South East London Integrated Medicines Optimisation Committee (SEL IMOC):

South East London glucagon-like peptide (GLP-1) analogue pathway for adults aged 18 years and over with Type 2 Diabetes Mellitus (T2DM).

Interim pathway to support care during the COVID-19 pandemic.

This guidance does NOT override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Developed by the SEL Diabetes Medicines Working Group on behalf of the SEL IMOC. If you have any queries or comments on this guideline please contact: LAMCCG.medicinesoptimisation@nhs.net

Date approved: February 2021

Review date: November 2021 or sooner if evidence/practice changes

South East London glucagon-like peptide (GLP-1) analogue pathway for adults aged 18 years and over with Type 2 Diabetes Mellitus (T2DM) during COVID-19

Initiation criteria

If triple therapy with metformin and 2 other oral anti-diabetic drugs is not effective, not tolerated or contraindicated, consider combination therapy of GLP-1 analogue, metformin and a sulfonylurea – see T2DM glycaemic control pathway in those whom:

- BMI ≥ 35kg/m^2 (adjust accordingly for ethnicity) and specific psychological or other medical problems associated with obesity **OR** BMI < 35kg/m^2 and where insulin would have significant occupational implications or weight loss would benefit other significant obesity related co-morbidities
- HbA1c > 58mmol/mol (7.5%) or greater than individually agreed threshold for intensification

- Ensure dietetic advice is provided prior to initiation of GLP-1 analogue therapy

If history of diabetes for > 10 years: please discuss with consultant, GLP-1 analogues are not substitutes for insulin – see T2DM glycaemic control pathway

- **If co-prescribed insulin, provision must be in place for ongoing specialist care advice and ongoing support from a consultant led multidisciplinary team in line with NICE guidance**
- Under exceptional circumstances, GLP-1 analogues can be initiated by specialist teams outside of NICE guidance in licensed combinations. A clinical rationale must be detailed within patient notes and in the transfer of care document

Initiation visit

- Review HbA1c, renal profile, lipid profile, and liver function tests (LFTs) and ensure appropriate for GLP-1 analogue use. If starting oral semaglutide and patient is taking levothyroxine, also review thyroid profile (see notes overleaf)
- Record weight and blood pressure
- Assessment of cautions, contra-indications, interactions, hepatic & renal parameters (see page 3-4)
- Review current anti-diabetic agents/doses (e.g. consider reduction of *sulfonylureas (SU) and/or insulin due to hypoglycaemia risk)* and review licensed combinations. SU may be withdrawn where clinically necessary. See notes overleaf re retinopathy complications

Agree with the patient most appropriate GLP-1 analogue (based on patient factors)

LIRAGLUTIDE (VICTOZA®)	DULAGLUTIDE (TRULICITY®)	SEMAGLUTIDE▼ (OZEMPIC®)	SEMAGLUTIDE▼ (RYBELSUS®)
ONCE DAILY INJECTION	ONCE WEEKLY INJECTION	ONCE WEEKLY INJECTION	ONCE DAILY ORAL TABLET

Patient education

- Lifestyle interventions to support therapy & need for HbA1c & weight reduction for continuation at 6 months
- Dose, timing of dose, missed dose & sick day rules (see Sick Day Rules guidance)
- Blood glucose monitoring requirements (including driving in line with Driver and Vehicle Licensing Agency(DVLA) guidance)
- Hypoglycaemia risk and actions to be taken e.g. dose reduction of concomitant medications (in particular insulin and sulfonylureas (SU))
- Side effects (see overleaf)
- For injections: subcutaneous use only. Educate on injection technique, storage & safe sharps disposal
- For oral tablet: educate on method of administration
- Ensure adequate contraception if relevant
- Follow up requirements and share contact details for the team
- Provision of written educational material where relevant
- Provide blood form for repeat renal profile before next appointment

Notes:

- For people already stable and well controlled on GLP-1 analogues in combinations previously recognised by NICE, therapy can be continued however should be monitored closely to ensure therapy remains effective.
- Exenatide standard release (Byetta®), Exenatide modified release (Bydureon®) and lixisenatide (Lyxumia®) have now been removed from the local formulary. For people who are already stable and well controlled on Byetta®, Bydureon® or Lyxumia®, therapy can be continued however should be monitored closely to ensure therapy remains effective.

***Please note:** information is not exhaustive, please see Summary of Product Characteristics (SPC) at www.medicines.org.uk for more information including details of interaction with other medicinal products.

