NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Diabetes, management of Type 2 Diabetes Mellitus

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

Version Number:	3
Does this version include changes to clinical advice:	Yes
Date Approved:	13th November 2024
Date of Next Review:	30th June 2027
Lead Author:	Deborah Morrison
Approval Group:	Medicines Utilisation Subcommittee of ADTC

Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Type 2 Diabetes Mellitus Management

Table of Contents

1 Introduction

This updated guideline is written to incorporate the 2022 Consensus report from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) [1] into the previous NHS GGC guidelines last updated in 2019. This consensus statement incorporates the evidence from the preceding 5 years, and takes a more holistic approach, including increased emphasis on the social determinants of health. This statement is a natural progression from the most recent SIGN update (154) [2] with increasing emphasis on use of SGLT-2 inhibitors (SGLT-2i), including for non-diabetes indications, and GLP-1 Receptor Agonists (GLP-1RA) becoming the preferred third line option. It also reflect the recent Scottish Quality Prescribing in Type 2 Diabetes Guide:

https://www.gov.scot/publications/quality-prescribing-strategy-type-2-diabetes-mellitus-guide-improvement-2024-2027/documents/

Finally, it includes information about tirzepatide which has recently (April 2024) received SMC approval.

There is an increasing emphasis on aiming for remission particularly in those newly diagnosed. SIGN guidelines for the prevention of type 2 diabetes are currently in development and should be available in 2024. These will provide guidance for those individuals who are high risk for developing diabetes but not yet fulfilling diagnostic criteria.

It is established that the majority of individuals with type 2 diabetes are best managed in primary care. Reconfiguration of secondary care services to allow for easy access to timely specialist support when required supports this model. Those individuals where their diabetes care is optimised are monitored in primary care, freeing up secondary capacity to promptly review those who need additional input.

Appendix 1 & 2 provides a very basic summary of the key prescribing advice, and should be used in the context of this wider document.

2 Diagnosis & Initial management of Type 2 Diabetes

2.1 Initial patient discussion

- Explain diagnosis – direct to appropriate literature/support (Diabetes UK, My Diabetes My way) and to the NHS GGC Type 2 Diabetes Online Hub (https://www.nhsggc.scot/your-health/type-2-diabetes-hub/)
- Ensure weight is documented in clinical notes (to allow automatic referral to the Type 2 hub)
- Encourage to take up offer of Structured Education (currently Control It Plus) and advise they will be automatically referred to Glasgow & Clyde Weight Management Service (GCWMS).
- As per SIGN Guidelines, consider setting HbA1c target of <48 initially *without* medical therapy.
- Discuss possibility of diabetes remission.

2.2 Diagnostic uncertainty

- Consideration of the individual phenotype, rather than age, is increasingly important as an increasing number of young people are developing T2D.
- Typical phenotype of individual with T2D:
    - Overweight (or increasing weight trajectory) or central obesity
    - Other features of metabolic dysfunction (dyslipidaemia, hypertension, polycystic ovary disease, history of gestational diabetes)
    - Preceding history of impaired fasting glucose or gestational diabetes
    - Family history of T2D (present in 30% of those newly diagnoses). Typically this is across wider family on one or both sides
    - South Asian ethnicity confers increased risk – likely to develop Type 2 diabetes with a lower BMI, and younger age

- Features less in keeping with Type 2 diabetes at presentation, or in initial management
    - 'Normal' BMI (taking into account different BMI targets for ethnicity)
    - Rapid weight loss
    - Evidence of ketosis (blood ketones ≥ 0.6mmol/l or urine 2+ or higher)
    - Family history of autoimmune conditions
    - Younger age and no family history of type 2 diabetes
    - Significant alcohol excess/history of pancreatitis
    - Poor response to T2D medications with worsening HbA1c, *at any age*, particularly in context of weight loss may indicate slow evolving Type 1 Diabetes
    - Strong vertical transmission where age of diagnosis is <40 years in more than 2 generations may indicate monogenic inheritance (MODY) and referral to secondary care would be appropriate.
    - Certain medical conditions e.g. haemochromatosis, history of transplant.

If patient is not typical of type 2 diabetes, such as with the features above, consider seeking second opinion e.g. SCI Gateway referral to secondary care/discussion at a community Diabetes MDT.

If Type 1 diabetes is strongly suspected, regardless of age, check for ketones and for same day discussion with diabetes specialists/medical receiving. Type 1 diabetes should not be referred via SCI Gateway, unless already discussed with a clinician.

2.3 Lifestyle/weight management & Remission

People with Type 2 diabetes should be encouraged to achieve and maintain a healthy BMI, as this will help manage the condition and decrease the potential need for escalating medical therapy. General lifestyle advice around diet, stopping smoking and being less sedentary is important. For all people newly or recently diagnosed with type 2 diabetes, remission should be considered the primary aim of any initial intervention. Results from the well-publicised DiRECT study have shown significant remission rates (HbA1c <48mmol/mol) for overweight patients with type 2 diabetes within 6 years of diagnosis if significant weight loss achieved (86% of people who lost more than 15kg on the programme were in remission after a year, as were 57 per cent of people who lost 10–15kg, and 34 per cent who lost 5–10kg) [3]. Five year follow up shows that of those in remission at year 2, 26% remained in remission at 5 years and serious adverse events were nearly half the rate in the intervention group compared to the original control group [4].

