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SPECIAL REPORT

GLP-1 Agonists — Medtech Friend or Foe?

Contents

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Key takeaways

- Recently, demand for GLP-1 agonists has been rapidly increasing. These medications have been all the 'buzz', with their popularity fueled by social media, celebrity endorsements by the likes of Elon Musk, and increased marketing spend by pharma manufacturers (e.g., Novo Nordisk, Eli Lilly).

- GLP-1s are a game changing drug class with potential to create meaningful impact on the treatment of diabetes and/or obesity and related complications/ comorbidities (e.g., sleep apnea, osteoarthritis, cardiovascular disease, chronic kidney disease).

- As a result, investors, fearful that GLP-1s will soften demand for certain procedures and reduce total addressable markets for some medical devices, have been exiting Medtech, leaving affected market players with reduced stock prices.

- Medtech OEMs and ecosystem players, like DMEs, CMOs, etc., are rightfully curious about the actual impacts of GLP-1s on their businesses in the near- and long-term.

- Impacts from GLP-1s will vary across conditions/markets. The addressable patient population, depending on condition, is much more nuanced than may initially seem — not everyone that wants to take a GLP-1 is eligible and may see the benefits from the therapy, and in most cases, only a fraction will be able take it on its own without the support of a medical device.

- There are still some very real headwinds affecting GLP-1 usage in the near and long-term (e.g., supply shortages, high costs, noncomprehensive payer coverage and questions around the likelihood for long-term coverage, long-term clinical concerns, durability of clinical results, low adherence, etc.) that are likely to temper the impacts of GLP-1s. Hence, the noise and the associated selloff we are seeing on the stock markets feels overdone.

- We do believe that GLP-1s have the potential to have a sizeable impact on improving the health of patients and treatment paradigms. However, as we will detail below, typically GLP-1s are likely to be complementary to existing standard of care vs. displacing in nature.

- The interest in GLP-1s from the public is likely to drive rates of diagnosis for certain conditions (e.g., obstructive sleep apnea, type 2 diabetes, etc.), and therefore, device usage. Individuals, who were previously reluctant to visit the doctor, may do so, attempting to secure prescriptions for the coveted GLP-1s. This will allow the doctors to evaluate and diagnose the patients' underlying/comorbid diseases, and potentially prescribe the necessary medical devices for treatment.

- We discuss potentially positive and neutral impact from GLP-1 agonists, and where we allude to any negative repercussions, it often comes down to potential decreases in the rate of growth vs. actual drops in medical device usage in the proximate future.

Introduction

Since the arrival of glucagon-like peptide-1 (GLP-1) agonists, it's hard to have a conversation about diabetes, weight loss, cardiovascular (CV) disease or a broad array of other topics without talking about these drugs. And with patient success stories ranging from (allegedly) Mindy Kaling to (confirmed) Elon Musk, having taken these medications, it's not hard to see why. GLP-1 agonists have demonstrated impressive results when it comes to weight loss in some individuals.
So, what are GLP-1 agonists?

GLP-1 agonists are noninsulin injectable (and oral) medications that were developed predominantly to help manage blood sugar (glucose) levels in people with type 2 diabetes. The U.S. Food and Drug Administration (FDA) approved the first GLP-1 agonist (exenatide) in 2005. Recently, however, these drugs have reached a new level of popularity, fueled by social media (e.g., users, who have partnerships with telehealth companies that prescribe GLP-1 agonists, talking about their weight loss on TikTok), celebrity endorsements (too many to list) and increased spending on marketing by associated pharmaceutical manufacturers (e.g., Novo Nordisk, Eli Lilly).

A recent study found that marketing spend has risen by 23% for Ozempic, 38% for Rybelsus and more than 1,000% for Wegovy. Ozempic and Rybelsus had a combined marketing spend of $245 million.[1]

