

GLP-1 Analogue Prescribing guidance

A guide to optimisation and discontinuation

Developed in partnership with the specialist teams at:

The Shrewsbury and Telford Hospital 
NHS Trust

Shrewsbury and Telford Hospital Trust


Shropshire Community Health
NHS Trust

Shropshire Community Trust

GLP-1 Analogue Naïve patients

[1] If triple therapy with metformin + 2 other oral drugs is not effective, not tolerated or contraindicated, consider combination therapy with metformin, a sulfonylurea and a GLP-1 analogue for adults with type 2 diabetes who:

have a 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.

Ensure all patients using Insulin and commencing GLP-1 Analogue are initiated under specialist service.

Prior to any prescription please complete GLP-1 template to record baseline HbA1c and weight

Commence weekly subcutaneous GPL-1 analogue [2]

Both semaglutide and dulaglutide are suitable for patients with established cardiovascular disease (secondary prevention)
Consider [Semaglutide](#) where weight of concern
Consider [Dulaglutide](#) for patients with risks for cardiovascular disease (primary prevention)

Due to the lack of available cardiovascular outcome trial data for oral semaglutide this should only be considered as a second line option for patients suitable for a GLP-1 where the subcutaneous route of administration is not tolerated or advisable.

Titrate oral [Semaglutide](#) 3mg once daily for 1 month, then increase [Semaglutide](#) to 7mg once daily maintenance dose

Consider increasing maintenance dose to 14mg once daily for further glycaemic control

Titrate subcutaneous [Semaglutide](#) 0.25mg weekly for 1 month 1 pen to last four weeks (needles included with device). Then increase to [Semaglutide](#) 0.5mg weekly Next strength pen to last four weeks

Consider increasing [Semaglutide](#) to 1mg weekly if limited response Next strength pen to last four weeks

Assess for side effects if not tolerated consider trial of alternative weekly subcutaneous agent

Commence [Dulaglutide](#) 1.5mg weekly

Assess for side effects -if not tolerated, stop and refer back to specialist service to avoid clinical inertia

Following GLP-1 commencement: Interim assessment 3 months—are metabolic parameters (weight and HbA1c) moving in the right direction?

Reassess 6 months
 Weight = loss of 3%
 HbA1c = reduction of 11mmol/mol
 • Side effects = well tolerated?

Yes—both targets achieved

No

Zero targets achieved?

Refer back to specialist service to avoid clinical inertia

One of 2 targets achieved?

Discuss next steps with patient—choose 1 option:

1. Increase semaglutide to 1mg weekly for time limited trial of 3 months
 2. Switch agent to dulaglutide 1.5mg weekly for time limited trial of 3 months
- Withdraw agent:**
3. Trial SGLT2i if not tried
 4. Refer for insulin

Recheck HbA1c and weight at 3 months
 If no further positive metabolic response refer back to specialist service to avoid clinical inertia

NICE Criterion [1]— Only continue GLP-1 Analogue therapy if the person with type 2 diabetes has had a beneficial metabolic response (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)

Continue

Assess annually that GLP-1 Analogue is making a positive contribution to disease control. If metabolic parameters of weight and HbA1c are not maintained take steps to reinforce healthy lifestyle, consider a change in therapy and refer where necessary

Existing GLP-1 Analogue users achieving NICE targets and not prescribed newer weekly agent

NICE Criterion— Only continue GLP-1 Analogue if the person with type 2 diabetes has had a beneficial metabolic response (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). [1]

Since the initial NICE guidance for GLP-1 initiation was released many new GLP-1 therapies have entered the market including an oral preparation. In addition, the results from the cardiovascular outcome trials are now available for existing GLP-1 treatments (Gold standard three component MACE; composite of CV death, nonfatal MI (including silent MI), or nonfatal stroke) [2,3]. To ensure that our patients receive the most beneficial outcomes from GLP-1 treatment, existing GLP-1 therapy should be reviewed. Treatments should be evidence based, improve health and be acceptable to patients.