Diabetes UK, the American Diabetes Association, and the European Association for the Study of Diabetes consensus definition of remission is "an HbA1c less than 48mmol/mol, in the absence of glucose lowering therapy, for a period of at least 3 months" [5].

2.4 Type 2 Diabetes Online Hub

The Type 2 Diabetes Online Hub is a new online resource in NHS GGC and more information is available here: https://www.nhsggc.scot/your-health/type-2-diabetes-hub/. Automatic referral for those newly diagnosed (once coded as Type 2 Diabetes) will happen as follows:

1. All patients newly diagnosed with T2D (irrespective of BMI) will be offered the Control It Plus structured education programme delivered by Health Care Professionals (HCPs).

2. All patients newly diagnosed with T2D AND have a BMI≥25 will be automatically invited to opt in the Glasgow and Clyde Weight Management Service (GCWMS). An up to date weight (within 12 months) and a height is required. If this information is not available then automatic referral will not happen.

Initial findings suggest Control It Plus programme is well received by those who attend. *The initial conversation with their health care professional at the time of diagnosis seems key in the person's decision to opt in.* The majority of people will access Control It Plus online but pilots of face to face deliver are ongoing for those without the means to attend virtually.

Where it is not appropriate for the patient to be automatically referred to the Type 2 diabetes hub please alert the hub to this by emailing (ggc.type2diabeteshub@ggc.scot.nhs.uk) or phoning 0141 531 8901 (Opening Hours: Monday – Friday, 08:30-16:30). Examples might be the patients BMI is ≥25 due to ascites, or presence of a terminal illness.

These are the same contact details that patients can use to self-refer, even if they have previously declined an offer. Patients who have been diagnosed with T2D in the past can still be referred or self-refer for Control It Plus and/or GCWMS on the above details.

Triage destination for patients with Type 2 Diabetes within GCWMS:

Community Weight Management Service (currently Weight Watchers/Slimming World)		Specialist Weight Management Service	
T2DM	BMI ≥25 (22.5*) *(patients who meets surgical criteria will be triaged to specialist service)*	T2DM	BMI≥45
T1DM	BMI ≥30 (27.5*)	T1DM	BMI≥45
Impaired fasting glucose/ impaired glucose tolerance/	BMI ≥25 (22.5*)	Potential bariatric surgery patient (as per criteria)	BMI≥35

* ethnicity at higher risk of diabetes

2.5 Specialist Weight Management Services

Access to lifestyle and specialist weight management services including bariatric surgery is available for eligible patients. Individuals can self refer (0141 211 3379), or HCPs can refer via SCI Gateway (primary care) or Trakcare (secondary care)

2.5.1 Consideration for Bariatric Surgery

Patients referred to GCWMS will be seen in specialist services if the fit these criteria:

- ✓ Type 2 Diabetes diagnosed within last ≤10yrs AND
- ✓ aged ≤ 55 years AND
- ✓ BMI ≥35 AND ≤ 60kg/m^2

If a GP or Consultant wishes a patient who is outside the current surgery criteria to be considered as an exceptional case for surgery, they can ask for the case to be considered at the Bariatric Exceptional Referrals panel. A full outline of the case should be submitted in writing to below (correct as of April 2023):

Alexandra Frew, Clinical Service Manager, General Surgery - North Sector, 4th Floor Walton Building, Glasgow Royal Infirmary. Email: Alexandra.Frew@ggc.scot.nhs.uk

3 Targets and intensification of therapy

3.1 HbA1c Targets

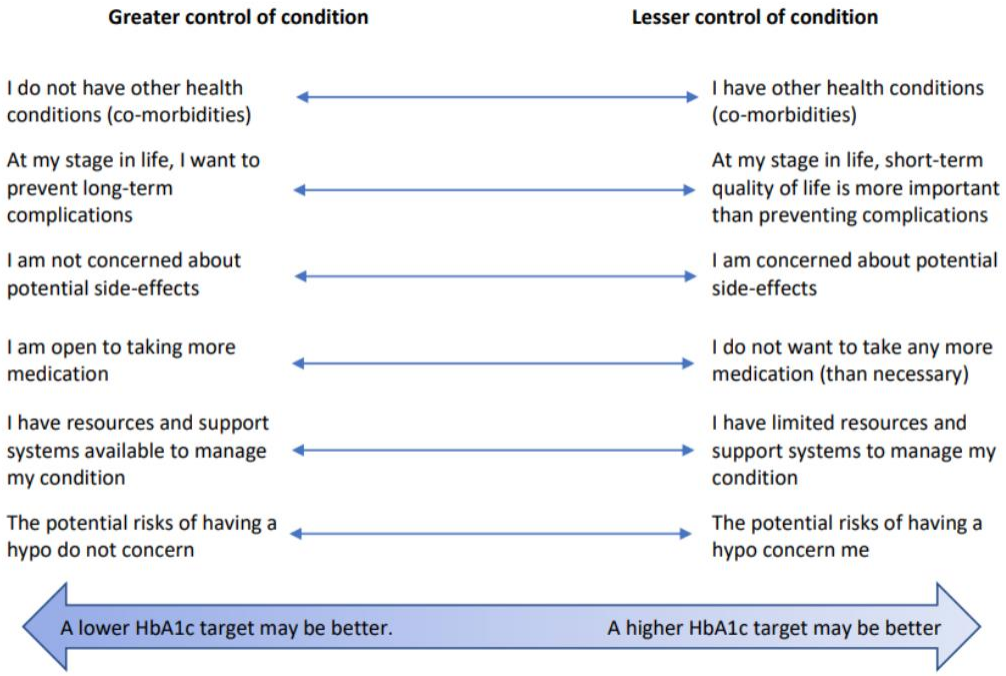
HbA1c targets should be individualised, and when not reaching target should prompt review and escalation of treatment. SIGN 154 [2]:

