Glucose Management in Adults with Type 2 Diabetes

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

Classification of Diabetes is important for determining therapy. Age of onset and body mass index should not be the sole factors precluding a confident categorisation of newly diagnosed diabetes.

Rescue therapy at any phase of treatment: For symptomatic hyperglycaemia, consider Gliclazide or Insulin. Review treatment when blood glucose control achieved.

First line non-pharmacological therapy: Diet and lifestyle advice (weight and physical activity) and referral to Diabetes Structured Education

Assess individualised Hba1c target, cardiovascular risk, and kidney function.

Does the patient have an ESTABLISHED Cardiorenal disease*?

*Coronary heart disease, acute coronary syndrome, previous myocardial infarction, stable angina, prior coronary or other revascularisation, cerebrovascular disease, peripheral arterial disease and chronic kidney disease

No

Yes

Chronic kidney disease (CKD)

If already taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate), offer an **SGLT-2 inhibitor** (in addition to the ARB or ACE inhibitor) if patient's estimated glomerular filtration rate (eGFR) met NICE Dapagliflozin for treating chronic kidney disease TA1075 and Empagliflozin for treating chronic kidney disease TA942 criteria. See guidance here for further information about safely initiating SGLT-2 inhibitors for adults in T2DM.

Metformin - Titrate weekly to minimise side effects up to maximum tolerated dose. ***[MR if GI disturbance]*** Clinical benefit should be reviewed at least 4 weeks post initiation.

If high risk of CVD *[QRisk≥10% or an elevated lifetime risk of cardiovascular disease (CVD)]*

As soon as Metformin tolerability is confirmed, **consider adding SGLT-2 inhibitor** (Dapagliflozin, Empagliflozin **with proven CVD benefit)** to reduce CVD risk even if Hba1c target achieved**.** **(**Consider using SGLT-2inhibitor alone if metformin contraindicated.)

If not at high risk of CVD. Continue Metformin alone, monitoring Hba1c and any CVD risk or status change.

If metformin contraindicated, consider other drug classes.

Chronic Heart Failure or Established Atherosclerotic CVD

Metformin - Titrate weekly to minimise side effects up to maximum tolerated dose. ***[MR if GI disturbance]*** Clinical benefit should be reviewed at least 4 weeks post initiation.

AND

As soon as Metformin tolerability is confirmed, **offer SGLT-2 inhibitor** (Dapagliflozin, Empagliflozin with proven CVD benefit) to reduce CVD event risk.

If Metformin contraindicated, offer SGLT-2

Treatment options if further interventions are needed:

Hba1c not controlled below individual's target:	**Became at risk or established CVD status**
Switching or adding:	Switching or adding:
DPP-4 inhibitor or Pioglitazone or Sulfonylurea if not already prescribed	SGLT-2 inhibitor (Dapagliflozin, Empagliflozin with proven CVD benefit) if not already prescribed

Switch or add treatments from different drug classes up to triple therapy. (Dual therapy if metformin is contraindicated)

Further treatment options if Hba1c not controlled below individual's target.

GLP-1 analogues (Semaglutide, Dulaglutide) or **GLP-1 &GIP analogues** (Tirzepatide)

If triple therapy with metformin and 2 other oral drugs is ineffective, not tolerated or contraindicated, **consider triple therapy by switching one drug (DPP-4 inhibitor or glitazone or sulfonylurea) for** a **GLP-1** or **GLP-1 &GIP analogues** only if the patients:

- have a body mass index (BMI)* of 35 kg/m2 or more, and specific psychological or other medical problems associated with obesity, OR
- have a BMI lower than 35 kg/m2, and:

- for whom insulin therapy would have significant occupational implications or

– weight loss would benefit other significant obesity related comorbidities.

*Use lower BMI thresholds (usually reduced by 2.5 kg/m2) for people from South Asian, Chinese, other

Insulin

Consider Insulin therapy when dual therapy has not continued to control HbA1c to below individual's target.

