Choosing glucose-lowering medication in those with indicators of high-risk or established atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD) or heart failure (HF)

Use metformin unless contraindicated or not tolerated
- Continue metformin unless contraindicated (remember to adjust dose/stop metformin with declining eGFR)
- Add an SGLT2i or GLP-1 RA with proven CV benefit\(^1\) (consider adding independence of individualised \(\text{HbA1c}\) target)
- If individualised \(\text{HbA1c}\) target achieved and already on dual therapy or multiple glucose-lowering therapies when adding SGLT2 or GLP-1 RA, consider stopping or reducing dose of other glucose-lowering therapy to reduce the risk of hypoglycaemia

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 CV benefit\(^1\)

OR

SGLT2i with proven CV benefit\(^2\) if eGFR adequate\(^3\)

If \(\text{HbA1c}\) above target

If further intensification is required or patient is 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 CV benefit\(^2\)
- DPP-4i if not on GLP-1 RA
- Basal insulin\(^2\)

If \(\text{HbA1c}\) above target

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate\(^3\) add GLP-1 RA with proven CV benefit\(^4\)

HF or CKD predominates
- Particularly HFpEF (LVF <45%)
- CKD: Specifically eGFR 30–60 ml min\(^{-1}\) (1.73 m\(^2\)) 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 adequate\(^5\)

OR

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate\(^3\) add GLP-1 RA with proven CV benefit\(^4\)

Avoid T2D in the setting of HF
Choose agents demonstrating CV safety:
- For patients on a SGLT2i, consider adding GLP-1 RA with proven CV benefit\(^1\)
- DPP-4i (not saxagliptin) in the setting of HF if not on GLP-1 RA
- Basal insulin\(^2\)
- SU\(^2\)

1. Proven CV benefit means it has label indication of reducing CV events.
2. Be aware that SGLT2i labelling varies by region and individual agents 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 3K progression in CVOTs. Empagliflozin has primary renal outcome data from CREDENCE. Dapagliflozin has primary heart failure outcome data from DAPA-HF.
4. Caduet with GLP-1 RA in EURO
d. Dapagliflozin and/or spironolactone have demonstrated CV safety
6. Low dose may be better tolerated though less well studied for CV effects
7. Choose second-generation SU to lower risk of hypoglycaemia. Glumetizide has shown similar CV safety to DPP-4
LVH = Left Ventricular Hypertrophy; HFpEF = Heart Failure Reduced Ejection Fraction
UACR = Urine Albumin-to-Creatinine Ratio; UEF = Left Ventricular Ejection Fraction

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Updates to the 2018 consensus report are indicated in magenta text.