> *"An HbA1c target of 7.0% (53 mmol/mol) among people with type 2 diabetes is reasonable to reduce the risk of microvascular and macrovascular disease. A target of 6.5% (48 mmol/mol) may be appropriate at diagnosis. Targets should be set with individuals in order to balance benefits with harms, in particular hypoglycaemia and weight gain."*

Good glycaemic control in the initial years after diagnosis likely provide a legacy effect in terms of reductions in CV morbidity and mortality [6]. There is less evidence for tight glycaemic control in older age groups and possibility of harm, particularly from hypoglycaemia. Suggested targets available from Scottish Quality Prescribing for Type 2 Diabetes Mellitus guidance (see Table page 6). Further information is available in a recent review of Type 2 Diabetes in older adults [7].

3.2 Individualisation of treatment aims

Decision aid shows characteristics and considerations that individuals and clinicians can consider when determining individual glycaemic control targets. Figure below and table overleaf adapted from Quality Prescribing for Type 2 Diabetes Mellitus: A Guide for Improvement 2022-2025 itself adapted from ADA/NICE, and supported by SIGN 154.



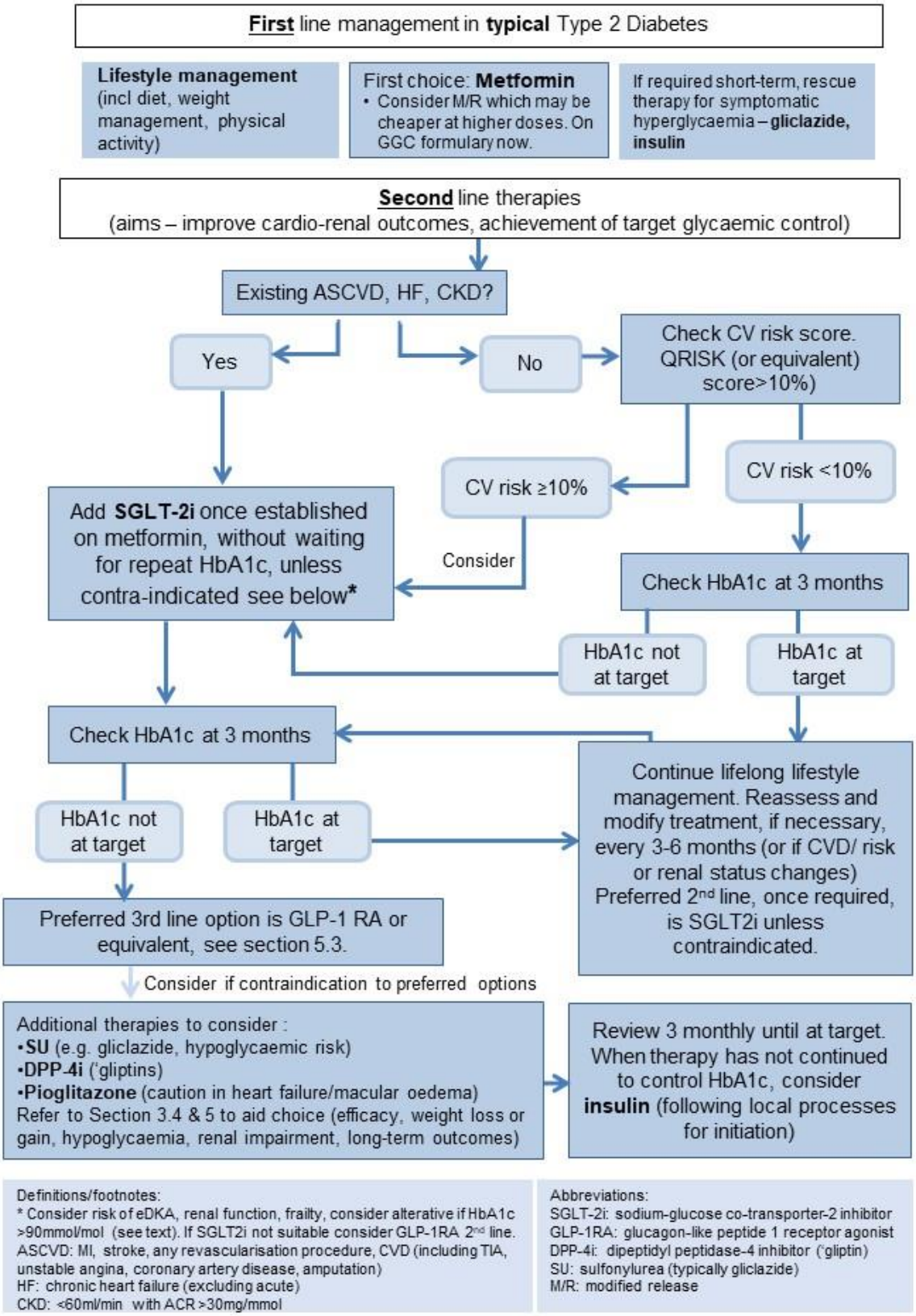
Management of T2DM in frailty. Adapted from *Strain et al.Type 2 diabetes mellitus in older people: a brief statement of key principles of modern day management including the assessment of frailty….* https://doi.org/10.1111/dme.13644

