-the-hype-and-demand. Accessed on 11 April 2024.
18. Suran M. As Ozempic's Popularity Soars, Here's What to Know About Semaglutide and Weight Loss. J Am Med Assoc. 2023;329(19):1627-9.
19. Yang A. National Geographic. Ozempic Is a Serious Drug with Serious Risks. Here's What to Know.2023. Available at: https://www.nationalgeographic.com/science/article/ozempic-tiktoks-favorite-weight-loss-drug-is-unproven. Accessed on 11 April 2024.
20. Blum D. The New York Times. 2022. Available at: https://www.nytimes.com/2022/11/22/well/Ozempic-diabetes-weight-loss.html. Accessed on 11 April 2024.
21. Whitley H, Trujillo J, Neumiller J. Special Report: Potential Strategies for Addressing GLP-1 and Dual GLP-1/GIP Receptor Agonist Shortages. Clin Diabetes. 2023;41(3):467-73.
22. FDA Medications Containing Semaglutide Marketed for Type 2 Diabetes or Weight Loss. 2024. Available at: https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/medications-containing-semaglutide-marketed-type-2-diabetes-or-weight-loss. Accessed on 11 April 2024.
23. Putka S. Diabetes patients also struggle to access GLP-1 agonists: patients are making substitutions, crossing state lines, stopping care because of shortages. 2023. Available at: https://www.medpagetoday.com/special-reports/features/102773#:~:text=All%20three%20of%20the%20most,loss%20and%20is%20expected%20to. Accessed on 10 March 2024.
24. Mailhac A, Pedersen L, Pottegard A, Sondergaard J, Mogensen T, Sorensen H, Thomsen R. Semaglutide (Ozempic®) Use in Denmark 2018 Through 2023-User Trends and off-Label Prescribing for Weight Loss. Clin Epidemiol. 2024;16(1);307-18.
25. U.S. Food and Drug Administration. FDA drug shortages. 2023 Available at: https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm. Accessed on 10 March 2024.
26. Beba H, Ranns C, Hambling C, Diggle J, Brown P. PCDS consensus statement: a strategy for managing the supply shortage of the GLP-1 RAs Ozempic and Trulicity. Diabetes Primary Care. 2022;24(5):147-9.
27. Long B, Pelletier J, Koyfman A, Bridwell R. GLP-1 agonists: A review for emergency clinicians. Am J Emergency Med. 2024;78(1) 89-94
28. Hantel A, Siegler M, Hlubocky F, Colgan K, Daugherty C. Prevalence and severity of rationing during drug shortages: a national survey of health system pharmacists. J Am Med Assoc. 2019;179(5):710-1.
29. Frías J, Bonora E, Nevarez Ruiz L. Efficacy and safety of dulaglutide 3.0 mg and 4.5 mg versus dulaglutide 1.5 mg in metformin-treated patients with type 2 diabetes in a randomized controlled trial (AWARD-11). Diabetes Care. 2021;44(3):765-73.
30. Frías J, Auerbach P, Bajaj H. Efficacy and safety of once weekly semaglutide 2·0 mg versus 1·0 mg in patients with type 2 diabetes (SUSTAIN FORTE): a double-blind, randomised, phase 3B trial. Lancet Diabet Endocrinol. 2021;9(9):563-74.
31. Trujillo J, Nuffer W, Ellis S. GLP-1 receptor agonists: a review of head-to-head clinical studies. Therapeutic Adv Endocrinol Metabol. 2015;6(1):19-28.
32. Novo Nordisk.Webpage.2023. Available at: https://www.novonordisk-us.com/supply-update.html. Accessed on 30 April 2024.
33. Pawlowski A, Wong C, Cohen M, Adams R, Gosk S. Canada cracks down on U.S. patients buying Ozempic in British Columbia. Webpage. 2023. Available at https://www.today.com/health/news/ozempic-weight-loss-canada-rcna77601. Accessed on 30 April 2024.
