Shropshire Clinical Commissioning Group

Telford and Wrekin Clinical Commissioning Group

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

[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/m^2 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/m^2 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 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)

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

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 agent

Commence Dulaglutide 1.5mg weekly

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?

No

Zero targets achieved?

Refer back to specialist service to avoid clinical inertia

One of 2 targets achieved?

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)

Yes—both targets achieved

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

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. Refer for insulin
4. Trial SGLT2i if not tried

Recheck HbA1c and weight at 3 months

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

[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 Dec 2019, dci190066; **DOI:** 10.2337/dci19-0066

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.

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 agent that has shown superiority for CV outcomes.

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

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

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 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

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/m^2 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/m^2 AND for whom insulin therapy would have significant occupational implications **OR** weight loss would benefit other significant obesity related comorbidities.

[1] NICE Type 2 Diabetes in Adults: Management NG28. Available at: https://www.nice.org.uk/guidance/ng28 [3] Diabetes Care 2011 May; 34(Supplement 2): S279-S284. https://doi.org/10.2337/dc11-s231