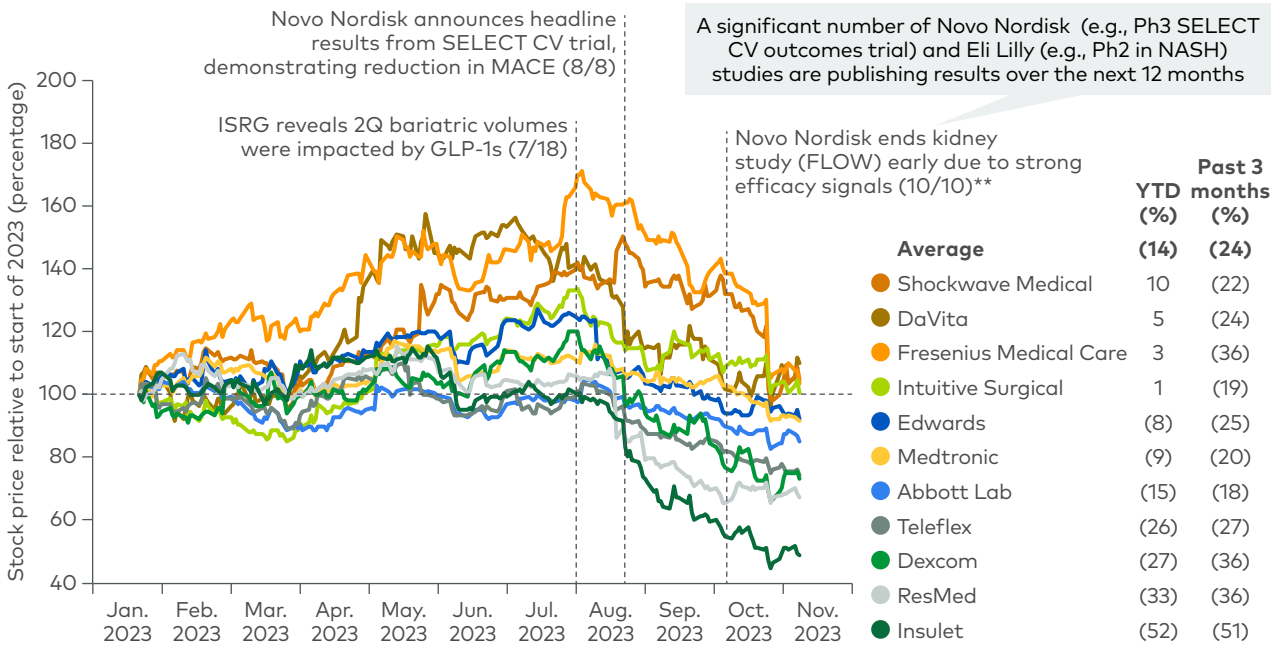
The current landscape for medtech original equipment manufacturers (OEMs)

GLP-1s are currently seen as a game-changing drug class with meaningful impact on the treatment of diabetes and/or obesity and related complications/comorbidities (e.g., sleep apnea, CV disease, chronic kidney disease, osteoarthritis).

As a result, investors — fearful that GLP-1s will soften demand for certain procedures and reduce total addressable markets for some medical devices — have been exiting medtech, leaving affected market players with reduced stock prices (see Figure 1).

Medtech OEMs and ecosystem players, such as durable medical equipment manufacturers and contract manufacturing organizations, are rightfully curious about the potential impact of GLP-1s on their businesses.

Figure 1
Select large medtech OEM stock performance, year to date*



*Data pulled 10/25/2023
**Results to remain blinded until trial completion and are expected to be read out in first half of 2024
Note: OEM=original equipment manufacturer; ISRG=Intuitive Surgical Inc.; GLP-1s=glucagon-like peptides-1; MACE=major adverse cardiovascular events; NASH=nonalcoholic steatohepatitis
Source: Company websites; Yahoo Finance

GLP-1 agonists and how they work

GLP-1 agonists mimic the function of GLP-1, a naturally occurring hormone produced by the small intestine, by attaching to cell receptors. In the body, GLP-1 triggers insulin release from the pancreas, blocks glucagon secretions, slows digestion (specifically, the emptying of the stomach) and increases post-food intake satiety (by affecting areas of the brain that are responsible for controlling hunger).

For type 2 diabetics, GLP-1 agonists help reduce blood sugar spikes through slower stomach emptying and increased insulin release.

The satiety achieved by GLP-1 agonists decreases food intake, appetite and hunger, which can in turn drive weight loss.

The current GLP-1 agonist market in the US

Currently (as of mid-November 2023), there are 13 GLP-1 agonists approved in the U.S. 10 assets are approved for treatment of Type 2 diabetes, but only Novo Nordisk's Wegovy and Saxenda and Eli Lilly's Zepbound are approved for treating obesity.

Beyond diabetes and obesity, GLP-1 agonists are also being evaluated for positive effects on nonalimentary, metabolic indications such as peripheral vascular disease and Alzheimer's disease (see Figure 2). These other indications represent longer-term opportunities but could add to an already growing pool of addressable patients as clinical evidence around GLP-1 agonists continues to emerge.

