NHS
South West London

Semaglutide oral (Rybelsus®)

Summary

Semaglutide, a glucagon-like peptide 1 (GLP-1) mimetic, is available as an oral tablet (Rybelus®) or as a subcutaneous injection (Ozempic®). Where a patient is being considered for the oral option, prescribers should discuss that there are injectable options in the same class with proven cardiovascular benefits, and less variation in absorption.

Treatment with oral semaglutide is restricted to patients:

- Prescribed in line with NICE NG28 guidelines **and** SW London Joint Formulary **and**
  - With genuine needle-phobia **or**
  - Where third party assistance from healthcare staff e.g. community services staff -DSN/district nursing is required for the administration of their injectable GLP-1 mimetic

Semaglutide oral (Rybelsus® 3mg, 7mg and 14mg tablets) is Amber-2 status on the SW London Joint Formulary, which means:

A minimum of 2 month's supply is from the specialist team to reach the maintenance dose of 14mg daily dose; once patient's stabilised on 14mg daily dose, primary care can continue the treatment, with review by Diabetes Specialist teams who initiated this medication.

If semaglutide is selected from all the available GLP-1 mimetics on the SWL formulary for a patient, the preferred route of administration is by subcutaneous injection. This is due to the positive cardiovascular data with Ozempic® that does not extend to the oral formulation, which has a highly variable absorption profile.

Selecting a GLP-1 mimetic therapy

As per NICE NG28 guidelines, if triple therapy with metformin and two other oral drugs is ineffective, not tolerated or contraindicated, a GLP-1 mimetic can be considered for adults with type 2 diabetes (T2DM) who:

- Have a body mass index (BMI) of 35 kg/m2 or higher (adjust accordingly for people from Black, Asian and other minority ethnic groups) **and** specific psychological or other medical problems associated with obesity **or**
- Have a BMI lower than 35 kg/m2 **and**:
  - For whom insulin therapy would have significant occupational implications **or**
  - Weight loss would benefit other significant obesity related comorbidities

Where a patient is being considered for the oral option, prescribers should discuss with the patient that there are injectable options in the same class with proven cardiovascular benefits, and with less variation in absorption.

If a patient fulfils the prescribing criteria above for oral semaglutide, please also consider cardioprotective data, variation in bioavailability below before making a clinical decision.

Continuation of GLP-1 mimetic therapy

GLP-1 mimetic therapy must only be continued if the adult with T2DM has had a beneficial metabolic response, which is **a reduction of at least 11 mmol/mol (1.0%) in HbA1c and weight loss of at least 3% of initial body weight in 6 months,** if not met consider alternative treatment options.

Cardioprotective data for oral semaglutide

- One trial assessed the incidence of cardiovascular (CV) events in patients treated with oral semaglutide (Rybelsus®) compared to placebo and showed that oral semaglutide was non-inferior to placebo. However, the trial was not powered to demonstrate superiority or that oral semaglutide led to a reduction in Major Adverse Cardiac Events (MACE), which has been demonstrated for the injectable form of semaglutide
- PIONEER 6 was not powered to demonstrate superiority of oral semaglutide over placebo: i.e. whether it was associated with a reduction in MACE, as has been demonstrated with subcutaneous semaglutide in the Sustain 6 trial
- The European Public Assessment Report (EPAR) for oral semaglutide (Rybelsus®) notes that, due to the large variability in exposure to the drug and the different route of administration, it remains uncertain if oral semaglutide exhibits the same cardiovascular effect. It may not be appropriate to extrapolate the results
- Therefore, the trial of cardiovascular safety was unable to demonstrate if oral semaglutide was superior to placebo in the prevention of cardiovascular events
- A larger CV outcomes study of oral semaglutide (SOUL) is currently underway. The subcutaneous preparation of semaglutide has demonstrated superiority over placebo for this outcome

Counselling Points for oral semaglutide

Due to the large variation in bioavailability, for optimal effect, it is vital that the patient is counselled with the following:

- Take on **an empty stomach** at any time of the day
- **Swallow tablet whole with a sip of water (up to half a glass of water equivalent to 120 ml)**. Tablets should not be split, crushed or chewed, as it is not known whether this affects absorption of semaglutide
- **Wait at least 30 minutes before eating or drinking or taking other oral medicinal products**. Waiting less than 30 minutes decreases the absorption of semaglutide

If the treatment response is lower than expected, the treating clinician should be aware that the absorption of semaglutide is highly variable and may be minimal (2 to

4% of patients will not have any exposure), and that the absolute bioavailability of semaglutide is low.

