

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



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 adequate³

OR

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate² add GLP-1 RA with proven CVD benefit¹

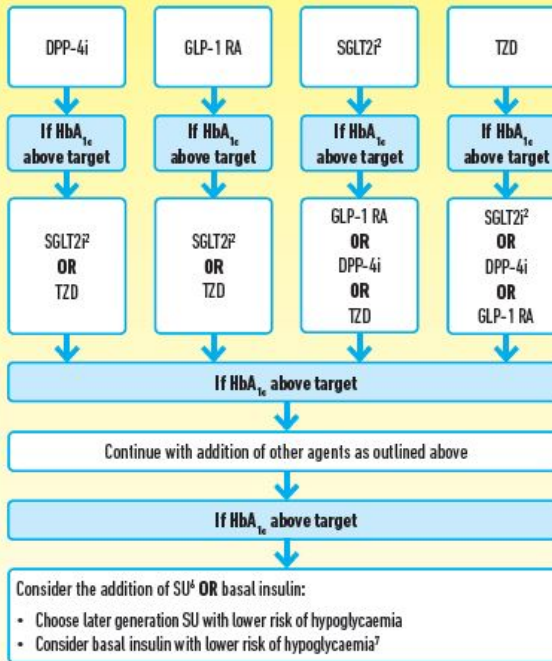
If HbA_{1c} above target

Avoid TZD in the setting of HF
Choose agents demonstrating CV safety:

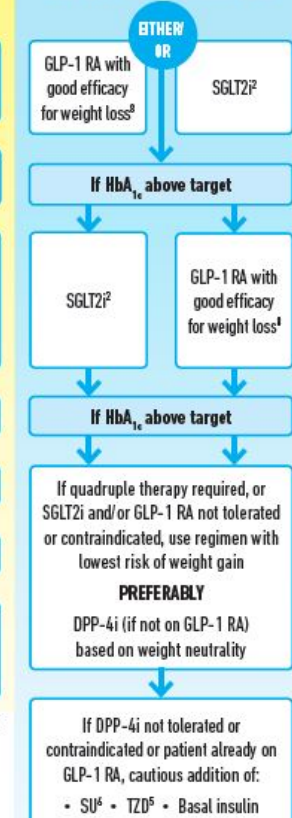
- For patients on a SGLT2i, consider adding GLP-1 RA with proven CVD benefit¹
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin⁴
- SU⁶

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

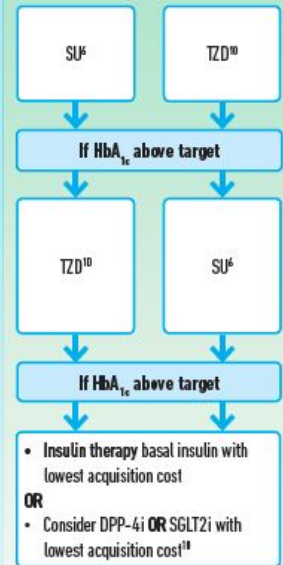
COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA



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.

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

Updates to the 2018 consensus report are indicated in magenta font

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

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 CVD benefit¹ (consider adding independently of individualised HbA_{1c} target)
- If individualised HbA_{1c} target achieved and already on dual therapy or multiple glucose-lowering therapies when adding SGLT2i 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%)



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



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OR
If SGLT2i not tolerated or contraindicated or if eGFR less than adequate² add GLP-1 RA with proven CVD benefit^{1,4}

If HbA_{1c} above target

If HbA_{1c} above target

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- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit¹
- DPP-4i if not on GLP-1 RA
- Basal insulin⁵
- TZD⁴
- SU⁷

• Avoid TZD in the setting of HF
Choose agents demonstrating CV safety:

- 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 insulin⁵
- SU⁷

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 CREDENCE. Dapagliflozin has primary heart failure outcome data from DAPA-HF

4. Caution with GLP-1 RA in ESRD
5. Degludec and U100 glargine have demonstrated CVD safety
6. Low dose may be better tolerated though less well studied for CVD effects
7. Choose later generation SU to lower risk of hypoglycaemia, Glimpiride has shown similar CV safety to DPP-4i

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

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