	Treatment target		De-escalation threshold	
	Levels	Therapy considerations	Levels	Suggested interventions
Mild frailty (CFS scale 4-5) The older fit adult	58 mmol/mol (7.5%)	• Caution initiating new agents that may cause hypoglycaemia (e.g., SU) • Caution initiating agents that may exaggerate weight loss **if** undesirable (e.g., GLP-1RA) • Consider co-morbidities, e.g., ASCVD, HF, CKD.	<53 mmol/mol (7.0%)	If HbA1c below threshold: • Discontinue or reduce sulfonylurea • Review insulin therapy that may cause hypoglycaemia.
Moderate frailty (CFS scale 6)	64 mmol/mol (8.0%)	• SGLT-2i* have positive long-term outcomes in people with ASCVD, HF, CKD • Pioglitazone may increase risk of heart failure (avoid). • DPP-4i and longer-acting insulins have demonstrated safety	<58 mmol/mol (7.5%)	If HbA1c below threshold: • Discontinue or reduce sulfonylurea • Review insulin therapy that may cause hypoglycaemia. Avoid pioglitazone (risk of heart failure).
Severe to very severe frailty (CFS scale 7-8)	70 mmol/mol (8.5%)	As moderate frailty plus: • Although additional long-term benefits for SGLT-2i* and GLP-1RA, consider if long-term benefits will be realised. • Consider once-daily morning NPH insulin or analogue alternatives if symptomatic nocturnal hyperglycaemia. • Educate carers and relatives regarding risk of hypoglycaemia	<64 mmol/mol (8.0%)	As moderate frailty plus • Insulins consider: - withdraw short-acting insulins because of risk of hypoglycaemia. - review timings and suitability of NPH insulin with regard to risk of hypoglycaemia. • Avoid therapies that promote weight loss & may exacerbate sarcopenia, e.g., SGLT-2i, GLP-1RA

* For all patients: Consider appropriate dosage dependent on renal function. When medications are stopped or reduced it is important to recheck HbA1c in 3 months time.

3.3 Initial Pharmacological Management of Type 2 Diabetes

Based on NICE NG128, ADA/EASD, SIGN. For patients with a phenotype consistent with Type 2 diabetes.
Adapted from Quality Prescribing for Type 2 Diabetes Mellitus: A Guide for Improvement 2022-2025



Choice of medications should be guided by local prescribing formulary.

3.4 Other scenarios (or 4th line if already on metformin/ SGLT-2i/ GLP-1 RA):

The combination of metformin, SGLT-2i and GLP-1RA (including GLP-1/GIP agonists) is very effective at improving diabetes control. If a 4th line agent is required then gliclazide or pioglitazone could be considered unless there are clear indications for insulin. Advice can be sought on 4th line choices, or whether insulin is required, via community MDT or via SCI Gateway.

Scenario	Medication considerations
Low or normal weight, or losing weight in the context of a rising HbA1c. Possible history of pancreatic insult.	Review compliance with medications already prescribed. Consider gliclazide. This may be a trial to see if blood glucose improves. **No** improvement on gliclazide suggests **insulin** may be required. Seek specialist advice.
Steroid induced hyperglycaemia	Gliclazide is often preferred as can be titrated to blood glucose and steroid dose, with escalation to insulin if gliclazide not suffice. Insulin may be appropriate first line in palliative setting (See Diabetes UK Guideline https://www.diabetes.org.uk/professionals/position-statements-reports/diagnosis-ongoing-management-monitoring/end-of-life-care). Seek guidance as required.
Unable to tolerate or access preferred GLP-1RA, or lack of efficacy of GLP-1RA.	Consider use of dual receptor agonist e.g. tirzepatide instead of GLP-1RA.
Unable to tolerate GLP-1RA or dual agonists and concerns around use of medications that may require blood monitoring/have hypo risk	Consider pioglitazone. See Section 5.6 Drug Classes information and BNF. Consider SCI GW for advice or community MDT discussion re suitability.
Frail, elderly , or not suitable for a GLP-1RA	Review HbA1c target table to consider if need to escalate therapy. If so consider DPP-4i e.g. sitaglipin or linagliptin if CKD.
Chronic Kidney Disease (CKD)	If eGFR <45ml/min adjustments may need to be made. See BNF and CKD section 4 links below.
High suspicion of Type 1 Diabetes	This guideline does not apply and these patients should be discussed urgently with your local team.