In summary, the available data demonstrates the cardiovascular benefits of semaglutide injections (Ozempic®), such as the reduction in MACE, and does not extend to the oral formulations. The highly variable oral absorption of semaglutide should be considered. Overall, these factors should be discussed with your patient when deciding on the most appropriate formulation choice for them.

Frequently Asked Questions and Answers:

Can a GP initiate a patient on semaglutide tablets?

Semaglutide should only be initiated by Diabetes Specialist teams, with prescribing to continue during stabilisation for a minimum of 2 months to reach the maintenance dose of 14mg daily. Primary care may then be requested to continue prescribing with review by Diabetes Specialist teams who initiated this medication.

The oral tablet formulation is only recommended for patients with genuine needle-phobia or require assistance from healthcare staff e.g. community services staff - DSN/district nursing for the administration of their injectable GLP-1 mimetic.

Can I switch a patient from semaglutide injection to tablets?

If a patient has been stabilised on semaglutide injection and requires a switch to the oral tablet formulation either due to needle-phobia or to assist with administration, this should only be undertaken by Diabetes Specialist teams. A minimum of 2 month's supply must be provided from the Specialist. Once the patient is stabilised on 14mg daily dose, primary care may then be requested to continue the treatment, with review by Diabetes Specialist teams who initiated this medication.

Oral semaglutide 14mg once daily is comparable to subcutaneous semaglutide 0.5 mg once weekly. Due to the high pharmacokinetic variability of oral semaglutide, the effect of switching between oral and subcutaneous semaglutide cannot easily be predicted. An oral dose equivalent to 1.0 mg subcutaneous semaglutide has not been established.

What is the difference between prescribing injections and tablets?

There is a significant difference in potential outcomes for the patient, depending on the formulation selected.

Prescribing medication orally tends to be more convenient for the patient; however, there are no studies that demonstrate cardiovascular benefit of oral semaglutide, compared to placebo. Cardiovascular benefit has been demonstrated with the injectable formulation.

In addition, there is a significant difference in bioavailability with the oral formulation, based on the patient's adherence to the recommended method of administration. This difference can be so significant, that 2 to 4% of patients will not have any significant exposure to semaglutide. This is not a factor with the injections.

These two key points are why locally the advice is not to prescribe the oral formulation, unless for patients with genuine needle-phobia or those requiring healthcare assistance to administer the injectable formulation.

What are the essential points of discussion with patients required for semaglutide tablets?

If it is deemed necessary to prescribe the oral formulation, the patient should be made aware of the lack of cardioprotective benefits compared to the injectable/other GLP-1 mimetics, and the importance of adhering to the recommended method of administration to ensure the patient has optimal absorption.

What are the important prescribing issues to consider for semaglutide tablets?

- Semaglutide is a biologic medicine, therefore must be prescribed by brand name
- Semaglutide is a black triangle drug, report all suspected adverse drug reactions through the Yellow Card Scheme
- Taking two 7mg tablets to achieve the effect of a 14mg dose has not been studied, therefore prescribing two 7mg tablets for a 14mg dose is not recommended

References:

- BNF online (Last accessed 05/09/2022)
- Efficacy, safety and cardiovascular outcomes of once-daily oral semaglutide in patients with type 2 diabetes: The PIONEER programme (Last accessed 05/09/2022)
- Rybelsus - Summary of Product Characteristics (SmPC) (Last accessed 05/09/2022)
- SWL Joint Formulary (Last accessed 05/09/2022)

Document History

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