References: **1**. Summary of product characteristics for Victoza at www.medicines.org.uk 6.12.20. **2**. Summary of product characteristics for Ozempic at www.medicines.org.uk 6.12.20 **3.** NICE guideline NG28 Type 2 diabetes in adults: management. December 2015. **4.** MHRA guidance on pancreatitis and exenatide and dipeptidylpeptidase 4 inhibitors on 21.4.16. **5**. MHRA guidance on reporting ADRs on 21.4.16. **6**. Summary of product characteristics for Trulicity at www.medicines.org.uk 6.12.20 **7.** NHS Choices. Diabetic Retinopathy on 26.9.19 8. Summary of product characteristics for Rybelsus at www.medicines.org.uk 4.12.20 9. MHRA GLP-1 receptor agonists reports of DKA when insulin rapidly reduced or discontinued 4.12.20

South East London glucagon-like peptide (GLP-1) analogue pathway for adults aged 18 years and over with Type 2 Diabetes Mellitus (T2DM) during COVID-19

NHS

LIRAGLUTIDE (VICTOZA®) INJECTION

- Start 0.6mg daily
- Issue 1-3 months treatment
- Increase the dose to 1.2mg daily after at least one week
- Administer any time of day independent of meals, but preferably at the same time of day

DULAGLUTIDE (TRULICITY®) INJECTION

- Start 0.75mg or 1.5mg weekly (consider 0.75mg weekly for potentially vulnerable populations. See overleaf)
- Issue 1-3 months treatment
- Consider increasing dose to 1.5mg weekly if applicable
- Administer any time of day, with or without meals
- Missed injection: administer asap if ≥72 hours until the next dose. If <72 hours, miss the dose. Administer next dose on regular scheduled day. Day of weekly injection can be changed as long as last dose given ≥72hrs before

SEMAGLUTIDE▼ (OZEMPIC®) INJECTION

- Start 0.25mg weekly
- Increase the dose to 0.5mg weekly after 4 weeks. After at least 4 weeks, the dose can be increased further to 1mg weekly to further improve glycaemic control
- Issue 1-3 months treatment
- Administer once weekly at anytime of day, with or without meals. Missed dose: administer asap and within 5 days after the missed dose. If >5 days, skip missed dose. Next dose to be administered on regular scheduled day.
- Day of weekly injection can be changed as long as the time between 2 doses is at least 3 days (≥72hrs)

SEMAGLUTIDE▼ (RYBELSUS®) ORAL TABLET

- Start 3mg daily
- Increase dose to maintenance dose of 7mg once daily after 1 month. After at least 1 month with dose of 7mg once daily, dose can be increased to maintenance of 14mg daily to further improve glycaemic control
- Issue 1-3 months treatment
- To be taken on an empty stomach at any time of the day. Swallow whole with a sip of water (up to half a glass of water equivalent to 120ml). Tablets should not be split, crushed or chewed as it is not known whether this impacts absorption.
- Wait at least 30 minutes before eating or drinking or taking other oral medicinal products. Waiting less than 30 minutes decreases the absorption of semaglutide
- Taking two 7mg tablets to achieve the effect of a 14mg dose has not been studied and is not recommended
- Missed dose: skip the dose. The next dose should be taken the following day

Patient to contact initiating team if have side effects, and prior to any dose increase. If therapy stopped, refer back to T2DM glycaemic control pathway

1 month review

- **Tolerability and safety review:** Review renal profile (see box 1), side effects, injection sites & technique/administration of oral semaglutide, need for dose adjustment of anti-diabetic therapies, adherence with medication and lifestyle interventions
- **If continuing GLP-1 analogue:** Provide relevant patient education, issue prescription, arrange 3 month HbA1c check, follow up appointment and renal profile test (if not undertaken at one month). Continue to 3 month review box below.
- **If stopping therapy:** refer back to **T2DM glycaemic control pathway**

3 month review

- **Efficacy review:** Review weight and HbA1c reduction progress
- **Tolerability and safety review:** Review renal profile (see box 1) if not undertaken at one month, side effects, injection sites & technique/administration of oral semaglutide, need for dose adjustment of anti-diabetic therapies, adherence with medication and lifestyle interventions. Re-check thyroid function if patient is prescribed oral semaglutide and levothyroxine (see page 3)
- **If continuing GLP-1 analogue:** Provide relevant patient education, arrange for HbA1c & renal profile test at 6 months and book 6 month follow up. Continue to 6 month review box below and provide a 1 month prescription where required. Transfer prescribing to GP using "GLP-1 analogue information sheet" document
- **If stopping GLP-1 analogue:** refer back to **T2DM glycaemic control pathway**

