

## GLP-1 Receptor Agonists in Type 2 Diabetes

As detailed in Oxfordshire's local [Type 2 Diabetes Blood Glucose Management in Adults Guideline](#) and [NICE Guideline 28](#), GLP-1 Receptor Agonists are a treatment option that can be initiated by prescribers in Primary Care to manage blood glucose in patients with Type 2 Diabetes. NICE recommend use of a GLP-1 agonist in combination with metformin and a sulfonylurea if triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated. The recommendation is for patient with type 2 diabetes who:

- have a BMI of 35 kg/m<sup>2</sup> 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<sup>2</sup> and for whom insulin therapy would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.

This guideline aims to assist prescribers in deciding on the most appropriate GLP-1 Receptor Agonist for their patient. Before starting a patient on a GLP-1 Receptor Agonist, ensure patient is compliant with current medication and that all oral hypoglycaemic therapy is optimised. If the patient's HbA1c remains at 58 mmol/mol (7.5%) or greater (or above personalised agreed target), consider initiating a GLP-1 Receptor Agonist.

Prescribers should consider stopping treatment if there is no response within 6 months of initiating treatment. Non-responders would be defined by NICE criteria as patients who fail to decrease their HbA1c by 1% point (11 mmol/mol if measured in IFCC units) and lose 3% of their body weight. The [Agreement Form and Checklist](#) will assist with this.

Exenatide (Byetta and Bydureon) and Lixisenatide (Lyxumia): Previously, both lixisenatide and exenatide were included in local guidance as first line options. Trials on cardiovascular benefits for both lixisenatide and exenatide have found to be neutral, therefore the recommendation is to offer one of the options listed in the table below which have proven cardiovascular benefit. Only consider continuation of lixisenatide and exenatide in existing patients who are achieving treatment goals and are at low risk of cardiovascular disease.

It is good practice to discuss the possible risks of starting and not starting medication with patients. The table below is a quick reference guide, for additional advice please contact the Community Diabetes team. For full and up to date information, refer to the [Summary of Product Characteristics](#) (SPC) and [BNF](#).

|                                    | <b>Semaglutide</b><br><i>(SPC: Ozempic)</i>   | <b>Dulaglutide</b><br><i>(SPC: Trulicity)</i>  | <b>Liraglutide</b><br><i>(SPC: Victoza)</i>  |
|------------------------------------|---|--|--|
| <b>Cost per Month</b>              | £73.25 (needles included)   | £73.25 (needles integrated in device)  | 1.2mg: £78.48<br>1.8mg: £117.72<br>(needles not included)  |
| <b>Frequency of Administration</b> | Weekly<br>1 pen = 4 weekly doses  | Weekly<br>1 pen = 1 weekly dose  | Daily<br>1 pen = 15 doses/10 doses   |
| <b>Dosing</b>                      | Administered once weekly at any time of the day, with or without meals. <ul style="list-style-type: none"> <li>Start at 0.25mg/week for 1 month</li> <li>0.5mg/week for 1 month (could be ongoing dose)</li> <li>1.0mg/week can be used</li> </ul> <p>If a dose is missed, it should be administered as soon as possible and within 5 days after the missed dose.</p> | Administered once weekly at any time of day, with or without meals. <ul style="list-style-type: none"> <li>Monotherapy: 0.75mg/week</li> <li>Add on therapy: 0.75-1.5mg/week</li> </ul> <p>If a dose is missed, it should be administered as soon as possible if there are at least 3 days (72 hours) until the next scheduled dose.</p> | Administered once daily at any time, independent of meals. It is preferable that Victoza is injected around the same time of the day. <ul style="list-style-type: none"> <li>Start at 0.6mg for 1 week then increase to 1.2mg</li> <li>Can be increased to 1.8mg if partial response. If no response consider one of the more cost effective options.</li> </ul> |
| <b>CV Benefit</b>                  | Yes (26% MACE reduction) <sup>1</sup>   | Yes (12% MACE reduction) <sup>2</sup>  | Yes (13% MACE reduction at 1.8mg) <sup>3</sup>   |
| <b>Glucose Lowering</b>            | Greatest benefit <sup>4</sup>   | Benefit  | Benefit  |
| <b>Weight Loss</b>                 | Greatest benefit <sup>4</sup>   | Benefit  | Benefit  |
| <b>Renal Impairment</b>            | Do not use if eGFR <15ml/min  |  |  |
| <b>Side Effects</b>                | Most side effects are gastrointestinal. Nausea is likely to be temporary, advise patient to stop eating before full to minimise nausea. <ul style="list-style-type: none"> <li>Dulaglutide 1.5mg and Semaglutide 0.5 &amp; 1mg all have similar rates of side effects</li> <li>Dulaglutide 0.75mg has a lower risk of side effects</li> </ul>                         |  |  |
| <b>Contraindications</b>           | <ul style="list-style-type: none"> <li>Type 1 diabetes mellitus</li> <li>Treatment of diabetic ketoacidosis.</li> <li>Congestive heart failure NYHA class IV</li> <li>Patients under 18 years old</li> <li>Pregnancy and breast feeding</li> </ul>  | <ul style="list-style-type: none"> <li>Type 1 diabetes mellitus</li> <li>Treatment of diabetic ketoacidosis.</li> <li>Congestive heart failure.</li> <li>Patients under 18 years old</li> <li>Pregnancy and breast feeding</li> </ul>  | <ul style="list-style-type: none"> <li>Type 1 diabetes mellitus</li> <li>Treatment of diabetic ketoacidosis.</li> <li>Congestive heart failure NYHA class IV</li> <li>Patients under 18 years old</li> <li>Pregnancy and breast feeding</li> <li>Inflammatory Bowel Disease and diabetic gastroparesis</li> <li>Significant liver impairment</li> </ul>          |

