LOUISIANA DEPARTMENT OF HEALTH

Diabetes ECHO
SGLT-2 inhibitors

05/08/2025

Project ECHO®

Speaker:

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Tulane University

Speaker Disclosure

In the past 24 months, I have not had any financial relationships with any ineligible companies.

Disclaimer

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Objectives

- ADA guidelines on the SGLT2 inhibitors
- Clinical considerations
- Adverse effects

Case Scenario

Mr Smith is a 68-year-old male who comes to the clinic as a new patient for T2DM.

He was diagnosed with T2DM 8 years ago. His current medications include metformin 1000 mg PO BID with excellent compliance. His BMI 28 kg/m2. Point-of-care A1c in clinic today is 7.4%, and eGFR is 82 mL/min/1.73m2

He has a history of myocardial infarction at the age of 61 years and subsequently developed HFrEF (EF 33%).

Of the following medications, which single medication would you recommend that he start, after discussing with him and assuming no contraindications?

A. Glimepiride

B. Semaglutide

C. Dapagliflozin

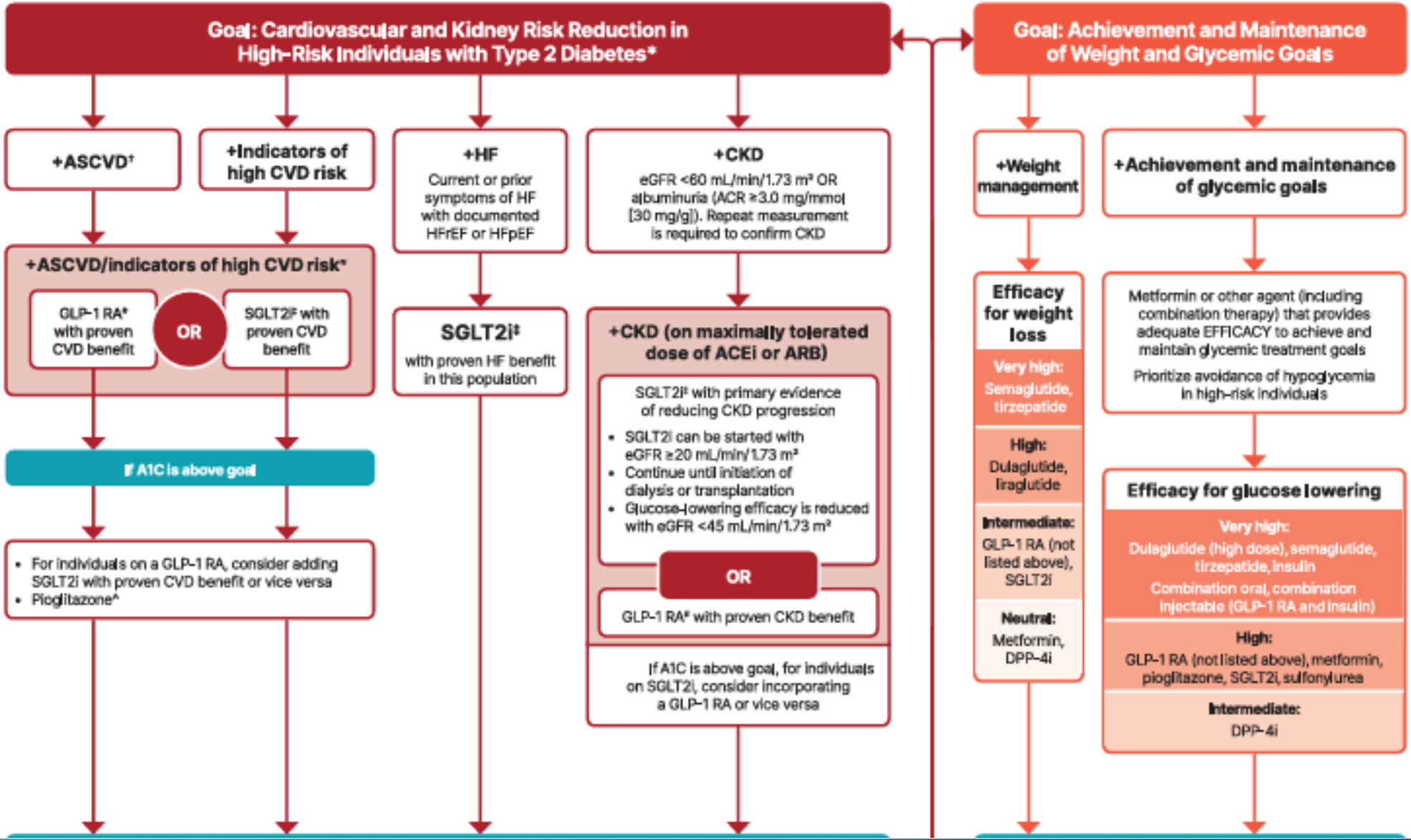