6 month review

- **Efficacy review. Continuation criteria:** HbA1c ↓ >11mmol/mol (1%) or individual target HbA1c **AND** weight loss ≥3% of initial body weight
- **Tolerability and safety review:** Review renal profile (see box 1), side effects, injection sites & technique/administration of oral semaglutide, need for dose adjustment of anti-diabetic therapies, adherence with medication and lifestyle interventions
- **If continuing GLP-1 analogue:** If co-prescribed with oral antidiabetic medication, provide relevant patient education and arrange for discharge to GP. If co-prescribed insulin +/- oral antidiabetic medication, provide relevant patient education and ensure ongoing support from a consultant led multidisciplinary team dependent on local commissioning arrangements
- **If stopping GLP-1 analogue:** refer back to **T2DM glycaemic control pathway**

Box 1: renal function advice (to be read in conjunction with renal advice on page 4):

- If eGFR drop >10ml/min, review eGFR trend prior to initiation. Discuss with Doctor. Consider other causes, re-check profile within 4 weeks
- If eGFR drop 5-10ml/min, re-check at 6 months and if stable check and review at 12 months (may be via GP). If not stable, discuss with Doctor
- If eGFR drop <5ml/min, re-check at 6 & 12 months (may be via GP at 12 months). Discuss with Doctor if not stable

South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London: South East London Clinical Commissioning Group (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

South East London glucagon-like peptide (GLP-1) analogue pathway for adults aged 18 years and over with Type 2 Diabetes Mellitus (T2DM) during COVID-19

Contra-indications (CI) and cautions*

Contra-indications:

- Hypersensitivity to active substance or excipients

Not recommended:

- Acute pancreatitis
- In breast feeding and pregnancy or those considering pregnancy
- For treatment of diabetic ketoacidosis (DKA) or Type 1 diabetes
- Severe gastrointestinal (GI) disease e.g. gastroparesis

Cautions

- History of pancreatitis
- Risk factors for pancreatitis e.g. high alcohol intake, gall bladder or biliary disease, high triglycerides
- Limited/very limited experience in those aged ≥75 years
- Diabetic retinopathy: rapid improvement in glucose control (eg with insulin and GLP-1 analogues) has been associated with temporary worsening of diabetic retinopathy. Review recent retinopathy screening report prior to initiation and monitor closely for all patients.
- DKA has been reported in association with some GLP-1 analogues, particularly after discontinuation or reduction of concomitant insulin. If insulin dose is to be reduced, undertake in a stepwise manner with blood glucose self-monitoring. Discuss risk factors for and signs and symptoms of DKA and advise to seek immediate medical advice if these develop

	Not recommended in:	Caution in:	Other
LIRAGLUTIDE (VICTOZA®) INJECTION	• Heart failure NYHA IV • Patients with inflammatory bowel disease	• Thyroid disease	• Small gastric emptying delay may influence absorption of concomitantly administered oral medication however no dose adjustment needed as interaction studies did not show clinically relevant delays • Liraglutide should not be used during pregnancy or during breast-feeding
DULAGLUTIDE (TRULICITY®) INJECTION			• For those receiving oral medicinal products requiring rapid GI absorption or prolonged release formulations, the potential for altered drug exposure should be considered. • Dulaglutide should not be used during pregnancy and should not be used during breast-feeding
SEMAGLUTIDE ▼ (OZEMPIC®) INJECTION	• Heart failure NYHA IV	• Those with diabetic retinopathy (DR) treated with insulin: increased risk of developing DR complications. Monitor closely. Rapid improvement in glucose control has been associated with temporary worsening of DR, but other mechanisms cannot be excluded. • Those receiving oral medicinal products requiring rapid GI absorption	• Semaglutide should not be used during pregnancy. If a patient wishes to become pregnant, or pregnancy occurs, semaglutide should be discontinued. Semaglutide should be discontinued at least 2 months before a planned pregnancy due to the long half life • Semaglutide should not be used during breast-feeding
SEMAGLUTIDE ▼ (RYBELSUS) ORAL TABLET	• Heart failure NYHA IV • There is no therapeutic experience in patients with bariatric surgery	• Those with DR treated with insulin and injectable semaglutide (risk cannot be excluded for oral semaglutide): increased risk of developing DR complications. Monitor closely. Rapid improvement in glucose control has been associated with temporary worsening of DR, but other mechanisms cannot be excluded.	• Compliance with the dosing regimen is recommended for optimal effect. If treatment response lower than expected, be aware that the absorption of oral semaglutide is highly variable and may be minimal • Delays gastric emptying which may influence the absorption of other oral medicinal products • Total exposure of thyroxine was increased by 33% following a single dose of levothyroxine. Monitoring of thyroid parameters need to be considered when treating with semaglutide at the same time as levothyroxine. • Semaglutide should not be used during pregnancy. If a patient wishes to become pregnant, or pregnancy occurs, semaglutide should be discontinued. Semaglutide should be discontinued at least 2 months before a planned pregnancy due to the long half life • Oral semaglutide should not be used during breast-feeding

