CLOSER LOOK

MEMORANDUM

What thought leaders are saying about Novo Nordisk's semaglutide for glycemic control, weight loss, and adherence - FDA OPH by Payal Marathe - October 18, 2017

Executive Highlights

- Our senior therapy associate Ms. Payal Marathe spoke in favor of approval for Novo Nordisk's once-weekly GLP-1 agonist semaglutide at the October 18 EMDAC meeting. See the full text of her remarks below!

Good afternoon, and thank you for this opportunity to share my perspective on the therapeutic candidate semaglutide. My name is Payal Marathe, and I work for Close Concerns, a healthcare information company that aims to improve patient outcomes by making everyone smarter about diabetes and obesity. As far as disclosures, almost 300 for- and non-profit organizations, including today's sponsor, subscribe to our fee-based newsletter called Closer Look.

The Close Concerns team, myself included, attends more than 50 scientific meetings each year, conversing with a wide range of thought leaders in the diabetes and obesity fields. This exposure to the forefront of clinical research, and to the latest clinical opinions on best practice diabetes care, is what leads me to believe that semaglutide would be an enormously valuable addition to the diabetes treatment arsenal.

There seems to be little dispute in the diabetes community that semaglutide has shown profound and consistent A1c reductions and weight loss across an array of randomized controlled trials. There's tremendous enthusiasm among clinicians, diabetes educators, and patient advocates for the GLP-1 receptor agonist class, one of the only downsides being low adherence in the real world. As we've heard time and time again, the best medicine on the planet won't do any good if a patient doesn't take it. IMS Health published a report last year showing that poor adherence is responsible for between 4%-15% of diabetes complication costs incurred by the healthcare system: In the US, this amounted to a grand total of $4 billion, or more than $14,500 per patient lifetime. Enter semaglutide, a once-weekly GLP-1 receptor agonist that cuts injection burden into one-seventh, or one-fourteenth - this is much easier for patients to take. Too often, real-world evidence doesn't match up with data from randomized controlled trials because of worse adherence, but this is less likely to happen with once-weekly semaglutide. At Close Concerns, we can't wait to see the real-world findings on this very potent, very efficacious therapy.

Even within the highly-praised class of GLP-1 receptor agonists, semaglutide boasts potential to rise above the rest. One reason is the better adherence prospects. Additionally, semaglutide has shown superior A1c reductions and weight loss in a head-to-head comparison with another once-weekly candidate already on the market, dulaglutide. The impressive data speaks for itself, but I also want to quote one renowned thought leader who said a 0.4% A1c treatment difference is a "thrashing" in the head-to-head trial business, "half a drug's worth." Importantly, this study found no correlation between semaglutide treatment and diabetic retinopathy.

As best practice diabetes care shifts toward more comprehensive approaches, healthcare providers are favoring therapies that not only lower A1c but that also improve critical outcomes beyond A1c, including body weight, frequency and severity of hypoglycemia, and cardiovascular health. Semaglutide shines on all of these parameters. The agent seems to produce a level of weight loss unheard of with current options for chronic weight management, demonstrating superiority even to high-dose liraglutide, another GLP-1 receptor agonist manufactured by today's sponsor. Obesity is a clear public health problem in this country in its own right, though it's also inextricable from the type 2 diabetes epidemic, and it is vital - absolutely vital - that better therapies are made available to patients to support weight loss, which also improves

adherence (that's an added benefit). Semaglutide's glucose-dependent mechanism of action minimizes hypoglycemia risk, which is important because of the outrageous costs associated with hypoglycemia, and because fear of hypoglycemia causes 72% of primary care physicians and 79% of diabetes care specialists to treat diabetes less aggressively than they otherwise would. Based on these stats, it's no wonder glycemic control is sub-optimal at the population level, but approving semaglutide would be a step in the right direction, because you'd be adding a treatment option to the diabetes toolkit that efficiently lowers A1c without increasing hypoglycemia risk.

With all of these benefits in tow, it would truly be a shame to keep semaglutide away from people with diabetes in the real world, especially when the singular safety concern could be well-managed with proper patient selection, education, and monitoring for retinopathy risk factors - all of this, I think, could be clearly stipulated on a semaglutide product label. Let's not forget that the base rate of diabetic retinopathy is small in comparison to the rate of patients above their 7% A1c goal - it's also small in comparison to the rate of obesity in the United States (higher than 20% in all states and territories, reaching 38% of the adult population in West Virginia, according to the CDC's 2016 figures). The impact of retinopathy on patients should not be minimized, nor should the severe unmet need for more effective anti-diabetes therapies like semaglutide. Very soon, I hope to see this medicine out there, helping patients control their blood sugars and lose weight with easy-to-take weekly doses.

In closing, I'd like to again sincerely thank you for this time, and for all the work you do to get safe, effective therapies into patient hands.

-- by Payal Marathe and Kelly Close