Medication Review & Optimisation

- Reassess patient's status and medication effectiveness at every diabetes review. Stopping medicines that are not tolerated.
- Consider whether switching rather than adding drugs could be effective. Take into account the drug class specific advice below when optimising the glucose lowering therapy.
- Before thinking about changing treatments, taking into account factors such as: adverse effects, adherence to existing medicines, the need to revisit advice about diet and lifestyle, prescribed doses and formulations.
- Stopping medicines that have had no impact on glycaemic control or weight, unless there is an additional clinical benefit.
- At any point in the management of diabetes, where there is a new change to cardiovascular risk or status change, if a SGLT-2 inhibitors isn't already being used, addition of a SGLT-2 inhibitor (not ertugliflozin) ought to be considered. See guidance here for further information about safely initiating SGLT-2 inhibitors for adults in T2DM.
- Consider discussing pregnancy in all women at childbearing age. If planning for pregnancy, discuss the important of keeping glucose level to individual's target level, review medications choice and regimen as per SmPC and BNF. Offer folic acid 5mg daily and refer to pre-conception clinic as appropriate.

Sodium-glucose co-transporter-2 (SGLT-2 inhibitor) – *Dapagliflozin, Empagliflozin, Canagliflozin*

- The risk of diabetic ketoacidosis must be considered in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness. Stop & reassess for ketoacidosis immediately if these symptoms occur, regardless of blood glucose level. Ref: Drug Safety Update.
- SGLT-2 inhibitors block renal tubular glucose reabsorption and thus their glucose lowering efficacy depends on the amount of filtered glucose and glomerular filtration rate and is reduced in people with impaired eGFR. Additional glucose lowering therapies should be considered in people with T2D when eGFR is persistently impaired & HbA1c is above the individualised target.
- Noted there is insufficient evidence to support a cardiovascular benefit with Ertugliflozin.

Dipeptidyl peptidase-4 inhibitor (DPP-4 inhibitor) – *Alogliptin, Linagliptin, Saxagliptin, Sitagliptin*

- Not to be used inconjunction with GLP1 agents. These drugs work on the same pathway. DPP4 antagonist block DPP4, an enzyme which breaks down GLP and GIP. If patient has cardiovascular risk or CKD consider an SGLT-2 inhibitor in place of DPP-4 inhibitor, unless contraindicated, or not tolerated.

Glitazones - *Pioglitazone*

- Reassess the risk of concomitant use with insulin (risk of heart failure). Patients with active bladder cancer, history of bladder cancer or uninvestigated haematuria should not receive pioglitazone.

Sulfonylurea- *Gliclazide*

- Moderate to high risk of hypoglycaemia in older people.
- Glimepiride not suitable for use in elderly patients due to its long half-life which increases the risk of precipitating hypoglycaemia.
- Offer self-monitoring blood glucose meter and testing strips to support glucose monitoring at times relevant to driving. Provide DVLA Diabetes and Driving rule information, see Diabetes UK resources for further information: here.

Glucagon-like peptide 1 (GLP-1) – *Dulaglutide, Semaglutide*

- Only continue in those with a beneficial metabolic response after 6 months (reduction of ≥11 mmol/mol [1.0%] in HbA1c and weight loss of ≥ 3% of initial body weight).

Consider adjustments to oral therapy when GLP1 analogue initiated		
Triple oral therapy containing DPP-4 inhibitor:	Swap DPP-4 inhibitor for GLP-1 mimetic.	Consider reducing Sulfonylurea by 50% (if co prescribed)
Triple oral therapy without DPP-4 inhibitor:	Add in GLP-1 mimetic, reduce sulfonylurea by 50%.	Continue to review dose of sulfonylurea, reducing as necessary, as GLP-1 mimetic up titrated.

- An updated NatPSA alert on the shortage of GLP-1 issued on 3rd Jan 2024 note that supply of GLP-1 is not expected to return to normal until at least the end of 2024. Always consult BSW local formulary information prior prescribing. Further information can be found: here

Glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) - *Tirzepatide*

- Tirzepatide has not been studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy or diabetic macular oedema. Consider use with caution in these patients with appropriate monitoring.
- STOP any existing GLP-1 agent when Tirzepatide is initiated.
- When Tirzepatide is added to existing therapy of a sulfonylurea, a reduction in the dose of sulfonylurea may be considered to reduce the risk of hypoglycaemia. See adjustments to oral therapy table under GLP-1 box.