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press release

Rybelsus® ▼ (semaglutide tablets), the world's first and only oral GLP-1 RA, now available in the UK to treat type 2 diabetes

- *Rybelsus® (semaglutide tablets), referred to herein as oral semaglutide, is the world's first and only oral GLP-1 receptor agonist (GLP-1 RA) – the first 'protein in a pill' treatment for diabetes. It provides a new treatment option for adults in the UK with type 2 diabetes (T2D) to improve glycaemic control with an additional benefit of weight loss, in a convenient once-daily pill*[1,2,3,4]
- *Following 15 years of research and innovation, oral semaglutide is co-formulated with an absorption enhancer (SNAC), which allows it to be taken orally and absorbed from the stomach.*[5] *Previously, people with type 2 diabetes (T2D) who required GLP-1 RA treatment only had the option of an injectable treatment.*
- *Almost half (48.6%) of UK GPs reported that the injectable route of administration is a barrier to prescribing a GLP-1 RA.***[6]

Gatwick, UK, 01 September 2020 - Novo Nordisk announced today the launch of Rybelsus® (semaglutide tablets) in the UK, the world's first and only oral GLP-1 RA and first 'protein in a pill' treatment for T2D. Oral semaglutide is now available for physicians in the UK, including GPs, to prescribe for adults with insufficiently controlled type 2 diabetes (T2D) to improve glycaemic control.[1]

In the PIONEER clinical development programme, oral semaglutide 14mg demonstrated significantly greater HbA_{1c} reduction at one year*, with the additional benefit of consistent weight reduction, versus treatments used in the UK: sitagliptin, empagliflozin and liraglutide.[1,2,3,4] In addition, up to 7 out of 10 patients achieved target blood sugar (HbA_{1c}) of <53 mmol/mol (7%) with oral semaglutide.[1] These data reveal the benefits of this effective new treatment option, as despite the number of treatments currently available, 40% of adults with T2D in the UK fail to achieve target blood sugar of ≤7%.[7] This puts them at increased risk of diabetes-related complications.[7]

The link between diabetes and worse COVID-19 outcomes has elevated the importance of managing key drivers of uncontrolled T2D including blood sugar and weight, both of which may have been negatively impacted during lockdown.[8,9] As a pill, oral semaglutide can be prescribed

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by GPs and initiated virtually, whereas other GLP-1 RA treatments may require face-to-face appointments to teach injection technique.

Prof. Steve Bain, Professor of Medicine (Diabetes) at Swansea University Medical School, said: *"GLP-1 RAs are recognised as offering glycaemic control and weight loss benefits compared to other types of type 2 diabetes treatment, but are clinically underutilised because they are only available as injectables. Being able to offer patients the option of a GLP-1 RA in-a-pill may make it easier for physicians, including GPs, to intensify treatment earlier for people with T2D who are not controlled on their current treatment, helping them achieve their clinical treatment goals and reduce their risk of serious complications."*

Until now, GLP-1 RAs including semaglutide (available in a once-weekly subcutaneous formulation) could only be delivered by injection because, as they are a protein-based treatment, they would usually be broken down by stomach acid. Almost half (48.6%) of UK GPs reported that the injectable route of administration can be a barrier to prescribing a GLP-1 RA**, driven by lower patient adherence, and time taken to teach injection technique.[10,11] This can cause delays in treatment intensification and can prevent treatment goals being met.[10,12]

Oral semaglutide 14 mg is a cost-effective treatment option for the NHS compared to other treatments, including empagliflozin 25 mg and sitagliptin 100 mg.[13] Treatment costs of oral semaglutide may be offset by cost savings due to the avoidance of diabetes-related complications.***[13] In the long-term, this could lead to potential cost savings for the NHS, where the burden of poor glycaemic control and the associated long-term complications can come at a high cost.[13] Reducing the need for secondary care referral for GLP-1 RA treatment initiation may also lead to increased NHS efficiencies and cost savings, and by reducing the time needed to initiate GLP-1 RA therapy in all settings, it could also provide NHS capacity benefits.[14]

Oral semaglutide is priced at parity with other GLP-1 RAs in the UK,[15] and the cost-effectiveness of GLP-1 RAs has already been determined in national guidelines including The National Institute for Health and Care Excellence (NICE) and the Scottish Medicine Consortium (SMC).[16]

NICE has confirmed that it will not perform a single technology appraisal (STA) for oral semaglutide. Novo Nordisk is now working with the NHS to ensure that physicians, including GPs, in England and Wales can access oral semaglutide for their patients. Oral semaglutide will also be reviewed as part of the NICE guidelines update for type 2 diabetes, and a decision is expected from the Scottish Medicine Consortium (SMC) later in 2020.