D. Sitagliptin

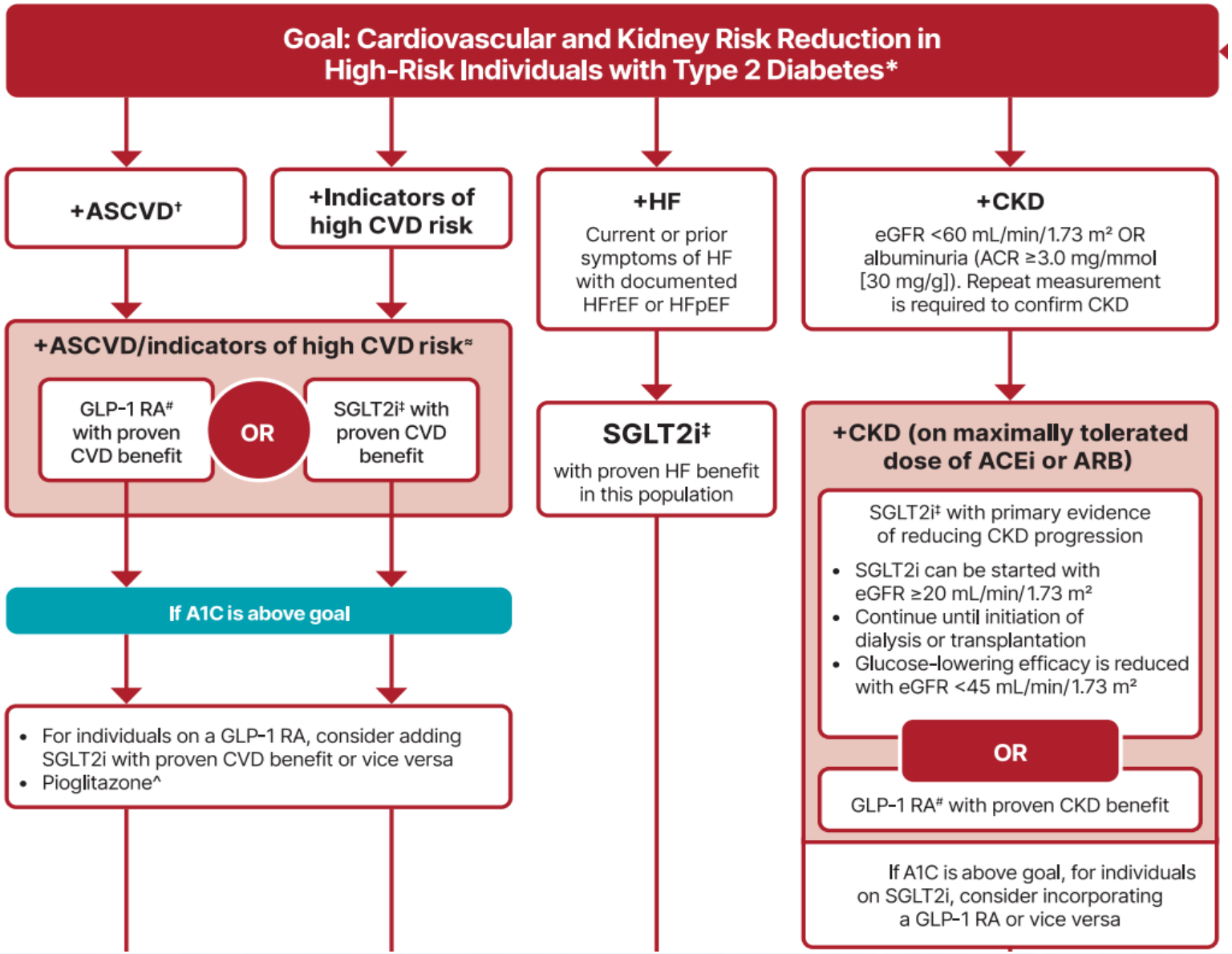
E. Basal insulin

Currently Available Agents

SGLT2i

Dapagliflozin	5, 10 mg daily
Canagliflozin	100, 300 mg daily
Empagliflozin	10, 25 mg daily
Ertugliflozin	5, 15 mg daily


Goal: Cardiovascular and Kidney Risk Reduction in High-Risk Individuals with Type 2 Diabetes*
+ASCVD†
+Indicators of high CVD risk
+HF
Current or prior symptoms of HF with documented HFrEF or HFpEF
+CKD
eGFR <60 mL/min/1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). Repeat measurement is required to confirm CKD
+ASCVD/indicators of high CVD risk*
GLP-1 RA# with proven CVD benefit
OR
SGLT2i‡ with proven CVD benefit
If A1C is above goal
• For individuals on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit or vice versa
• Pioglitazone^
SGLT2i‡
with proven HF benefit in this population
+CKD (on maximally tolerated dose of ACEi or ARB)
SGLT2i‡ with primary evidence of reducing CKD progression
• SGLT2i can be started with eGFR ≥20 mL/min/1.73 m²
• Continue until initiation of dialysis or transplantation
• Glucose-lowering efficacy is reduced with eGFR <45 mL/min/1.73 m²
OR
GLP-1 RA# with proven CKD benefit
If A1C is above goal, for individuals on SGLT2i, consider incorporating a GLP-1 RA or vice versa
Goal: Achievement and Maintenance of Weight and Glycemic Goals
+Weight management
+Achievement and maintenance of glycemic goals
Efficacy for weight loss
Very high:
Semaglutide, tirzepatide
High:
Dulaglutide, liraglutide
Intermediate:
GLP-1 RA (not listed above), SGLT2i
Neutral:
Metformin, DPP-4i
Metformin or other agent (including combination therapy) that provides adequate EFFICACY to achieve and maintain glycemic treatment goals
Prioritize avoidance of hypoglycemia in high-risk individuals
Efficacy for glucose lowering
Very high:
Dulaglutide (high dose), semaglutide, tirzepatide, insulin
Combination oral, combination injectable (GLP-1 RA and insulin)
High:
GLP-1 RA (not listed above), metformin, pioglitazone, SGLT2i, sulfonylurea
Intermediate:
DPP-4i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OR
GLP-1 RA# with proven CKD benefit
If A1C is above goal, for individuals on SGLT2i, consider incorporating a GLP-1 RA or vice versa