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|-----------------|--|--|--|
| <b>Cautions</b> | <ul style="list-style-type: none"> <li>An increased risk of developing diabetic retinopathy complications has been observed. Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy, caution in those with a high HbA1c (&gt;9%, 75mmol/mol) and/or retinopathy grade R2/R3/M1/P1.</li> <li>Therapeutic experience in patients ≥75 years of age is limited</li> <li>severe hepatic impairment</li> <li>delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products</li> </ul>      | <ul style="list-style-type: none"> <li>Patients ≥ 75 (0.75 mg once weekly can be considered as a starting dose)</li> <li>delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products</li> </ul> | <ul style="list-style-type: none"> <li>Monitor INR on warfarin</li> <li>Thyroid Disease</li> <li>delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products</li> </ul> |
|                 | <p><b>All:</b> Be alert to the signs and symptoms of acute pancreatitis. Instruct patients to seek prompt medical care if they experience persistent severe abdominal pain. Discontinue GLP-1 Receptor Agonist if pancreatitis is suspected. If pancreatitis is confirmed, appropriate supportive treatment should be initiated and the patient carefully monitored until recovery and a GLP-1 Receptor Agonist should not be restarted.</p>   |  |  |
|                 | <p><b>All:</b> <a href="#">MHRA safety alert</a>: Serious and life-threatening cases of diabetic ketoacidosis have been reported in patients with type 2 diabetes on a combination of a GLP-1 agonist and insulin, particularly after rapid discontinuation or reduction of concomitant insulin. GLP-1 receptor agonists are not substitutes for insulin, and any reduction of insulin should be done in a stepwise manner with careful glucose self-monitoring. If unsure, please contact the Community Diabetes Team for advice on <a href="mailto:diabetesdialogue@nhs.net">diabetesdialogue@nhs.net</a>.</p> |  |  |
|                 | <p><b>All:</b> When added to existing therapy of sulfonylurea or insulin, a reduction in the dose of sulfonylurea or insulin should be considered to reduce the risk of hypoglycaemia. NICE recommend seeking specialist care advice and ongoing support from a consultant-led multidisciplinary team when offering a GLP-1 mimetic in combination with insulin. Contact the Community Diabetes Team for advice on <a href="mailto:diabetesdialogue@nhs.net">diabetesdialogue@nhs.net</a>.</p>   |  |  |
| <b>Storage</b>  | <ul style="list-style-type: none"> <li>Before first use: Store in a refrigerator (2°C to 8°C)</li> <li>After first use: Store below 30°C or in a refrigerator (2°C to 8°C).</li> </ul>   | <ul style="list-style-type: none"> <li>Store in a refrigerator (2 °C – 8 °C).</li> <li>In use: Trulicity may be stored unrefrigerated for up to 14 days at a temperature not above 30 °C.</li> </ul>   | <ul style="list-style-type: none"> <li>Before first use: Store in a refrigerator (2°C–8°C).</li> <li>After first use: Store below 30°C or store in a refrigerator (2°C–8°C).</li> </ul>  |
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## References

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