Figure 2
Currently marketed GLP-1 agonists, by indication

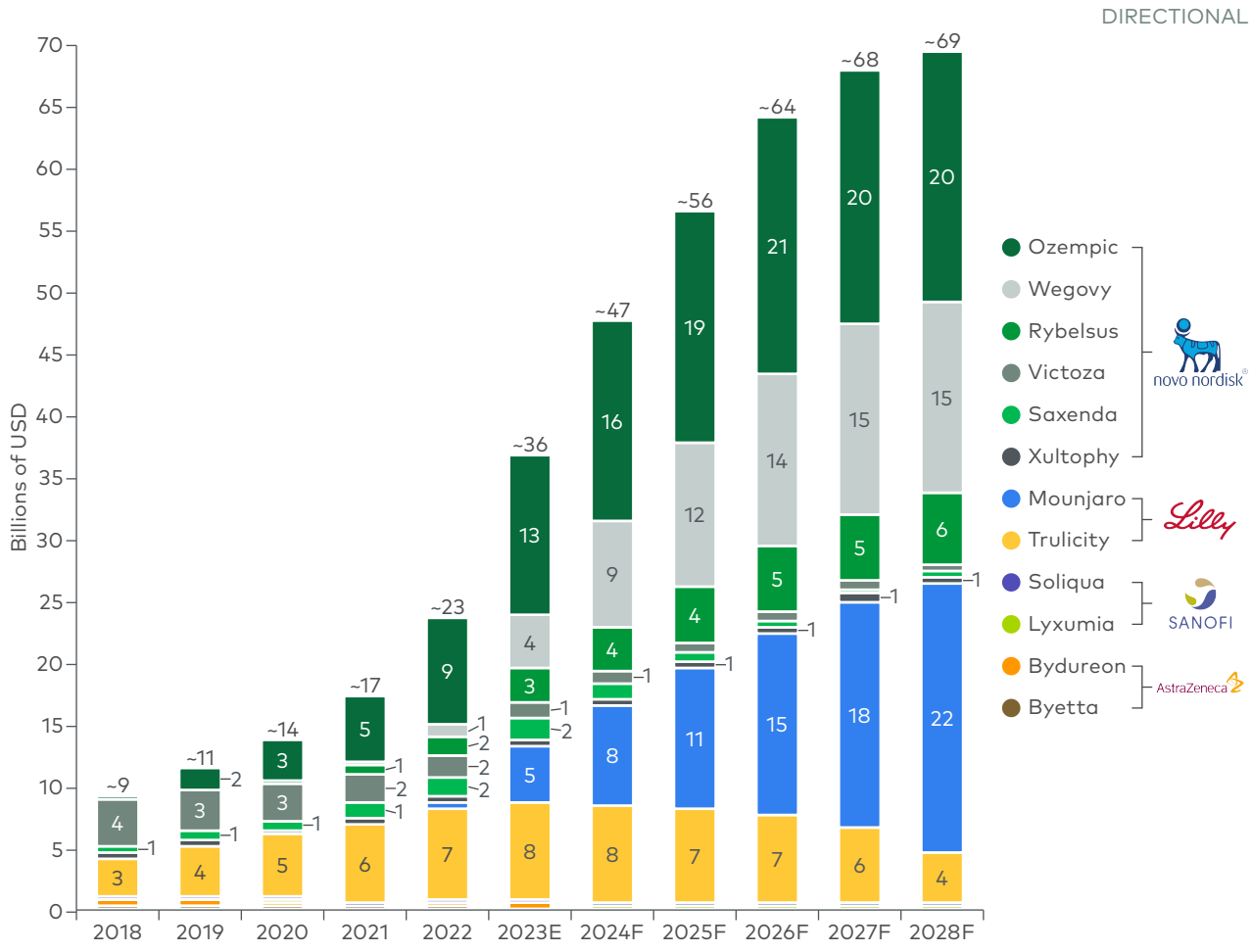
Manufacturer	Asset	2023 pro forma WW revenue ($B)	Dosage frequency	FDA approval date for first indication	Score					
					Type 2 diabetes	Obesity	NASH	Alzheimer's disease	Cardiovascular disease	Others
novo nordisk®	Ozempic	~$12.9	0.25-1 mg 1x weekly	12/5/2017	√		Phase III	Phase III	√*	• Chronic kidney disease: Phase III • Peripheral vascular disease: Phase III
	wegovy	~$4.4	0.25-2.4 mg 1x weekly	6/4/2021	Phase III	√		Phase III		• Endometriosis: Phase II
	Rybelsus semaglutide tablets	~$2.7	7-14 mg tab. 1x daily	9/20/2019	√	Phase III		Phase III	√*	
	Victoza	~$1.3	0.6-1.8 mg 1x weekly	1/25/2010	√	Phase III			√*	• Parkinson's disease: Phase II
	Saxenda	~$1.6	0.6-3 mg 1x daily	12/23/2014		√				• Smoking cessation: Phase II
	Xultophy	~$0.5	10-50 units 1x daily	11/21/2016	√					
Lilly	mounjaro	~$4.5	2.5-15 mg 1x weekly	5/13/2022	√	Preregis-tration**	Phase II		Phase III (heart failure)	• Obstructive sleep apnea: Phase III
	trulicity	~$7.9	0.5-4 mg 1x weekly	9/18/2014	√				√*	
SANOFI	SOLIQUA	~$0.2	15-60 units 1x daily	11/21/2016	√					
	Lyxumia^	~$0.2	10-20 mg 1x daily	7/27/2016	√					
AstraZeneca	BYDUREON	<$0.3	2 mg 1x weekly	1/27/2012	√					
	Byetta	<$0.01	5-10 mg 2x daily	4/28/2005	√					