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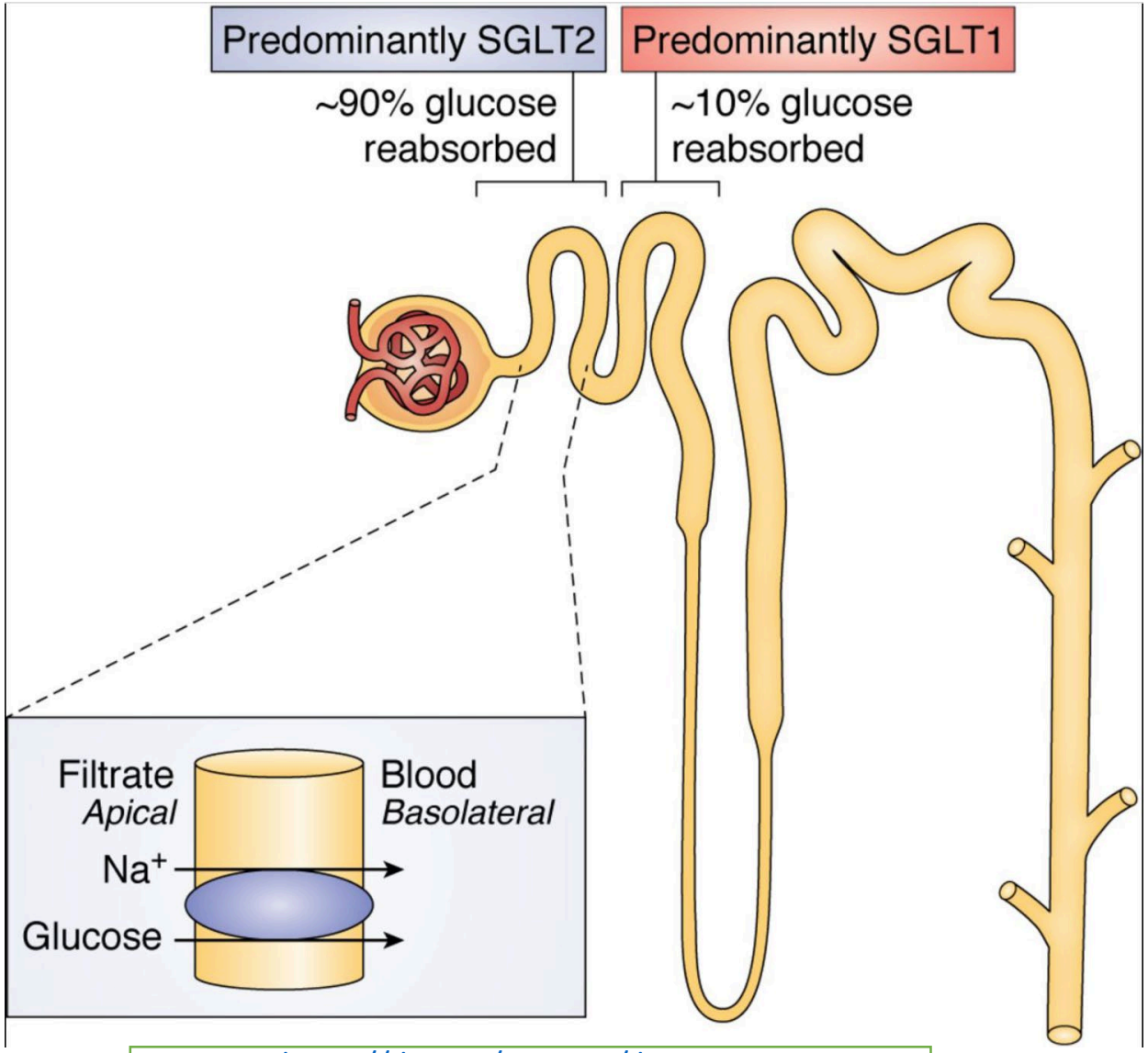
D. Sitagliptin
E. Basal insulin

In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT-2i with proven benefit should be made **irrespective of the A1c.**

