GLP-1 Analogue Prescribing guidance
A guide to optimisation and discontinuation

Developed in partnership with the specialist teams at:

Shrewsbury and Telford Hospital Trust
Shropshire Community Trust
GLP-1 Analogue Naïve patients

**Titrate 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. Assess for side effects if not tolerated; consider trial of alternative weekly agent.

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

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

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.
3. Refer for insulin.
4. Trial SGLT2i if not tried.

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

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

Commence weekly 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).

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

Interim assessment 3 months—are metabolic parameters (weight and HbA1c) moving in the right direction?

Yes—both targets achieved

No
- Zero targets achieved?
- One of 2 targets achieved?

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)

Consider increasing Semaglutide to 1mg weekly if limited response. Next strength pen to last four weeks.

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.
3. Refer for insulin.
4. Trial SGLT2i if not tried.

Withdraw agent:
1. Refer back to specialist service to avoid clinical inertia.
2. Recheck HbA1c and weight at 3 months.

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

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

**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.

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[1] NICE Type 2 Diabetes in Adults: Management NG28. Available at: https://www.nice.org.uk/guidance/ng28
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. 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.

**Prescribing considerations**

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

- **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**
  - 1.2mg dose - no evidence for improved CV outcomes
  - Daily dose - patient may find weekly option more acceptable
  - Complicated injectable device - patient may find self-administration easier with newer weekly agent
  - 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

**Switch to either Semaglutide 0.25mg and titrate or Dulaglutide 1.5mg weekly.**

Where patients are using insulin refer to specialist service for switch over.

Assess at 6 months to ensure metabolic improvements maintained

**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 agent that has shown superiority for CV outcomes.**

**PATIENT HAS ESTABLISHED CARDIOVASCULAR DISEASE**

**SEМAGLUTИDE**

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

**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

**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

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

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

- □ 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
- □ 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.