*For patients who also have diabetes
**If tirzepatide is approved for weight loss, it will likely get a new brand name and dosage to differentiate it from Mounjaro, which is the same drug but only labeled for diabetes treatment
^Lyxumia is known as Adlyxin in the U.S. and as of 1/1/23 has been discontinued by Sanofi in the U.S.
Note: GLP-1=glucagon-like peptide-1; FDA=Food and Drug Administration; NASH=nonalcoholic steatohepatitis; WW=worldwide
Source: Evaluate Pharma; Company press releases and websites

What do analysts believe the sales forecasts for GLP-1 agonists will look like over the next 5 years, and why?

The top five assets, Ozempic, Wegovy, Rybelsus, Mounjaro and Trulicity, are estimated to comprise about 90% of 2023 worldwide pro forma sales. Expansion into other indications, primarily obesity, drives much of forecasted GLP-1 agonist sales growth over the next five years, with Mounjaro forecast to grow fastest, according to analysts. While Ozempic and Wegovy mimic the GLP-1 hormone, Mounjaro affects an additional metabolic hormone called glucose-dependent insulinotropic polypeptide and has shown evidence that it may achieve the best weight reduction efficacy of all marketed GLP-1 agonists. This dynamic drives Mounjaro forecasted sales up to approximately $21 billion in 2028, according to analyst consensus (see Figure 3).

Figure 3
Historical and projected WW revenue of currently marketed GLP-1 agonist products (2018-2028F)



Note: GLP-1=glucagon-like peptide-1; WW=worldwide
Source: Evaluate Pharma

A body mass index (BMI) ≥ 30 characterizes obesity in adults, whereas a BMI > 40 characterizes severe obesity. Obesity is highly prevalent in the U.S., with 42.4% of the U.S. adult population considered obese (140+ million Americans) and 9.2% severely obese (30+ million Americans).[2] Comparatively, 37+ million Americans have diabetes (about 1 in 10), and approximately 90%-95% of them have type 2 diabetes.[3]

Patients may often have diabetes and be obese, but the two conditions can occur independently. Obese and/or diabetic patients are at heightened risk for other medical conditions and comorbidities (e.g., CV disease, hypertension, chronic kidney disease), which often lead to costly healthcare spending and follow-up care. Thus, the annual cost of diabetes in the U.S. amounts to $327 billion,[4] and $173 billion for obesity[5] (there may be some overlap in costs driven by patients who are both diabetic and obese). As such, GLP-1 agonists have garnered significant attention as potential breakthrough drugs in helping combat type 2 diabetes, and recently, even more so, obesity and other related conditions.

Additionally, a number of high-dose oral GLP-1 agonists, which are currently showing similar results to injectable GLP-1 agonists, are in clinical trials (see Figure 4). Oral drugs typically have higher patient adherence rates than do injectables, so there is a lot of excitement about them. Currently, only Rybelsus, an oral tablet, is FDA approved for type 2 diabetes.

