Shropshire, Telford and Wrekin Clinical Commissioning

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

V4.0 Shropshire and Telford & Wrekin CCG Medicines Management Team. Approved by APC August 2020. Reviewed October 2021. Approved December 2021

Review Date: December 2023 or earlier in response to new local/national guidance.

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 subcutaneous GPL-1 analogue [2]

Both Dulaglutide and Semaglutide are suitable for patients with established cardiovascular disease (secondary prevention)

Consider Dulaglutide for patients with risks for cardiovascular disease (primary prevention) - REWIND trial

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.

Commence Dulaglutide 1.5mg weekly.

Dulaglutide 0.75mg may be considered as a starting dose in potentially vulnerable patients.

Consider increasing Dulaglutide from 1.5mg to 3mg weekly if limited response after at least 4 weeks

Consider increasing Dulaglutide to 4.5mg weekly if limited response at 3mg, after at least 4 weeks

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

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

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

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?

No

Zero targets achieved?

Refer back to specialist service to avoid clinical inertia

One of 2 targets achieved?

Yes—both 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)

Discuss next steps with patient—choose 1 option:

1. Increase doses of selected s/c GLP-1 for time limited trial of 3 months
2. Switch to alternative s/c weekly GLP-1 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

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

[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 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

- 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

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

- 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

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

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

Prescribing considerations

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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[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

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
4.0	08/10/2021	Document updated to reflect new higher doses and clinical data available for dulaglutide impact on weight reduction. Circulated to APC members Dec 21 for information.	CH