South East London Type 2 Diabetes Mellitus (T2DM) Glycaemic Control Management Pathway for Adults

This guidance was developed by the SEL Diabetes Medicines Working Group on behalf of the SEL IMOC

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South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London Integrated Care System: NHS South East London (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 Type 2 Diabetes Mellitus (T2DM) Glycaemic Control Management: Overview

At all appointments, reinforce person centered diet and lifestyle advice, check medication adherence and develop a collaborative care plan with the person who has diabetes

STEP ONE

THINK INSULIN if BMI <22 or symptomatically hyperglycaemic – see immediate treatment box (page 3)
Agree individualised HbA1c target – refer to page 3
Refer to structured education programme and offer lifestyle and diet advice. If HbA1c ≥ 48 mmol/mol move to step two

Assess HbA1c, cardiovascular risk and kidney function

STEP TWO
Please see prescribing information on page 3 & 4 for further information on appropriate choice of medication

Not at high CVD risk (QRISK2 <10%)

Offer:
Metformin

If gastro-intestinal (GI) disturbance, offer:
Metformin MR

If metformin contraindicated (C/I)

Consider:
DPP-4 inhibitor (gliptin) or Pioglitazone or Sulfonylurea (SU)

A SGLT2 inhibitor for some people***: Canagliflozin or dapagliflozin or empagliflozin in line with NICE TA390 or ertugliflozin in line with NICE TA572:
Can be used as monotherapy when metformin not tolerated or C/I when diet and exercise do not provide adequate glycaemic control only if DPP4i would otherwise be prescribed and SU or pioglitazone is not appropriate. **Review DKA risk before starting: see page 3**

Consider patient factors when agreeing choice of therapy. See page 3 for more information

High risk of CVD (QRISK2 ≥10%)

Offer:
Metformin

If GI disturbance, offer
Metformin MR

And as soon as metformin tolerability is confirmed**, **consider**

SGLT2 inhibitor with proven cardiovascular (CV) benefit***
Review DKA risk before starting: see page 3

If metformin contraindicated (C/I)

Consider:
SGLT2 inhibitor alone***

Chronic heart failure or established atherosclerotic CVD*

Offer:
Metformin

If GI disturbance, offer
Metformin MR

And as soon as metformin tolerability is confirmed**, **offer:**

SGLT2 inhibitor with proven cardiovascular (CV) benefit***
Review DKA risk before starting: see page 3

If metformin contraindicated (C/I)

Offer:
SGLT2 inhibitor alone***

Recheck HbA1c after 3 months. If the person's HbA1c is not below the individually agreed target, or the person develops CVD or a high risk of CVD, move to STEP 3 (see page 2)

*Established atherosclerotic CVD includes coronary heart disease, acute coronary syndrome, previous myocardial infarction, stable angina, prior coronary or other revascularisation, cerebrovascular disease (ischaemic stroke and transient ischaemic attack) and peripheral arterial disease. ** Start metformin alone to assess tolerability before adding SGLT2 inhibitor. ***At the time of publication, the SGLT2 inhibitors with proven cardiovascular benefit are canagliflozin, dapagliflozin and empagliflozin. DPP-4 inhibitor = dipeptidyl peptidase 4 inhibitor, SGLT2i – sodium glucose co-transporter 2 inhibitor

South East London Type 2 Diabetes Mellitus (T2DM) Glycaemic Control Management: Overview

At all appointments, reinforce person centered diet and lifestyle advice, check medication adherence and develop a collaborative care plan with the person who has diabetes

STEP THREE & FOUR
Please see prescribing information on page 3 & 4 for further information on appropriate choice of medication

If the person's HbA1c is not below the individually agreed target despite steps 1 and 2 above, or the person develops CVD or a high risk of CVD, please follow steps below

At any point if HbA1c is not below the individually agreed target

Switching or adding treatments. Consider:

DPP-4 inhibitor (gliptin) or Pioglitazone or Sulfonylurea

or SGLT2 inhibitors may also be an option (see below): Review DKA risk before starting: see page 3