Figure 4
Oral GLP-1 drugs on the market and in development

Drug	Approved and pipeline indications		Dosage
	Type 2 diabetes	Obesity	
novo nordisk® RYBELSUS® semaglutide tablets	√	Phase III trial	Up to 14 mg 1x daily
Lilly Orforglipron	Phase II trial concluded	Phase II trial	Up to 45 mg 1x daily
Pfizer Danuglipron	Phase III trial		Up to 200 mg 2x daily
novo nordisk® OASIS 1	Phase III(a) trial		50 mg 1x daily

Novo intends to file for regulatory approval in the U.S. and U.K. in 2023

Note: GLP-1=glucagon-like peptide-1
Source: Evaluate Pharma; Company press releases and websites

Implications for medtech companies and the use of GLP-1 agonists in the treatment of other diseases

There are a multitude of headwinds facing GLP-1 agonist use, including high costs, noncomprehensive payer coverage, and questions around the likelihood of long-term coverage, supply shortages, long-term clinical concerns, durability of clinical results, low adherence, etc. These headwinds result in differential impacts of GLP-1s across patient populations; segmentation is critical to understanding their impact, as use of GLP-1 and their effect will vary based on BMI, comorbidities, payer mix, socioeconomic status, and so on. And even if the headwinds are overcome, the addressable patient population, depending on condition, is much more nuanced than it may initially seem — not everyone who wants to take a GLP-1 is eligible and able to see benefits from the therapy, and in most cases, only a fraction will be able to take the drug on its own without the support of a medical device.

The SELECT trial showed groundbreaking results of GLP-1 agonists in the reduction of MACE (major adverse cardiovascular events), including for example CV (cardiovascular) death, across patients with a BMI of at least 27 and a preexisting condition of CVD (cardiovascular disease). Therefore, underlying diseases driving Medtech markets should see growth in underlying patient populations as a result of GLP-1 agonists impact on reduced mortality. Have the market frenzy on Medtechstock prices factored that incremental patient population in? We doubt it.

The headwinds include:

- **GLP-1 agonists are expensive drugs**, and payer coverage is not comprehensive. Significant uncertainty exists around payer coverage and market access for GLP-1 agonists in the future. Most commercial payers cover GLP-1 agonists for diabetes and weight loss but have restrictions (e.g., patient qualification, step therapy) for the latter indication. Some insurers are cutting back coverage given the surge in demand and high lifetime cost of the medications. ResMed CEO Michael Farrell recently estimated a $480,000 "lifetime cost" for a 40-year-old obstructive sleep apnea (OSA) patient who takes a GLP-1 agonist full time (40 years x 12 months x $1,000 estimated cost of drug).[6] Furthermore, GLP-1 agonists that are indicated for diabetes are required to be covered at a class level for treatment of diabetes under Medicare Part D. However, obesity and weight loss medications are excluded

from coverage in Medicare Part B and Part D by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003.[7] Thus, for patients who are not covered, the out-of-pocket cost for GLP-1 agonists is between $800 and $1,300 per month, meaning that few patients can afford the drugs.

- **GLP-1 agonists are in short supply** given the increased demand for these products for licensed and off-label indications. Novo Nordisk CEO Lars Fruergaard commented that it could "take quite some years" before the company fully meets demand for semaglutide, sold as both Ozempic and Wegovy.[8] Supply is likely to increase as more plants are established and additional oral options are made available.

- **Beyond access challenges, there are clinical concerns** surrounding GLP-1 agonists. GLP-1 agonists have considerable side effects, including nausea, diarrhea and vomiting, which can prevent certain patients from taking the medications. Moreover, the long-term effects of GLP-1 agonists remain unknown. New research indicates that patients using GLP-1 agonists could be at risk of more serious gastrointestinal issues such as biliary disease, pancreatitis, bowel obstruction and gastroparesis.[9] Though these side effects appear rare, it is possible that as more people use these drugs for longer, more side effects may emerge. There are also contraindications (e.g., pregnancy, personal or family history of medullary carcinoma of the thyroid).

- **Finally, market stakeholders question patient adherence**, performance in the real world and weight gain after cessation of therapy with GLP-1 agonists. A recent analysis of real-world pharmacy and medical claims data highlighted that 68% of new patients who began taking GLP-1 agonists were no longer doing so after one year.[10] Real-world weight loss outcomes may also be lower than those seen during clinical trials, where GLP-1 agonist administration was conducted in addition to a specific diet and physical activity. What's more, a clinical trial demonstrated that patients regained two-thirds of the weight initially lost over a 12-month period, suggesting ongoing treatment is needed to preserve improvements in weight and health.[11] This means that if patients are to be treated with GLP-1 agonists, they will likely require indefinite therapy if they want to sustain benefits. This boomerangs back to the point above around affordability of these medications.

Diving a bit deeper, what does this mean for medtech companies? How should we think about the impact of GLP-1s on relevant device categories — especially device categories that some believe will be heavily affected (e.g., continuous glucose monitoring and diabetes care, OSA, orthopedics, CV)?