Please refer via SCI gateway or via MDT for advice if unclear on next steps. Please see next section for more detailed information on individual medications

4 Diabetes and Chronic Kidney Disease (CKD)

Please see updated guidelines available on clinical guidelines platform Renal section for management and referral criteria: https://rightdecisions.scot.nhs.uk/ggc-clinical-guidelines/renal-medicine/ .

GP Notebook has an excellent table that summarises renal considerations for the main diabetes medications available at https://gpnotebook.com/simplepage.cfm?ID=x201810177124437326

Appendix 2 has a prescribing guide for SGLT-2i which includes in patients with CKD.

5 Drug Classes

5.1 Metformin

Metformin should be considered first line treatment for people with type 2 diabetes.

Titrated from 500mg once a day gradually aiming for optimum dose of 1g twice daily. Metformin is much better tolerated when taken with meals e.g. with breakfast and with evening meal. Generally accepted patients will continue with metformin unless not tolerated or contraindicated due to prognostic benefit. Long acting metformin (M/R) is now on the formulary and can be used, and may be less costly at the 1g M/R tablets.

5.2 SGLT-2 inhibitors (SGLT-2i, 'flozins)

SGLT-2i with proven CV benefit preferred, and guided by local formulary. Where metformin is not tolerated or contraindicated, they are appropriate 1st line. Where metformin has been tolerated and in:

- Individuals with no CV comorbidities and no evidence of CKD:
    - SGLT-2i are second line therapy and should be added in if HbA1c is not to target 3 months after initiation of metformin
- Individuals with CV comorbidities and/or evidence of CKD:
    - SGLT-2i should be added in as soon as tolerability of metformin has been established.

Caution in frail/elderly patients due to potential risk of postural hypotension and/or dehydration.

****SGLT-2i SAFETY****

1) Ensure awareness of association with euglycaemic diabetic ketoacidosis (eDKA) and need to withhold SGLT-2i during inter-current illness. Written information for patient can be found here, and patient specific medications be added before sharing with the patient:

https://rightdecisions.scot.nhs.uk/polypharmacy-guidance/medicines-sick-day-guidance/

2) SGLT-2i should be withheld for at least 1 day before elective surgery sometimes more. Follow local guidance/advice provided by surgical teams.

Reduced effect on glycaemic control in presence of CKD. Consider other agents to improve glycaemic control if eGFR <45ml/min. See Appendix 2 for choice of SGLT-2i.

Cautions for prescribing in following scenarios:

- Elderly at risk of volume depletion
- Predisposing features to DKA/eDKA
    - Pancreatic insufficiency
    - Drug or alcohol abuse
    - Low/ultra-low carb or keto diets
    - Excessive alcohol intake.
- Frequent bacterial urine infection or genitourinary yeast infections
- Foot ulceration – suggest request advice from specialist services there may be an overall benefit in using e.g if oedema is complicating healing.

SGLT-2i may still be appropriate to prescribe and seek specialist input if required.

5.3 GLP-1 receptor agonists (GLP-1RA) including dual agents e.g tirzepatide

GLP-1RA therapy should be considered as a 3rd agent when available. This class of medications is:

- Safe and generally well tolerated
- Most frequent side-effects are GI upset and often settle within 2-3 weeks of initiation.
- Very few contraindications to use. See 'Initiation of GLP-1RA in Primary Care Guideline' available on the NHS GGC Guidelines platform https://rightdecisions.scot.nhs.uk/ggc-clinical-guideline-platform/endocrine/community-management/
- In individuals with type 2 diabetes and established CVD, GLP-1RA with proven CV benefit (currently liraglutide [8] dulaglutide [9] or subcutaneous semaglutide [10]) are preferred. Injectable GLP-1RA as described are first-line GLP1-RA; oral GLP-1RA are a second line option if patient refuses or not appropriate for an injectable (or supply issues).

DPP-4i ('gliptins) should **not** be prescribed alongside GLP-1 RA.

With increasing evidence of safety, efficacy and ease of use NHSGGC formulary has been updated to reflect that GLP-1RA can be initiated in either primary or secondary care by clinicians experienced in the treatment of diabetes. Referral to cDSN will still be indicated if patient also on insulin, or to secondary care if concern re medical comorbidity. Please refer to Primary care GLP-1RA guidelines on NHS GGC clinical platform as above. This is being updated to include tirzepatide. GLP1-RA or dual agents such as tirzepatide can be as used second line when SGLT-2i is contraindicated or other specific clinical reason.

5.3.1 Tirzepatide

Tirzepatide is a dual agonist (GLP-1 receptor agonist and GIP agonist). Similar to more established GLP-1RA, tirzepatide decreases blood sugar levels by increasing insulin production and lowering liver glycogenesis. Similarly it supports weight loss by decreasing appetite and slowing the movement of food from the stomach into the small intestine. People feel full more quickly and for a longer period of time.

The Scottish Diabetes Group Consensus statement reports:
"Tirzepatide, in addition to other oral anti-diabetic medicines, should be considered in adults with T2DM, where glycaemia is insufficiently controlled, as an adjunct to a reduced-calorie diet and increased physical activity and:

- ***Generally after a trial of GLP-1 RA**. This guidance is based on the lack of confirmed cardiovascular benefit at present.*
- *As an alternative to GLP-1 RAs in the following instances:*
    - *Where there are supply issue with existing GLP-1 RAs*
    - *High risk individuals in where greater weight loss will have a positive benefit on obesity related complications e.g. young onset, Obstructive Sleep Apnoea etc."*

Similar NHS GGC formulary guidance applies to initiating tirzepatide as to GLP-1RA above. Cardiovascular outcome data is awaited and therefore where relevant and available medications in this class with CV benefit would routinely be preferred, taking account of availability.