SGLT-2i in dual therapy: Canagliflozin or dapagliflozin or empagliflozin or ertugliflozin with metformin if SU C/I or not tolerated or person is at significant risk of hypoglycaemia or its consequences

SGLT-2i in triple therapy:
Canagliflozin or empagliflozin with metformin and SU, or metformin and pioglitazone
Dapagliflozin with metformin and SU
Ertugliflozin with metformin and DPP-4i only when diet and exercise do not provide adequate glycaemic control only if the disease is uncontrolled on metformin and DPP-4i and a SU and pioglitazone is not appropriate

SGLT-2i with insulin: Canagliflozin or dapagliflozin or empagliflozin in combination with insulin with or without other antidiabetic drugs

Consider patient factors when agreeing choice of therapy. See page 3 for more information

Recheck HbA1c after 3 months. If the person's HbA1c is not below the individually agreed target, switch or add treatments from different drug classes up to triple therapy (dual if metformin C/I)

At any point if cardiovascular risk or status changes

If person has or develops high risk of CVD (QRISK2 ≥10%)

Switching or adding treatments **Consider:**

SGLT2 inhibitor with proven CV benefit*** Review DKA risk before starting: see page 3

If person has or develops chronic heart failure or established atherosclerotic CVD*

Switching or adding treatments **Offer:**

SGLT2 inhibitor with proven CV benefit*** Review DKA risk before starting: see page 3

When to consider insulin

- When dual or triple therapy has not controlled HbA1c to below person's individual target, also consider insulin-based therapy (+/- other drugs).
- If HbA1c is >11mmol/mol above individualised target, initiation of insulin is preferred.
- Patient preference
- BMI < 22kg/m^2 or person symptomatically hyperglycaemic, or clinical need arises - see immediate treatment box (page 3)
- When contra-indications or cautions to other therapies limit options

Insulin should only be initiated by accredited health professionals e.g. community diabetes team or specialist healthcare professional. Please follow local guidance on insulin initiation. In line with NICE, human isophane (NPH) insulin is recommended first line basal insulin in T2DM for most people

When to consider GLP-1 analogues

If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or C/I, consider triple therapy by switching one drug for a GLP-1 analogue in those whom:

- have BMI of ≥35 kg/m^2 (adjust accordingly for people from Black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity

or

- have BMI <35 kg/m^2 and: – for whom insulin therapy would have significant occupational implications or – weight loss would benefit other significant obesity related comorbidities.

See page 3 for link to SEL GLP-1 analogue pathway

When to review

Measure HbA1c:

- **Every 3-6 months until HbA1c is stable on unchanging therapy**
- **6 monthly once HbA1c and therapy stable**

As a minimum diabetes reviews need to be undertaken annually

South East London: Type 2 Diabetes Mellitus (T2DM) Glycaemic Control Management: Prescribing information and overview notes

Immediate treatment

If BMI < 22kg/m^2 or person symptomatically hyperglycaemic, seek advice from diabetes team as early insulin initiation or sulfonylurea therapy may be required. See early/urgent insulin initiation guideline. Insulin should be initiated by an accredited health professional e.g. community diabetes team, specialist healthcare professional trained in insulin initiation.

NB: Insulin may be initiated at any step based on clinical need

Treatment targets

- Discuss and agree individualised HbA1c targets. Encourage people to reach & maintain target levels unless it results in any adverse effects (including hypoglycaemia), or where achieving HbA1c target impairs quality of life. Consider other reasons for low HbA1c e.g. deteriorating renal function or sudden weight loss.
- Where T2DM is managed either by lifestyle and diet +/- a single drug not associated with hypoglycaemia, support people to aim for HbA1c of 48 mmol/mol (6.5%). If taking a drug associated with hypoglycaemia, support people to aim for HbA1c of 53 mmol/mol (7.0%).
- Consider relaxing target HbA1c on a case by case basis, with particular consideration for people who are older or frailer, if: (i) they are unlikely to achieve long term risk reduction benefits e.g. people with reduced life expectancy (ii) tight BG control would put them at risk if hypoglycaemia developed e.g. risk of falling, have impaired hypoglycaemia awareness or if they drive or operate machinery as part of their job (iii) intensive management would not be appropriate e.g. if they have significant co-morbidities. Consider using the NICE patient decision aid to support discussions on agreeing target HbA1c levels
- For guidance on HbA1c targets for women with type 2 diabetes who are planning a pregnancy or are pregnant, refer to NICE guideline on diabetes in pregnancy.