Most medtech companies serve patients with health conditions that can be treated (at least in part) by GLP-1 agonists, namely patients with diabetes and comorbidities of diabetes and/or obesity (e.g., OSA, CV disease, osteoarthritis and chronic kidney disease). Specifically, devices such as continuous glucose monitors (CGMs) for diabetes care, continuous positive airway pressure (CPAP) machines for OSA, orthopedic implants (e.g., knee, hip), CV devices (e.g., pacemakers, valves), bariatric surgery devices (e.g., surgical robots and consumables for robotically assisted bariatric surgery) and dialysis equipment have been noted as possibly vulnerable to disruption from use of GLP-1 agonists by patients.

Below, we've described what may happen in some of the main areas that are sparking concern and debate. However, each market has various nuances and is therefore likely to be impacted differently by GLP-1s — for some, the argument for complementary usage is strong, and for others, the impact on the patient population is potentially a bit more negative for medtech companies. However, what remains true across all is that significant headwinds exist for GLP-1 use, including access and uncertainty around the long-term effects, and are unlikely to be meaningfully mitigated. Although we do acknowledge it's hard to predict exactly what will happen, our opinion is that the medtech sell-off is overplayed and that demand across the medtech markets is likely to continue to be strong. And as we mentioned above, the expansion of the patient population due to the reduction in mortality rates, should in fact expand the eligible patient pool for many areas as patients age.

So, let's play out what might happen to the use of these devices.

Diabetes care and CGM usage

- In diabetes care, there is a question about whether GLP-1 agonists could supplant use of CGMs if meaningful GLP-1-induced weight loss allows diabetic patients to regenerate enough beta cell functionality (beta cells are pancreatic cells that produce the insulin hormone that controls glucose levels in the blood) to return A1C to normal levels. Furthermore, others note that GLP-1 agonists could help prediabetic patients at risk of developing type 2 diabetes slow disease progression, further limiting their future need for CGMs.

- However, many experts (including us) believe that use of GLP-1 agonists is complementary to CGM usage, as CGMs can support dose titration of GLP-1 agonists. Expert physicians we have spoken to suggest that they will continue to prescribe diabetes devices alongside GLP-1 agonists for this exact reason. Dexcom analyzed Optum insurance claims and found that CGM use increased among patients on insulin after being prescribed GLP-1 agonists and that CGM use roughly quadrupled for basal insulin or noninsulin patients after being prescribed GLP-1s, indicating tailwinds to CGM use resulting from GLP-1s. Underlying this complementarity is a rapidly growing CGM device market driven by increasing CGM penetration among diabetic patients, especially type 2 patients.

- In terms of who could be impacted to the point of no longer needing a CGM, only a small portion of type 2 normal and basal insulin patients are expected to meaningfully reduce BMI enough (i.e., by 15%+) to regenerate beta cell functionality and no longer need to use a CGM. Additionally, young (ages 18-40) overweight/obese patients with prediabetic A1C levels may also be able to return their A1C levels to normal, slightly reducing the future pool of type 2 diabetes patients requiring CGMs. Nonetheless, physicians are increasingly treating this large and growing patient population with GLP-1 agonists in combination with CGMs, with patients sometimes even paying out of pocket.

- Finally, even with some reductions in addressable patients due to meaningful weight loss, CGM current and future usage is unlikely to be largely impacted, as the underlying market growth far outpaces the impact of GLP-1 agonists. The CGM market has significant runway for growth across its addressable population (type 1 diabetics, type 2 intensively managed/normal insulin and type 2 basal insulin), with wide underpenetration across type 2 patients currently. Favorable recent reimbursement changes are likely to support CGM proliferation in the type 2 diabetic population.

OSA and CPAP machine usage

- Obesity increases the risk of developing OSA. Approximately 70% of all OSA patients are obese. As such, many are curious whether patients who achieve significant weight loss due to GLP-1 agonists will be able to reduce many OSA-related symptoms (e.g., daytime sleepiness) and move away from using CPAP machines, a common treatment for OSA. For example, the SCALE Sleep Apnea randomized controlled trial demonstrated that liraglutide (an older GLP-1 agonist) resulted in a small portion of OSA patients losing weight and seeing a reduction in their apnea-hypopnea index (AHI). Currently, there is limited evidence for use

of GLP-1 agonists in OSA, but clinical trials (e.g., SURMOUNT-OSA: a study of tirzepatide in participants with OSA)[12] are underway.

- The vast majority of OSA cases remain undiagnosed (approximately 80%).[13] A portion of the undiagnosed patients with mild or moderate cases of OSA may also be affected by usage of GLP-1 agonists, who similarly may achieve meaningful weight loss. Some market stakeholders are also excited about leveraging GLP-1 agonists to treat OSA patients because they may have added benefits for common OSA comorbidities (e.g., hypertension, diabetes, obesity, atherosclerotic CV diseases).