Across the PIONEER trials, oral semaglutide was well-tolerated and had an adverse event profile consistent with the GLP-1 RA class, with the most common adverse reactions being nausea, diarrhoea and, when used with insulin and/or sulfonylurea, hypoglycaemia.[1] In PIONEER 6, a

trial among people with T2D and established cardiovascular disease (CVD), chronic kidney disease (CKD), or CV risk factors, the cardiovascular risk profile of oral semaglutide was non-inferior to placebo, in addition to standard of care.[17]

Pinder Sahota, Corporate Vice President and General Manager, Novo Nordisk UK, said: *"We have been working hard for 15 years to make an orally administered GLP-1 a reality because we recognised a real need among people with T2D and their treating physicians for a non-injectable option. Novo Nordisk has invested approximately £1.8 million in UK R&D for oral semaglutide, so we are proud to now be working with the NHS to make this treatment option available to the millions of people with T2D in the UK, in what represents a significant turning point in diabetes care."*

**primary endpoints at week 26 met*

***Based on the results of a 2014 published survey of UK physicians on their perceptions of GLP-1 receptor agonists*

****Based on the willingness-to-pay threshold of £20,000 per Quality Adjusted Life Years (QALY) gained*

*****END*****

About Rybelsus®

Rybelsus® (semaglutide tablets), an analogue of the naturally occurring hormone glucagon-like peptide-1 (GLP-1), is the first and only GLP-1 RA in a pill.[1] For 15 years, Novo Nordisk has been researching a way to deliver GLP-1 RA treatment in a pill, without the protein being broken down by stomach acid. Novo Nordisk has formulated semaglutide (previously only available as a once-weekly subcutaneous injection) with an absorption enhancer (SNAC), which allows it to be taken orally and absorbed from the stomach.[5] In the EU and UK, Rybelsus® is indicated for the treatment of adults with insufficiently controlled T2D, to improve glycaemic control as an adjunct to diet and exercise:[1]

- As monotherapy when metformin is considered inappropriate due to intolerance or contraindications
- In combination with other medicinal products for the treatment of diabetes

It is administered once daily and is approved for use in two maintenance dosages, 7 mg and 14 mg. The starting dose is 3 mg daily for 4 weeks.

Tolerability of oral semaglutide

- Gastrointestinal disorders were the most frequently reported adverse reactions in clinical trials, including nausea, diarrhoea and vomiting, of mild to moderate severity, and of short duration.[1]
- Compliance with the dosing regimen is required for the optimal effect of oral semaglutide. Absorption of semaglutide is highly variable and may be minimal (2-4% patients will not have any exposure).[1]
- Patients treated with semaglutide in combination with a sulfonylurea and/or insulin may have an increased risk of hypoglycaemia.[1]
- Oral semaglutide contains 23 mg sodium per tablet.[1]
- For patients with diabetic retinopathy, treated with insulin and subcutaneous semaglutide, an increased risk of developing diabetic retinopathy complications has been observed. Caution should be exercised when using oral semaglutide in patients with diabetic retinopathy.[1]
- Oral semaglutide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.[1]

About GLP-1 RAs

Oral semaglutide is a glucagon-like peptide-1 receptor agonist (GLP-1 RA). GLP-1 is a naturally occurring hormone which helps to regulate blood glucose and appetite, and supports the cardiovascular (CV) system.[1] Semaglutide mimics GLP-1 by binding to and activating the GLP-1 receptor. This leads to a reduction in blood glucose, appetite and the preference for high-fat foods, which also helps to reduce body weight.[1]

About the PIONEER clinical trial programme

PIONEER (Peptide Innovation for Early Diabetes Treatment) is the global phase 3a clinical trial programme that investigated Rybelsus® (semaglutide tablets) for the treatment of type 2 diabetes. The clinical trial programme involved 9,543 people with type 2 diabetes across 10 clinical trials – this included 311 people with type 2 diabetes in the UK, across 33 sites. The programme evaluated the tolerability and efficacy of Rybelsus® in people with type 2 diabetes vs other glucose-lowering therapies for type 2 diabetes, including SGLT-2i, DPP-4i, GLP-1 receptor agonists and as an add-on to insulin.[1]

About Novo Nordisk

Novo Nordisk is a leading global healthcare company, founded in 1923 and headquartered in Denmark. Our purpose is to drive change to defeat diabetes and other serious chronic diseases such as obesity and rare blood and endocrine disorders. We do so by pioneering scientific breakthroughs, expanding access to our medicines and working to prevent and ultimately cure disease. Novo Nordisk employs about 43,100 people in 80 countries and markets its products in around 170 countries. For more information, visit novonordisk.co.uk, Facebook, Twitter, LinkedIn, YouTube.

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▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See mhra.gov.uk/yellowcard for how to report side effects.

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