

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY)

NO

INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD OR HF[†]

Consider independently of baseline HbA_{1c} or individualised HbA_{1c} target

ASCVD PREDOMINATES

- Established ASCVD
- Indicators of high ASCVD risk (age ≥55 years + LVH or coronary, carotid, lower extremity artery stenosis >50%)

PREFERABLY

- GLP-1 RA with proven CVD benefit¹
- OR
- SGLT2i with proven CVD benefit¹ if eGFR adequate²

If HbA_{1c} above target

If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit¹
- DPP-4i if not on GLP-1 RA
- Basal insulin⁴
- TZD⁵
- SU⁶

HF OR CKD PREDOMINATES

- Particularly HFREF (LVEF <45%)
- CKD: Specifically eGFR 30-60 ml min⁻¹ [1.73m]⁻² or UACR >30 mg/g, particularly UACR >300 mg/g

PREFERABLY

- SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate²
- OR
- If SGLT2i not tolerated or contraindicated or if eGFR less than adequate² add GLP-1 RA with proven CVD benefit¹

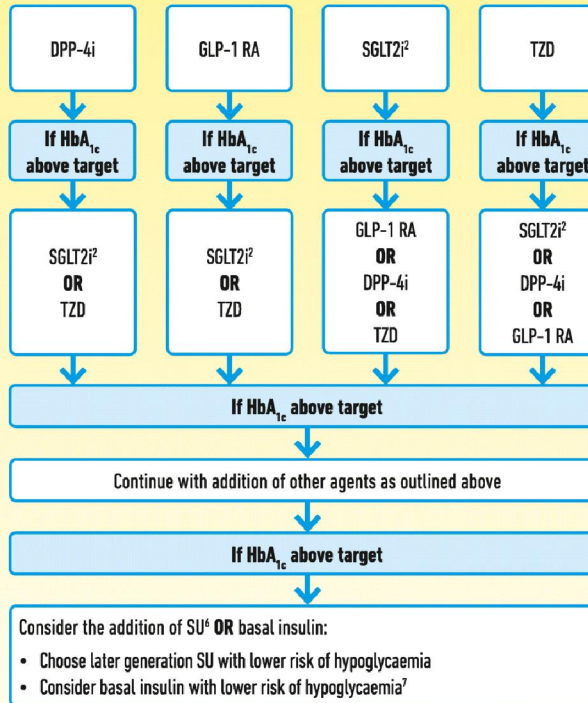
If HbA_{1c} above target

Choose agents demonstrating CV safety:

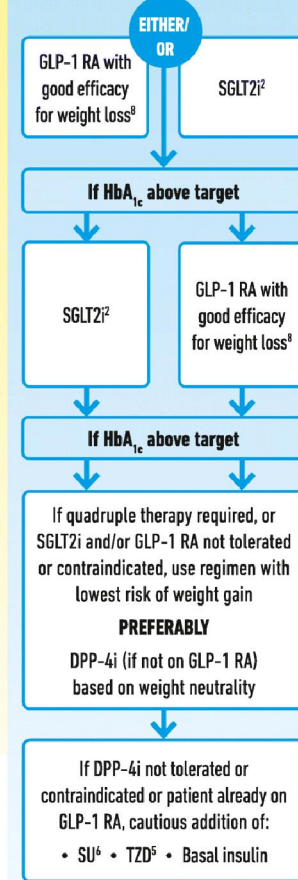
- Avoid TZD in the setting of HF
- For patients on a SGLT2i, consider adding GLP-1 RA with proven CVD benefit¹
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin⁴
- SU⁶

If HbA_{1c} above individualised target proceed as below

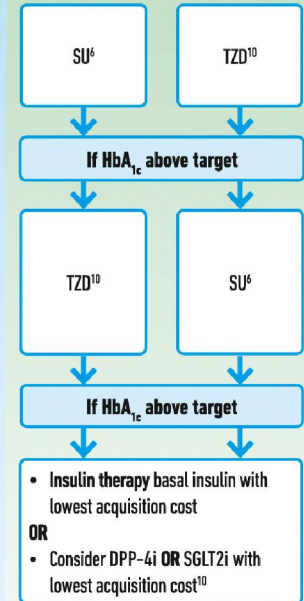
COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA



COMPELLING NEED TO MINIMISE WEIGHT GAIN OR PROMOTE WEIGHT LOSS



COST IS A MAJOR ISSUE⁹⁻¹⁰



1. Proven CVD benefit means it has label indication of reducing CVD events.

2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use

3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CRENDENCE, Dapagliflozin has primary heart failure outcome data from DAPA-HF

4. Degludec and U100 glargine have demonstrated CVD safety

5. Low dose may be better tolerated though less well studied for CVD effects

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

Updates to the 2018 consensus report are indicated in magenta font

6. Choose later generation SU to lower risk of hypoglycaemia, Glimepiride has shown similar CV safety to DPP-4i

7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin

8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide

9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycaemia and lower priority to avoid weight gain or no weight-related comorbidities)

10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

LVH = Left Ventricular Hypertrophy; HFREF = Heart Failure reduced Ejection Fraction
UACR = Urine Albumin-to-Creatinine Ratio; LVEF = Left Ventricular Ejection Fraction