- However, despite the above, while weight loss can provide meaningful improvements in OSA, reduction in AHI is unpredictable and it usually does not lead to a complete cure, with many sleep apnea patients still needing additional therapies such as CPAP. Thus, GLP-1 agonists may only reduce the need for CPAP machines among a small proportion of mild and moderate cases, marginally decelerating growth in current and new CPAP users. CPAP usage is expected to remain unaffected for patients with severe cases of OSA (about 30% of the total CPAP users). Numerous physicians also remain skeptical about patient ability to maintain a healthy weight after stopping GLP-1 agonist therapy, a prerequisite for preventing OSA symptoms from returning.

- Similar to CGMs, underlying market growth will continue to drive CPAP usage. Higher diagnosis rates (e.g., due to increased public awareness of sleep disorders) are expected to support CPAP market growth, even if GLP-1 agonists slightly decrease the number of addressable patients for CPAP machines in the mild/moderate OSA and undiagnosed segments of the market.

- If OSA was to become an on-label indication for GLP-1 agonists, it could further drive awareness of sleep apnea, which could in turn affect CPAP usage positively. As is the case with some payers/physicians in diabetes care, to qualify for a GLP-1 agonist, the patient could be required to first try or be treated in tandem with a CPAP machine. GLP-1 agonists could be administered to those who do not tolerate device-based therapy.

Other patient populations and medtech markets affected by GLP-1 agonists:

Osteoarthritis

- Obesity is a risk factor for osteoarthritis (OA), a common reason for joint replacement surgery. However, patients who now have the degenerative condition cannot get rid of the ailment by losing weight and will require treatment. What's more, for this patient population, GLP-1 agonists may provide upside for large joint devices. Doctors are often hesitant to perform surgery on patients with a BMI > 40, which is considered morbidly obese, given that they are more likely to experience serious complications both during and after surgery than someone of average weight. Thus, severely overweight patients in need of orthopedic surgery (approximately 10% of patients)[14] may be more likely to qualify for joint replacement surgery if they are able to lose the necessary weight by taking GLP-1 agonists.

- So, that begs the question, will patients taking GLP-1 in the future be able to keep their weight in check and prevent OA from developing in the first place? Data from the first National Health and Nutrition Examination Survey (NHANES I) indicates that obese women had nearly four times the risk of knee OA as compared to nonobese women; for obese men, the risk was nearly five times greater.[15] However, obesity remains only one of the contributors to OA, alongside infection, injury, deformity, etc. Therefore, OA is still likely to be relatively prevalent and it may simply take longer for patients to need surgery. GLP-1s help achieve some weight loss, but many patients will continue to be clinically overweight and some clinically obese. Moreover, any decline in addressable population will likely be offset by the patients qualifying for orthopedic surgery in the foreseeable future. Finally, those patients taking GLP-1s will need to pair the medication use with a healthier diet and physical activity to achieve sustainable weight loss. Given the need for increased levels of exercise, patients are more likely to sustain sports injuries, leading to a higher number of orthopedic interventions.

Bariatric surgery

- Bariatric surgery is currently the most efficient treatment for severe obesity, resulting in durable weight loss, improvement of CV risk factors and obesity-related comorbidities, and reduced all-cause mortality. Bariatric surgery is typically an option if a patient's BMI is > 40 (i.e., morbid obesity) or BMI is 35-39.9 (i.e., obesity) and the patient has an obesity-related condition (e.g., type 2 diabetes, hypertension, severe OSA).[16] These patients are also likely candidates for GLP-1 agonists to support weight loss, and we do expect some of these patients will want to try and will try GLP-1 agonists.

- However, patients with morbid obesity may not achieve sufficient weight loss (e.g., 15%+) with GLP-1s to reduce health risks or obtain desired results, leaving patients to seek bariatric surgery at a later date. Obese patients who take GLP-1s but have low adherence or limited sustained weight loss, experience negative side effects, and/or find the drugs to be cost prohibitive may also ultimately receive bariatric surgery. As such, there may be a softening in demand in the near term for bariatric surgery, but it is likely to rebound.

- What's more, there are patients who experience weight regain after bariatric surgery (between 1 and 2 in 5 patients[17,18]), reducing the benefits of the procedure. There is no standard therapy for weight regain after bariatric surgery, but a recent study suggests that two-thirds of the weight regained can be safely lost with GLP-1s.[19] This opens up a use case where GLP-1s can be employed in tandem with bariatric surgery, especially for morbidly obese patients.