34. Government of Canada. Health Canada. Update on the supply of Ozempic and other GLP-1 receptor agonists: Notice. Webpage. 2023 Available at: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-

products/drug-shortages/information-consumers/supply-notices/ozempic.html. Accessed on 30 April 2024.
35. Campbell P. Semaglutide Shortage Prompts FDA Warning to Patients, Providers. Webpage. 2023. Available at: https://www.hcplive.com/view/semaglutide-shortage-prompts-fda-warning-to-patients-providers. Accessed on 30 April 2024.
36. Panic G, Yao X, Gregory P, Austin Z. How do community pharmacies in Ontario manage drug shortage problems? Results of an exploratory qualitative study. Can Pharmacists J. 2020;153(6):371-7.
37. Skydsgaard N. Reuters. Novo Nordisk Says EMA Raised Safety Signal on Drugs Including Semaglutide. 2023. Available at: https://www.reuters.com/business/healthcare-pharmaceuticals/novo-nordisk-shares-slip-ema-drug-safety-signal-2023-06-22/. Accessed on 11 April 2024.
38. European Medicines Agency. Science Medicine Health. Shortage of Ozempic (Semaglutide) 2023. Available at: https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/medications-containing-semaglutide-marketed-type-2-diabetes-or-weight-loss. Accessed on 11 April 2024.
39. Phakey S, Shen A. Impact of semaglutide and dulaglutide shortages on Pharmaceutical Benefits Scheme prescriptions supplied for type 2 diabetes treatment. Aust J General Pract. 2024;53(1):57-61.
40. Massy-Westropp M. UNSW Sydney. What We Can Learn from the Ozempic Shortage. 2023. Available at: https://www.unsw.edu.au/newsroom/news/2023/02/what-we-can-learn-from-the-ozempic-shortage#:~:text=The%20Ozempic%20shortage%20illustrates%20the,current%20dearth%20of%20such%20medications. Accessed on 11 April 2024.
41. TGA about the Ozempic (Semaglutide) Shortage 2022 and 2023. 2023. Available at: https://www.tga.gov.au/safety/shortages/information-about-major-medicine-shortages/about-ozempic-semaglutide-shortage-2022-and-2023. Accessed on 11 April 2024.
42. Mattingly A. The role of outsourcing facilities in overcoming drug shortages. J Am Pharmac Assoc. 2021;61(1):110-14.
43. Arillota D, Floresta G, Guirguis A, Corkery J, Catalani V, Martinotti G, Sensi S, Schifano F. GLP-1 Receptor Agonists and Related Mental Health Issues; Insights from a Range of Social Media Platforms Using a Mixed-Methods Approach. Brain Sci. 2023;13(11):1503.
44. Landsverk G. Shortages of a 'game changer' weight-loss drug are driving people to buy potentially risky knockoff versions. 2023. Available at: https://www.insider.com/buy-compounded-semaglutide-online-risks-wegovy-ozempic-2023-1. Accessed on 10 March 2024.
45. Belluz J. Obesity in the Age of Ozempic. 2023. Available at: https://www.vox.com/science-and-health/23584679/ozempic-wegovy-semaglutide-weight-loss-obesity. Accessed on 11 April 2024.
46. Davis N. The Guardian. New Diabetes Drugs Do Not Tackle Root Causes of Obesity, Experts Warn. 2023. Available at: https://www.theguardian.com/society/2023/feb/05/new-diabetes-drugs-do-not-tackle-root-causes-of-obesity-experts-warn. Accessed on 11 April 2024.
47. FDA Ozempic Prescribing Information. 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/209637Orig1s009lbl.pdf. Accessed on 11 April 2024.
48. Nanayakkara N, Huang M, Jenkins A, Cohen N. The Impact of GLP-1 receptor agonist shortages on glycaemic control: Findings from an Australian specialist diabetic clinic. Diab Res Clin Pract. 2024;213(1):111740.

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