Self-monitoring of blood glucose (SMBG)

Please refer to SEL Guide SMBG in Adults and Young People Self-monitoring of Blood Glucose - selondonccg.nhs.uk

Metformin (biguanide)

Metformin reduces CV events in overweight and obesity to a greater extent than predicted by its glucose lowering effects.

- **Standard release:** usual dose is 2g -2.5g daily (max. dose 3g daily in 3 divided doses can be used in exceptional circumstances). Start at a dose of 500mg daily. Increase by 500mg every 2 weeks to reach a dose of 1g twice daily
- **Modified release (M/R)**: Initially 500mg once daily, increased every 10-15 days, max. 2g once daily with evening meal. If control not achieved use 1g twice daily with meals. If changing from standard release to M/R, people taking less than 2g daily of standard release can start on same daily dose of M/R
- **Kidneys:** Review metformin dose if eGFR <45ml/min (also review at 60ml/min if on >2g daily). Caution in those at risk of sudden deterioration in kidney function and those at risk of eGFR falling below 45ml/min. Stop/avoid metformin if eGFR <30mL/min. Please note: different dose recommendations exist in renal impairment dependent on dose preparation. See www.medicines.org.uk for further information. **Advise on sick day rules**
- If suspicion of vitamin B12 deficiency, monitor vitamin B12 serum levels

SGLT2 inhibitors

Please see South East London Guidance on Prescribing Sodium Glucose Co-transporter 2 inhibitors (SGLT-2i) in people with T2DM for Glycaemic Control for prescribing advice and advice on assessing and addressing modifiable risk factors for diabetic ketoacidosis (DKA)

DPP-4 inhibitors (DPP-4i) : 1st line sitagliptin, linagliptin in severe renal impairment

- Increased risk of pancreatitis: Dipeptidylpeptidase-4 inhibitors: risk of acute pancreatitis
- Patients on dual/triple therapy of DPP-4i with an SU or dual therapy with insulin may be at risk of dose related hypoglycaemia. Dose reduction of SU or insulin may be needed
- **Sitagliptin in kidneys:** reduce dose to 50mg daily if eGFR 30-44ml/min, reduce dose to 25mg daily if eGFR 15-29ml/min. See medicines.org.uk for advice on other DPP-4i and renal impairment
- Alogliptin and Saxagliptin are not on formulary. Initiation should weigh risk of heart failure.

Pioglitazone

- Safety & efficacy should be reviewed every 3-6 months in continued therapy.
- Contraindicated in people with heart failure/history of heart failure, uninvestigated macroscopic haematuria, DKA, hepatic impairment or current/history of bladder cancer
- Caution in: risk factors for heart failure or for those at increased risk of bone fractures, risk factors for bladder cancer, concomitant use with insulin, elderly.
- Patients on dual/triple therapy of pioglitazone with an SU or dual therapy with insulin may be at risk of dose related hypoglycaemia. Dose reduction of SU or insulin may be needed.

Sulfonylurea: Gliclazide is preferred SU in SEL

- Recommended patients taking an SU, self-monitor their blood glucose levels in line with SEL SMBG guidance and DVLA regulations – check DVLA website for up to date information.
- Caution in use of elderly, housebound, frail and in certain occupations e.g. operating heavy machinery.
- Provide education about risks of hypoglycaemia with SUs, particularly if renally impaired.
- **Kidneys**: gliclazide: use in caution for mild to moderate renal impairment (eGFR 30-60mL/min) due to increased risk of hypoglycaemia. AVOID in severe renal impairment (eGFR <30mL/min).
- **Liver**: AVOID in severe hepatic impairment due to increased risk of hypoglycaemia.