There may be an interaction with oral contraceptives so patients should be advised to consider alternative methods for 4 weeks after initiation and at dose changes until actual risk is clarified. See BNF for up to date information.

5.4 DPP-4 inhibitors (DPP-4i, 'gliptins)

DPP-4i can be considered where individuals are close to their individualised target and there are reasons for not using preferred SGLT-2i or GLP-1RA classes. Typically HbA1c reduction is 6mmol/mol, and they are well tolerated with minimal side-effects. They can be suitable for frail/elderly individuals. DPP-4i should **not** be prescribed alongside GLP-1RA.

5.5 Sulphonylureas (e.g gliclazide)

Sulphonylureas, typically gliclazide, should be considered as add on therapy when preferred options are not achieving HbA1c targets in type 2 diabetes. They may be considered 1st or 2nd line in patients who are not overweight or have a history of pancreatic insult.

Appropriate advice and access to blood glucose monitoring should be considered, in relation to risk of hypoglycaemia, and DVLA guidance. See NHS GGC Guidelines:
https://rightdecisions.scot.nhs.uk/media/2661/296-diabetes-self-monitoring-of-blood-glocuse.pdf

5.6 Thiazolidinediones (Pioglitazone)

Pioglitazone can be considered for lowering HbA1c in individuals where insulin resistance is evident and preferred options metformin/SGLT-2i/GLP-1RA are already being used/contra-indicated, or on a temporary basis while there are supply issues with GLP-1RA.

Pioglitazone should not be used in individuals where fluid retention is harmful e.g. with heart failure, problematic leg swelling, or macular oedema (including patients with a history of anti-VEGF intra-orbital injection therapy, even if eyes appear on follow-up in 'quiescent' phase). The risk of fracture should be considered during long-term use of pioglitazone. Where there is lack of experience or uncertainty around indication advice should be sought from secondary care via SCI Gateway or community MDT.

Patients prescribed pioglitazone should be made aware of the increased risk of peripheral oedema, heart failure, weight gain, bladder cancer and fractures.

It may be useful if individuals decline preferred options such as gliclazide or insulin due to the need for blood glucose monitoring or effects of these medications on occupation.

While it is contraindicated in heart failure there is some evidence of cardiovascular protection in those with Type 2 diabetes and evidence of CV disease or high risk of it, particularly from stroke, from the PROactive study [11].

5.7 Insulin

Oral metformin therapy should be continued when insulin therapy is initiated to maintain or improve glycaemic control. Consider stopping or reducing sulphonylurea therapy when insulin therapy is initiated. The benefits and risks of continuing other glucose-lowering agents should also be reviewed at this time on an individualised basis.

Insulin should be initiated for progression of type 2 diabetes by health professionals experienced in diabetes management typically community Diabetes Nurse Specialist (cDSN). As before, initiation of insulin would be discussed with GP or secondary care diabetes team.

Further details available on guideline 'Diabetes: Insulin Initiation and Adjustment, Patients with Type 2 Primary Care: Guidance for Diabetes Specialist Nurses' and the Community DSN updated Service Specification.
https://rightdecisions.scot.nhs.uk/media/2731/148-diabetes-insulin-initiation-amended.pdf

Appropriate advice and access to blood glucose monitoring should be considered, in relation to risk of hypoglycaemia, and DVLA guidance. See NHS GGC Guidelines: https://rightdecisions.scot.nhs.uk/media/2661/296-diabetes-self-monitoring-of-blood-glocuse.pdf

Referral to secondary care for insulin initiation may be appropriate but not limited to: where there is diagnostic uncertainty, women of childbearing age, or a new kidney injury/rapidly changing renal function for example.

6 Diabetes, Prevention and Management of Associated Complications

The NHS GGC Guidelines platform has been updated and has an excellent search function which allows for easy location of the required relevant guideline, e.g. renal, foot, hypertension and primary and secondary prevention of CV disease.

https://rightdecisions.scot.nhs.uk/ggc-clinical-guideline-platform/endocrine/

7 Pregnancy and Type 2 Diabetes (including pre-pregnancy)

All women with type 2 diabetes of child bearing age should be offered contraceptive advice and know to plan any pregnancy to optimise outcomes**. All women with Type 2 diabetes should be referred to their local secondary care type 2 service if considering pregnancy at any point in the future, or are at risk of unplanned pregnancy.** If patient is found to be actively planning a pregnancy referral to clinic is indicated urgently, potentially teratogenic therapies stopped, folic acid established at 5mg daily, and glycaemia optimised. Target HbA1c in pregnancy is <48mmol/mol, and if HbA1c above this target it may be appropriate for primary care teams to advise patients to take measures to prevent pregnancy until they have been seen in clinic and an individualised target agreed. If HbA1c is above 86 strongly advise women not to become pregnant due to the high risk of adverse pregnancy outcomes and initiate appropriate contraception [12].