Cardiovascular disease

- Patients with type 2 diabetes and obesity are at high risk of developing CV disease. There is evidence that GLP-1 agonists can reduce not only body weight and glycemia but also blood pressure, postprandial lipemia and inflammation, which could in turn help reduce CV events.[20] Topline results from the SELECT trial suggest a statistically significant roughly 20% reduction in major adverse CV events compared with placebo as noted above. Consequently, some cardiologists are enthused about GLP-1 agonists as a way to improve CV health.

- However, despite this, we expect the impact of GLP-1s on CV device utilization to be muted. First, there is strong growth in the underlying new CV patient population. Second, though obesity and type 2 diabetes are leading risk factors for CV disease, there are numerous other factors (e.g., smoking and secondhand smoke exposure, unhealthy diet, physical inactivity, kidney dysfunction) that contribute to the various disorders of the heart and blood vessels.

  Even in diabetic and obese individuals on GLP-1s, risk of CV disease remains high. Third, evidence underscores that surgery and medical devices provide demonstrated and sustainable clinical outcomes, while the same cannot be said of GLP-1 agonists. Hence, our expectation is that similar to other areas, GLP-1s will be a complementary treatment to cardiovascular devices — supporting patients but not fully eliminating them from the funnel. Additionally, it will be important to evaluate GLP-1 impact across the various types of CV devices (used to treat

different types of CV disease) going forward since effects are likely to vary and not all medtech companies may be affected the same.

Chronic kidney disease

- Diabetes and hypertension are the primary causes of chronic kidney disease (CKD), together accounting for more than 70% of end-stage renal disease (ESRD).[21] With increasing uptake of GLP-1s, it is natural to wonder what may happen to dialysis volumes if prevalence of diabetes and/or hypertension is significantly reduced via intake of GLP-1 agonists. Furthermore, there are studies that highlight that GLP-1s appear to have a nephroprotective action, which is expressed through both indirect (improvement of blood pressure and glycemic control, weight loss) and direct (restoration of normal intrarenal hemodynamics, prevention of ischemic and oxidative damage) effects.[22] This generates further interest in the future impact on dialysis volumes.

- It is possible that the number of patients who are diagnosed with CKD, and who consequently therefore progress to ESRD, may decline, but the existing patient base is large. Similar to orthopedic surgery, obese patients in need of a kidney transplant but who do not qualify due to high BMI could potentially take GLP-1 agonists to lose weight and access the treatment they require (though of course, the supply of kidneys is a large limiting factor as well). Hence, while we could theorize a slightly downward pressure on the number of patients on dialysis, there are a number of mitigants that may mute that impact.

- Although there are steps providers and patients can take to slow progression (including potentially taking GLP-1s), CKD is generally progressive and irreversible. There are currently more than 562,000 patients in the U.S. on dialysis. These individuals will continue to need dialysis unless they receive a kidney transplant. What's more, 37 million patients in the U.S. already have kidney disease,[23] and although GLP-1s may slow the decline of renal function toward ESRD, they cannot prevent it. Thus, though dialysis demand may be affected in the nearer term, the number of patients who will require dialysis in the future remains elevated given the extremely high number of existing patients with renal disease in the U.S. What's more, as discussed above, if GLP-1s are able to achieve cardiovascular mortality reductions (as the SELECT trial suggests), more patients may ultimately require dialysis.

Conclusion

Overall, we do believe in the potential power of GLP-1s and the impact they may have on treatments in various areas. However, we underscore that their impact across conditions/procedures and medtech device markets is likely to vary. We see GLP-1s as a friend (or perhaps a "frenemy") rather than a foe for most medtech companies. As we discussed, the headwinds affecting GLP-1s are very real and the drugs are unlikely to meet the needs of all eligible patients. This is perhaps evidenced by the recent announcement that Novo Nordisk recently paired up with GE HealthCare to develop a drug-free, noninvasive treatment for obesity and type 2 diabetes.[24]

Medtech companies and GLP-1 makers both have a multitude of upsides to pursue, some even in partnership with each other. By no means can we fully predict the impact that GLP-1 agonists will have on medtech markets at this point (though we have confidence that the above is likely to play out), and we'll be monitoring as more data is released and GLP-1s are used over a longer period of time.

For more information, please contact medtech@lek.com.

Endnotes

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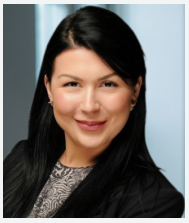

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