Other information: Patients **should not** be changed from an injectable GLP-1 analogue to oral semaglutide unless there is a valid clinical reason. Where this is the case, please refer to the Summary of Product Characteristics (SPC) at www.medicines.org.uk for more information on changing between preparations.

South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London: South East London Clinical Commissioning Group (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

Side effects*

1. **Hypoglycaemia:** consider dose reduction of concomitant medications to prevent hypos (in particular SU and insulin)
2. **Gastrointestinal effects**: nausea, vomiting, diarrhoea, abdominal pain listed as very common/common. Nausea likely at initiation and decreases over time. Caution with dehydration and renal function decline – advise on potential for dehydration and take precautions to avoid fluid depletion
3. **Reduced appetite**
4. **Diabetic retinopathy complications** :rapid improvement in glucose control (eg with insulin and GLP-1 analogues) has been associated with temporary worsening of diabetic retinopathy. Advise patients to immediately report any symptoms of worsening retinopathy e.g worsening vision (gradual or sudden), sudden vision loss, shapes floating in the field of vision (floaters), blurred or patchy vision, or eye pain.
5. **Pancreatitis:** counsel on characteristic symptoms and action to take- persistent, severe abdominal pain (sometimes radiating to the back). Patient to discontinue treatment and contact healthcare professional immediately
6. **Possible changes to international normalised ratio (INR) in patients on warfarin or coumarin derivatives**. More frequent monitoring recommended e.g. at initiation, dose change and cessation of liraglutide and semaglutide
7. **Renal function decline:** monitor as stated overleaf or more frequently if clinically indicated
8. **Rapid weight loss:** monitor patients for signs and symptoms of cholelithiasis
9. **Injection site reaction**: assess technique and ensure site rotation
10. **Headache 11. Increase in heart rate and tachycardia 12. Hypersensitivity**
13. **Small reduction in blood pressure 14.Cholelithiasis**

Note: For established medicines, report all serious suspected adverse drug reactions (ADRs) even if effect is well recognised. For black triangle drugs (▼), report all suspected ADRs. Report to https://yellowcard.mhra.gov.uk/

Hepatic and renal impairment*

	Hepatic impairment	Renal impairment
LIRAGLUTIDE (VICTOZA®) INJECTION	• No dose adjustment recommended in mild or moderate hepatic impairment. • Not recommended in severe hepatic impairment	• No dose adjustment in mild, moderate or severe renal impairment • Not recommended for end stage renal disease (<15ml/min)
DULAGLUTIDE (TRULICITY®) INJECTION	• No dose adjustment required in hepatic impairment	• No dose adjustment in mild, moderate or severe renal impairment • Not recommended for end stage renal disease (<15ml/min)
SEMAGLUTIDE▼ (OZEMPIC®) INJECTION	• No dose adjustment required in hepatic impairment. Experience in severe hepatic impairment is limited – exercise caution if used	• No dose adjustment in mild, moderate or severe renal impairment. Experience in severe renal impairment is limited • Not recommended for end stage renal disease (<15ml/min)
SEMAGLUTIDE▼ (RYBELSUS) ORAL TABLET	• No dose adjustment required in hepatic impairment. Experience in severe hepatic impairment is limited – exercise caution if used	• No dose adjustment in mild, moderate or severe renal impairment. Experience in severe renal impairment is limited • Not recommended for end stage renal disease (<15ml/min)

***Please note:** information is not exhaustive, please see Summary of Product Characteristics (SPC) at www.medicines.org.uk for more information including details of interaction with other medicinal products.