8 References

[1] M. J. Davies, V. R. Aroda, B. S. Collins and e. al, "Management of hyperglycaemia in type 2 diabetes. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)," *Diabetologia,* vol. 65, p. 1925–66., 2022.

[2] SIGN, "Pharmacological management of glycaemic control in people with type 2 diabetes (154).," 2017.

[3] M. E. J. Lean, W. S. Leslie, A. C. Barnes and etal, "Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial," *Lancet Diabetes Endocrinol,* vol. 7, p. 344–55, 2019.

[4] M. Lean, W. S. Leslie, A. C. Barnes and e. al, "5-year follow-up of the randomised Diabetes Remission Clinical Trial (DiRECT) of continued support for weight loss maintenance in the UK: an extension study," *Lancet Diab Endocrinol,* vol. 12, no. 4, pp. 233-246, 2024.

[5] M. C. Riddle, W. T. Cefalu, P. H. Evans and etal, "Consensus report: definition and interpretation of remission in type 2 diabetes," *Diabetes Care,* vol. 44, p. 2438–2444, 2021.

[6] R. R. Holman, S. K. Paul, M. A. Bethel and ETAL, "10-year follow-up of intensive glucose control in type 2 diabetes," *N Eng J Med,* vol. 359, p. 1577–89, 2008.

[7] W. D. Strain, S. V. Hope, A. Green and etal, "Type 2 diabetes mellitus in older people: a brief statement of key principles of modern day management including the assessment of frailty. A national collaborative stakeholder initiative," *Diabet Med,* vol. 35, p. 838–45, 2018.

[8] S. P. Marso, G. H. Daniels, K. Brown-Frandsen and etal, "Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes," *N Engl J Med,* vol. 28, no. 375, pp. 311-22, 2016.

[9] H. C. Gerstein, H. M. Colhoun, G. R. Dagenais and etal, "Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial," *Lancet,* vol. 294, p. 121–30, 2019.

[10] S. P. Marso, S. C. Bain, A. Consoli and etal, "Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes," *N Eng J Med,* vol. 375, p. 1834–44, 2016.

[11] E. Erdmann, J. Dormandy, R. Wilcox and etal, "PROactive 07: pioglitazone in the treatment of type 2 diabetes: results of the PROactive study," *Vasc Health Risk Manag,* vol. 3, p. 355–70, 2007.

[12] "Diabetes in pregnancy: management from preconception to the postnatal period [NG 3]," NICE Guidelines, 2015.

9 Appendix 1. Two page summary of T2D NHS GGC Guidelines

Type 2 Diabetes Intensification Summary

First Line Management in Typical Type 2 Diabetes

Lifestyle management (including diet, weight management physical exercise)

First Choice: metformin
- if GI upset consider M/R
- M/R may be cheaper at higher doses

If required for short term, rescue therapy for symptomatic hyperglycaemia – **sulphonylurea, insulin**

1. **Titrate metformin to 1g BD or max tolerated dose and CV risk assessment:**

Existing ASCVD, HF, CKD? → Add SGLT-2i* ('flozin) (as soon as metformin titrated)

At risk of ASCVD? (QRISK) score >10% → Consider SGLT-2i* ('flozin) (as soon as metformin titrated)

No additional ASCVD

Check HbA1c 3 months after medication established

2. **If above target HbA1c add SGLT-2i ('flozin) if not already on, or contraindicated**

3. **If above target HbA1c add GLP-1RA unless contraindicated. Consider Tirzepatide if GLP-1RA unavailable/contra-indicated/not effective**

*** Safe prescribing of SGLT2i**
Check eGFR suitable; Avoid if Hx of DKA; Consider reducing loop diuretic dose. Hypo risk if adding to SU/ insulin (consider reducing dose). Consider use of other agents if HbA1c >90mmol/mol
Patient counselling: Genital hygiene (5-fold risk genital thrush); Symptoms of DKA; Avoid excess alcohol
"Sick day rules" apply: Withhold if fasting/ dehydrated/ surgery or acutely unwell.

HbA1c targets for Type 2 Diabetes:
- Targets should be set with individuals in order to balance benefits with harms, in particular hypoglycaemia & weight gain.
- HbA1c target of <53 mmol/mol is reasonable to reduce the risk of microvascular and macrovascular disease
- HbA1c target of <48 mmol/mol may be appropriate at diagnosis/young
- Targets <58 are not suitable if on hypo causing medications e.g gliclazide or insulin
- If high risk from hypos e.g cognitive decline, loss of awareness consider target Hba1c 65-75mmol/mol, see section 3.2.

At every diabetes appointment consider multifactorial risk reduction: referral to GCWMS, smoking cessation, diet, exercise, BP control, dyslipidaemia. See Annual review guideline on clinical Decisions platform for further information.