GLP-1 analogues: dulaglutide, liraglutide and semaglutide are preferred in SEL

Please see South East London GLP-1 analogue pathway for more information and advice

For all people with T2DM, advise on sick day rules as part of consultation

See NICE Type 2 diabetes in adults: choosing medicines for further information on choosing between therapies and www.medicines.org.uk for further information on safe medicines use

South East London: Type 2 Diabetes Mellitus (T2DM) Glycaemic Control Management: Prescribing information and overview notes

Summary of medications for first line and further treatment

Drug Group	Weight Effects	Hypoglycaemia Risk	Renal Impairment	Hepatic Impairment
Metformin	None	Low ^	Dose reduction or avoid. Check BNF monographs/SPCs for eGFR thresholds	Withdraw if tissue hypoxia likely
SGLT2 inhibitors ('flozins')	Loss	Low ^	Dose reduction or caution or avoid. Check BNF monographs/SPCs for eGFR thresholds	Caution or avoid. Check BNF monographs/SPCs for severity
DPP-4 inhibitors ('gliptins')	None	Low ^	Dose reduction or caution (not for linagliptin) Check BNF monographs/SPCs for eGFR thresholds	Dose reduction or caution or avoid (not for linagliptin or sitagliptin). Check BNF monographs/SPCs for severity
Pioglitazone	Gain	Low ^	No warnings	Avoid
Sulfonylurea	Gain	Moderate ^ Higher risk in older and frail individuals	Dose reduction or caution or avoid. Check BNF monographs/SPCs for eGFR thresholds	Caution or avoid. Check BNF monographs/SPCs for severity

^ Hypoglycaemia risk may increase if used with insulin and/or sulfonylurea therapy. Consider reducing dose of sulfonylurea or insulin if clinically indicated

For further detailed information on individual drugs, please check: Summaries of Product Characteristics (SmPCs) and BNF

Choosing Medication: Considerations for when choosing, reviewing, and changing treatments

Diet & Lifestyle Advice	Choosing Treatments: Base choice on:	Reviewing and Changing Treatment: Consider & Discuss with individual:
At each point of contact with the individual, always reinforce advice about diet, lifestyle and patient education	The individual's clinical circumstances e.g. co-morbidities, contraindications, weight and polypharmacy risk	Stopping medication that is not having desired impact on glycaemic control or weight, unless it has additional benefits e.g. CV or renal benefits
	Individual's preference and needs	Stop medication that is not tolerated
	The effectiveness of the drug treatments in terms of: - Metabolic response - Cardiovascular protection - Renal protection	How to optimise current treatment regimen before changing treatment. Taking into account factors such as: - Adverse effects - Adherence to current treatments - Diet and lifestyle reinforcement - Prescribed doses and formulations
	Safety, tolerability of individual drugs	Whether switching a treatment could be effecting instead of adding a treatment
	Monitoring requirements, including SMBG needs	
	Licensed indications or combinations available	
	SEL formulary preferences and costs	

Adapted from NG28: choosing medicines for first-line and further treatment

References:

1. NICE clinical guideline 28 – type 2 diabetes, (Last accessed 28.04.22),
2. SmPCs for all agents, available via www.medicines.org.uk (last accessed 28.4.22),
3. Drug Safety Updates: SLGT2 inhibitors: updated advice on risks of DKA Drug Safety Update SGLT2i(Last accessed 08.03.2022),
4. Drug Safety Updates: SLGT2 inhibitors: updated advice on increased risk of lower limb amputations (Last accessed 08.03.2022),
5. Drug Safety Updates: SGLT2i: Reports of Fournier's gangrene (last accessed 08.03.2022)