

PHARMACOLOGIC TREATMENT OF HYPERGLYCEMIA IN ADULTS WITH TYPE 2 DIABETES



FIRST-LINE THERAPY depends on comorbidities, patient-centered treatment factors, including cost and access considerations, and management needs and generally includes metformin and comprehensive lifestyle modification[^]

ASCVD/INDICATORS OF HIGH RISK, HF, CKD†

RECOMMEND INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE‡

+ASCVD/INDICATORS OF HIGH RISK*

EITHER/OR
 GLP-1 RA with proven CVD benefit¹
 OR
 SGLT2i with proven CVD benefit¹

IF A1C ABOVE TARGET

- For patients on a GLP-1 RA, consider incorporating SGLT2i with proven CVD benefit and vice versa¹
- TZD²

+HF*

SGLT2i with proven benefit in this population¹

+CKD**

CKD and albuminuria (e.g., ≥200 mg/g creatinine)
 OR
 CKD without albuminuria (e.g., eGFR <60 mL/min/1.73 m²)

PREFERABLY
 SGLT2i with primary evidence of reducing CKD progression
 OR
 SGLT2i with evidence of reducing CKD progression in CVOTs
 OR
 GLP-1 RA with proven CVD benefit¹ if SGLT2i not tolerated or contraindicated

For patients with CKD (e.g., eGFR <60 mL/min/1.73 m²) without albuminuria, recommend the following to decrease cardiovascular risk

EITHER/OR
 GLP-1 RA with proven CVD benefit¹
 OR
 SGLT2i with proven CVD benefit¹

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA and vice versa

If A1C remains above target, consider treatment intensification based on comorbidities, patient-centered treatment factors, and management needs

NONE

Incorporate agents that provide adequate **EFFICACY** to achieve and maintain glycemic goals
Higher glycemic efficacy therapy: GLP-1 RA; insulin; combination approaches (Table 9.2)
 • Consider additional comorbidities, patient-centered treatment factors, and management needs in choice of therapy, as below:

MINIMIZE HYPOGLYCEMIA

No/low inherent risk of hypoglycemia: DPP-4i, GLP-1 RA, SGLT2i, TZD
 For SU or basal insulin, consider agents with lower risk of hypoglycemia^{3,4}

IF A1C ABOVE TARGET

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

MINIMIZE WEIGHT GAIN/PROMOTE WEIGHT LOSS

PREFERABLY
 GLP-1 RA with good efficacy for weight loss
 OR
 SGLT2i

IF A1C ABOVE TARGET

For patients on a GLP-1 RA, consider incorporating SGLT2i and vice versa
 • If GLP-1 RA not tolerated or indicated, consider DPP-4i (weight neutral)

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

CONSIDER COST AND ACCESS

Available in generic form at lower cost:
 • Certain insulins: consider insulin available at the lowest acquisition cost
 • SU
 • TZD

IF A1C ABOVE TARGET

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

1. Proven benefit refers to label indication (see Table 9.2)
2. Low dose may be better tolerated though less well studied for CVD effects
3. Choose later generation SU to lower risk of hypoglycemia
4. Risk of hypoglycemia: degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
5. Consider country- and region-specific cost of drugs

[^]For adults with overweight or obesity, lifestyle modification to achieve and maintain ≥5% weight loss and ≥150 min/week of moderate- to vigorous-intensity physical activity is recommended (See Section 5: Facilitating Behavior Change and Well-being to Improve Health Outcomes).
[†]Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.
[‡]Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.
[§]Refer to Section 10: Cardiovascular Disease and Risk Management.
^{**}Refer to Section 11: Chronic Kidney Disease and Risk Management and specific medication label for eGFR criteria.