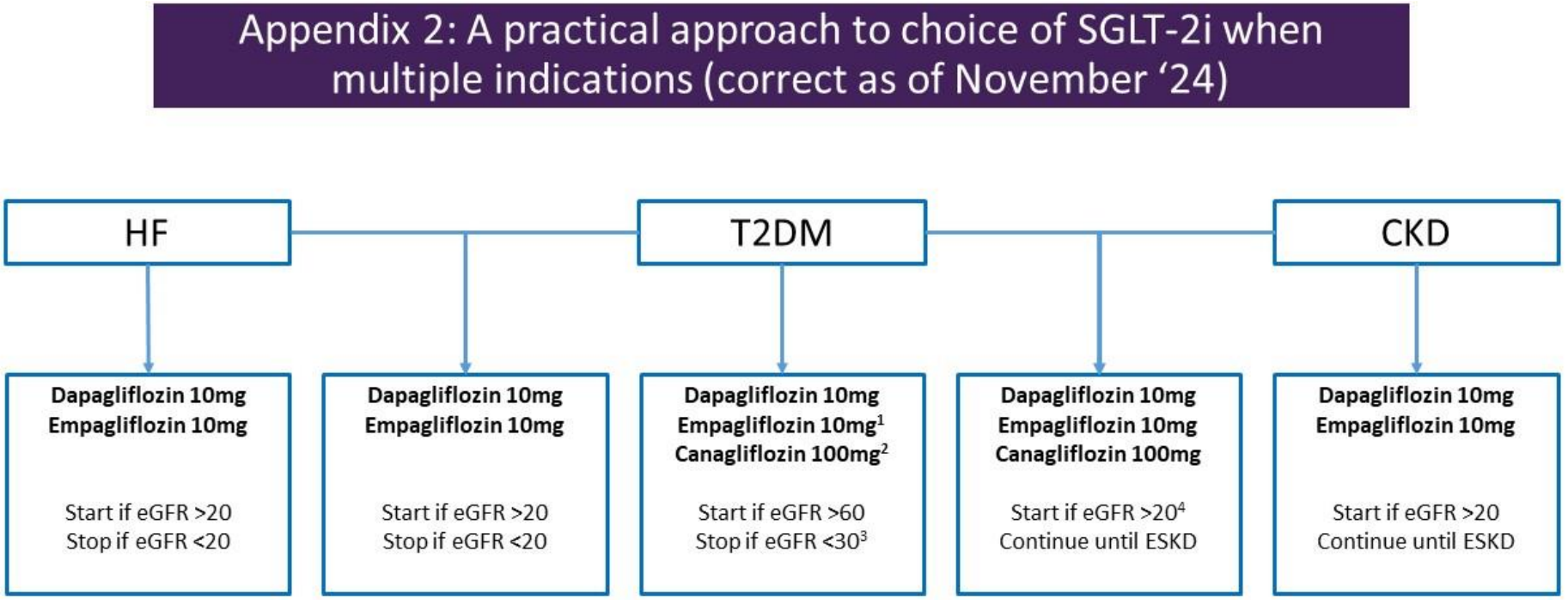
Two page summary of T2D NHS GGC Guidelines cont'd. 2/2

Other scenarios (or 4th line if already on metformin/ SGLT-2i/ GLP-1RA) (Table 3.4):

The combination of metformin, SGLT-2i and GLP1-RA is very effective at improving diabetes control. If a 4th line agent is required then gliclazide or pioglitazone could be considered unless there are clear indications for insulin. Advice can be sought on 4th line choices, or whether insulin is required, via community MDT or via SCI Gateway.

Scenario	Medication considerations
Low or normal weight, or losing weight in the context of a rising HbA1c. Possible history of pancreatic insult.	Review compliance with medications already prescribed. Consider gliclazide. This may be a trial to see if blood glucose improves. **No** improvement on gliclazide suggests **insulin** may be required. Seek specialist advice.
Steroid induced hyperglycaemia	Gliclazide is often preferred as can be titrated to blood glucose and steroid dose, with escalation to insulin if gliclazide not suffice. Insulin may be appropriate first line in palliative setting (See Diabetes UK Guideline https://www.diabetes.org.uk/professionals/position-statements-reports/diagnosis-ongoing-management-monitoring/end-of-life-care). Seek guidance as required.
Unable to tolerate or access preferred GLP-1RA, or lack of efficacy of GLP-1RA.	Consider use of dual receptor agonist e.g Tirzepatide instead of GLP-1 RA.
Unable to tolerate GLP-1RA or dual agonists and concerns around use of medications that may require blood monitoring/have hypo risk	Consider pioglitazone. See Section 5.6 Drug Classes information and BNF. Consider SCI GW for advice or community MDT discussion re suitability.
Frail, elderly , or not suitable for a GLP-1RA	Review HbA1c target table to consider if need to escalate therapy. If so consider DPP-4i e.g. sitaglipin or linagliptin if CKD.
Chronic Kidney Disease (CKD)	If eGFR <45ml/min adjustments may need to be made. See BNF and CKD section 4 links below.
High suspicion of Type 1 Diabetes	This guideline does not apply and these patients should be discussed urgently with your local team.

10 Appendix 2 – SGLT-2i prescribing guide



Notes

1. Increase dose to 25 mg od if inadequate glycaemic control and eGFR >60
2. Increase dose to 300 mg od if inadequate glycaemic control and eGFR >60
3. *All SGLT2i have limited glycaemic effect when eGFR<45. Consider discontinue any SGLT2i if eGFR <45, where used solely for glycaemic effect in T2DM
4. Canagliflozin threshold of initiation eGFR >30

Courtesy of Dr Nazim Ghouri