NOT FORMULARY

Twice Daily **Exenatide** (Byetta®) Weekly **Exenatide** (Bydureon®)

EXSCEL Trial (14752 pts over 3.2 years)
Median WEEKLY dose: 2mg
73% of participants established Cardiovascular disease
NOT Significant - HR 0.91 (0.83 to 1.00) p = 0.06

Liraglutide (Victoza®)

LEADER Trial (9340 pts over 3.8 years)
Median daily dose 1.78mg
81% of participants established Cardiovascular disease
Significantly fewer CV outcomes - HR 0.87 (0.78 to 0.97) p = 0.01

NOT FORMULARY

Lixisenatide (Lyxumia®)

ELIXA Trial (6068 pts over 2.1 years)
Median daily dose 20mcg
100% of participants established Cardiovascular disease
NOT significant—HR 1.02 (0.89 to 1.17) p = 0.81

Prescribing considerations

- No evidence for improved CV outcomes
- Multiple Daily dose - patient may find weekly option more acceptable
- Complicated injectable device - patient may find self administration easier with newer weekly agent

- 1.2mg dose - no evidence for improved CV outcomes
- Daily dose - patient may find weekly option more acceptable
- Daily dose more costly than weekly agents at evidence based 1.8mg dose

- No evidence for improved CV outcomes
- Daily dose - patient may find weekly option more acceptable
- Short duration of action leading to variable metabolic response

Recommend that all patients who have achieved NICE criterion for continuation of GLP-1 and where the therapy continues to offer a beneficial metabolic response should be offered a newer weekly subcutaneous agent that has shown superiority for CV outcomes. *Due to the current lack of CV outcome superiority data and the high pharmacokinetic variability of the oral preparation, switching existing GLP-1 analogue users to oral semaglutide is not recommended.*

PATIENT HAS ESTABLISHED CARDIOVASCULAR DISEASE

SEMAGLUTIDE

SUSTAIN-6 Trial (3297 pts over 2.1 years)
Median WEEKLY dose 0.5mg or 1mg.
83% of participants established cardiovascular disease
Baseline HbA1c = 72mmol/mol
Significantly fewer CV outcomes - HR 0.74 (0.58 to 0.95) p = 0.02

Based on clinical judgement and patient preference, consider switch to either Semaglutide 0.25mg and titrate or Dulaglutide 1.5mg weekly. Where patients are using insulin, further advice/ input may be sought from specialist as required. Assess at 6 months to ensure metabolic improvements maintained

PATIENT HAS RISK FACTORS FOR OR ESTABLISHED CARDIOVASCULAR DISEASE

DULAGLUTIDE

REWIND Trial (9901 pts over 5.4 years)
Median WEEKLY dose 1.5mg.
68.5% of participants risk factors for cardiovascular disease
Baseline HbA1c = 55mmol/mol
Significantly fewer CV outcomes - HR 0.88 (0.79 to 0.99) p = 0.026

[1] NICE Type 2 Diabetes in Adults: Management NG28. Available at: <https://www.nice.org.uk/guidance/ng28> [2] Buse J et al. 2019 Update to: Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2019 [3] <https://pmj.bmj.com/content/early/2019/12/04/postgradmedj-2019-137186>

Existing GLP-1 Analogue users not achieving NICE targets and not prescribed newer weekly agent

Confirm patient motivated to manage condition and persevere with treatment

Discuss options with patients

1. **Start newer weekly subcutaneous GLP-1 Analogue where GLP-1 Analogue therapy remains an appropriate option (see NICE criterion below).**

Switching to longer acting agents has been shown to improve metabolic responses further due to increased exposure times and compliance [3]

2. **Consider SGLT2 inhibitor (if not already taking)**
3. **Refer for insulin**

If swapping to newer weekly GLP-1 Analogue:

- Follow initiation process on page 2
- Input baseline measurements
- Recheck HbA1c and weight at 3 months

If no further positive metabolic response refer back to specialist service to avoid clinical inertia

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Version	Date	Changes	Editor
1.0	12/08/2020	Approved by APC	CJ
2.0	14/04/2021	Updated to include oral semaglutide to match Net formulary wording and incorporated specialist comments around SGLT-2 positioning, specialist input requirement for patients on insulin and strengthening of wording around clinical judgement and patient preference on those already stable on GLP-1 with superior CV outcomes (daily agents)	CMH
3.0	17/06/2021	Document updated to reflect new commissioning organisation	CMH
