

Glucagon-like peptide-1 (GLP-1) analogue factsheet

Glucagon like peptide-1 (GLP-1) is an incretin hormone; it decreases blood glucose levels in a glucose-dependent manner by enhancing the secretion of insulin, via GLP-1 receptors.

GLP-1 analogue medications (also called GLP-1 mimetics) exert their glucose lowering effects by binding to and activating the GLP-1 receptor sites. This potentiates glucose-dependent insulin secretion from the pancreatic beta cells.

Dipeptidylpeptidase-4 (DPP4) inhibitors exert their blood glucose lowering activity via the same pathway as GLP-1 analogues. If a DPP-4 inhibitor is being taken, it should be discontinued on starting a GLP-1 receptor agonist, as the combination does not provide additional blood glucose control (per National Institute for Health and Care Excellence (NICE) guidance).

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With the exception of people who use insulin, semaglutide (once weekly injection) and liraglutide (once daily injection) for intensification of treatment are considered suitable for initiation and prescribing in primary care, (as detailed below).

For people who use insulin, initiation of a GLP-1 remains a specialist area of practice (specialist initiated or specialist advised) and required ongoing support from the diabetes specialist nurse (DSN) team.

Semaglutide oral tablets are only considered appropriate for specialist use (specialist initiated or specialist advised) and are reserved for people with no pre-existing cardiovascular disease and have a phobia of needles (or as an alternative to injectable GLP-1s in case of serious supply chain issues). Please note that people prescribed oral semaglutide should be advised how to take the medicine correctly in line with product literature. Failure to take the product in line with these directions may result in reduced absorption.

Background

NICE guidance recommends <u>GLP-1 mimetics</u> as below.

If third-line treatment is ineffective, not tolerated, or contraindicated:

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Triple therapy with metformin and 2 other oral antidiabetic drugs

For people on triple therapy with metformin and 2 other oral antidiabetic drugs, consider combination treatment with metformin, a sulfonylurea, and a GLP-1 receptor agonist for people with:

- 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 conditions associated with obesity, or
- a BMI lower than 35 kg/m2, and insulin therapy would have significant occupational implications, or weight loss would benefit other significant obesity-related co-morbidities.

Note: a GLP-1 receptor agonist should only be continued if the person has shown a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months.

Insulin-based treatment

For people on insulin-based treatment, arrange referral or seek advice from the specialist diabetes team, for consideration of treatment with a GLP-1 receptor agonist plus insulin.

Note: if a GLP-1 receptor agonist is added to insulin or an insulin secretagogue (sulfonylurea or meglitinide), consider reducing the dose of the latter agents to reduce the risk of hypoglycaemia. If a DPP-4 inhibitor is being taken, it should be discontinued on starting a GLP-1 receptor agonist, as the combination does not provide additional blood glucose control

Prescribing quantities and directions

GLP-1 mimetic products are available as either an injectable medication or an oral tablet. They are either given as a once daily or weekly dose depending on the product. Some products need to be titrated before the maximum dose is reached.

All products come in a pack size which is sufficient for a one-month supply and care needs to be taken that larger quantities are not prescribed mistakenly. Monthly prescription quantities are generally encouraged to avoid waste and for safety reasons.

Products, costs and doses

Name of GLP-1 mimetic	Dose	Pack size and price	Packs needed for 1 month supply
Semaglutide (once weekly injection) Ozempic	0.25mg once weekly for 4 weeks then increased to 0.5mg once weekly for at least 4 weeks, then increased if necessary to 1mg once weekly	0.25mg/0.19ml, 1.5ml pre-filled pen (titration dose only), £73.25 0.5mg/0.37ml, 1.5ml pre-filled pen, £73.25 1mg/0.74ml, 3ml pre-filled pen, £73.25	1 pre-filled pen is sufficient for 4 weeks supply 0.25mg strength should not be added to repeat prescriptions
Liraglutide (once-daily injection) Victoza (second line - once daily administration)	Initially 0.6mg once daily for at least 1 week, then increased to 1.2mg once daily for at least 1 week, then increased if necessary to 1.8mg once daily	2 x 6mg/ml, 3ml pre- filled pens, £78.48 3 x 6mg/ml, 3ml pre- filled pens, £117.72	For a 1.2mg daily dose, 2 x 6mg/ml, 3ml pen will be sufficient for 30 days For a 1.8mg daily dose, 3 x 6mg/ml, 3ml pen will be sufficient for 30 days
Dulaglutide (once-weekly injection) Trulicity	0.75mg once weekly as monotherapy 1.5mg once weekly in combination treatment	4 x 0.75mg/0.5ml pre-filled pens, £73.25 4 x 1.5mg/0.5ml pre- filled pens, £73.25	Each pack contains 4 pre-filled disposable pens which is sufficient for 4 weeks

Name of GLP-1 mimetic	Dose	Pack size and price	Packs needed for 1 month supply
Semaglutide (oral tablets) Rybelsus 1. Consultant initiation or advised 2. Those with no pre-existing CVS disease and when needle phobic or no alternative GLP-1 because of supply issues (please see prescribing note about switching below)	3 mg once daily for one month. After one month, the dose should be increased to a maintenance dose of 7 mg once daily. After at least one month with a dose of 7 mg once daily, the dose can be increased to a maintenance dose of 14 mg once daily to further improve glycaemic control.	Rybelsus 3 mg tablets £78.48 /30 tablets Rybelsus 7 mg tablets £78.48 /30 tablets Rybelsus 14 mg tablets £78.48 /30 tablets	

Prescribing notes

The effect of switching between oral and subcutaneous (s.c.) semaglutide cannot easily be predicted because of the high pharmacokinetic variability of oral semaglutide. Exposure after oral semaglutide 14 mg once daily is comparable to s.c. semaglutide 0.5 mg once weekly. An oral dose equivalent to 1.0 mg of s.c. semaglutide has not been established (Rybelsus summary of product characteristics)

Prescribe all GLP-1s by brand.

Dose titration:

- Ozempic: multiple concentrations produced, take care, prescribe correct concentration for required dose
- Victoza: Only one concentration produced, dose titration achieved by varying volume of injection

Glucagon-like peptide-1 (GLP-1) as part of a weight management service

Liraglutide once-daily injection marketed as Saxenda.

NICE, (<u>technology appraisal TA664</u>), recommend that it is prescribed in secondary care by a specialist multidisciplinary tier 3 weight management service.

Saxenda should not be prescribed for diabetes.

At time of drafting, NICE guidance regarding use of semaglutide, (<u>Wegovy</u>), remains in development. It is understood that the decision to commence treatment will be part of a tier 3 or 4 weight management programme.