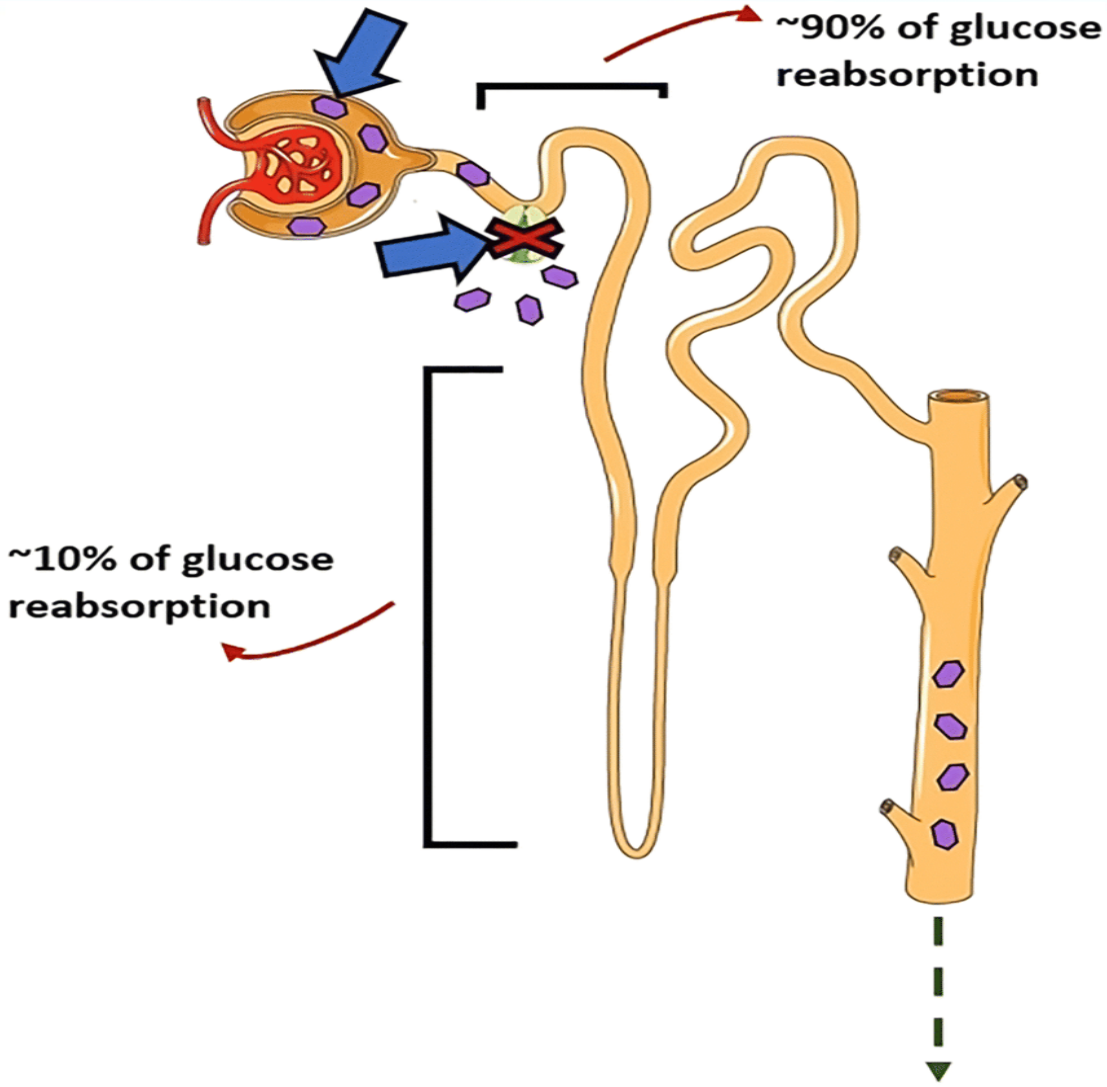
SGLT-2i have demonstrated their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, Hospitalization for HF, and kidney outcomes in individuals with T2DM and established or high risk CVD.

Mechanism of Action

SGLT2i



Perry et https://doi.org/10.1074/jbc.REV120.008387



Nashawi et al Heart Failure Reviews Jan 2022 DOI: 10.1007/s10741-020-09996-y

- At lower eGFR, SGLT2 inhibitors have reduced effect on glycosuria and glucose-lowering.
- Continue to have significant CV and renal risk reduction at low eGFR.
- SGLT2 inhibitors come in 2 dose levels.
- Glucose lowering effect is dose dependent
- Cardiorenal benefit is not dose dependent.

Low eGFR	High eGFR
CV/Renal benefit	CV/Renal benefit
	Glucose lowering benefit

Contraindications/Precautions/Adverse Effects

SGLT2i

- SGLT2 inhibitors should not be used specifically for the treatment of hyperglycemia in patients with:
- Type 1 diabetes
- Type 2 diabetes and eGFR <45 mL/min/1.73 m^2 (ertugliflozin), or

  <30 mL/min/1.73m^2 (empagliflozin, canagliflozin, dapagliflozin)
- Prior diabetic ketoacidosis (DKA)

- Increased risk of genital mycotic infections and urinary tract infections.
- Also, reports of fatal
  - Urosepsis and pyelonephritis
  - Necrotizing faciitis of the perineum (Fournier's gangrene)
- Volume loss

Monitor for signs of dehydration eg. lightheadedness, dizziness. Blood pressure and kidney function should be monitored.

Bersoff-Matcha et al Ann Intern Med. 2019;170(11):764. Epub 2019 May 7.
Nyirjesy P et al Curr Med Res Opin. 2012 Jul;28(7):1173-8. Epub 2012 Jun 14.

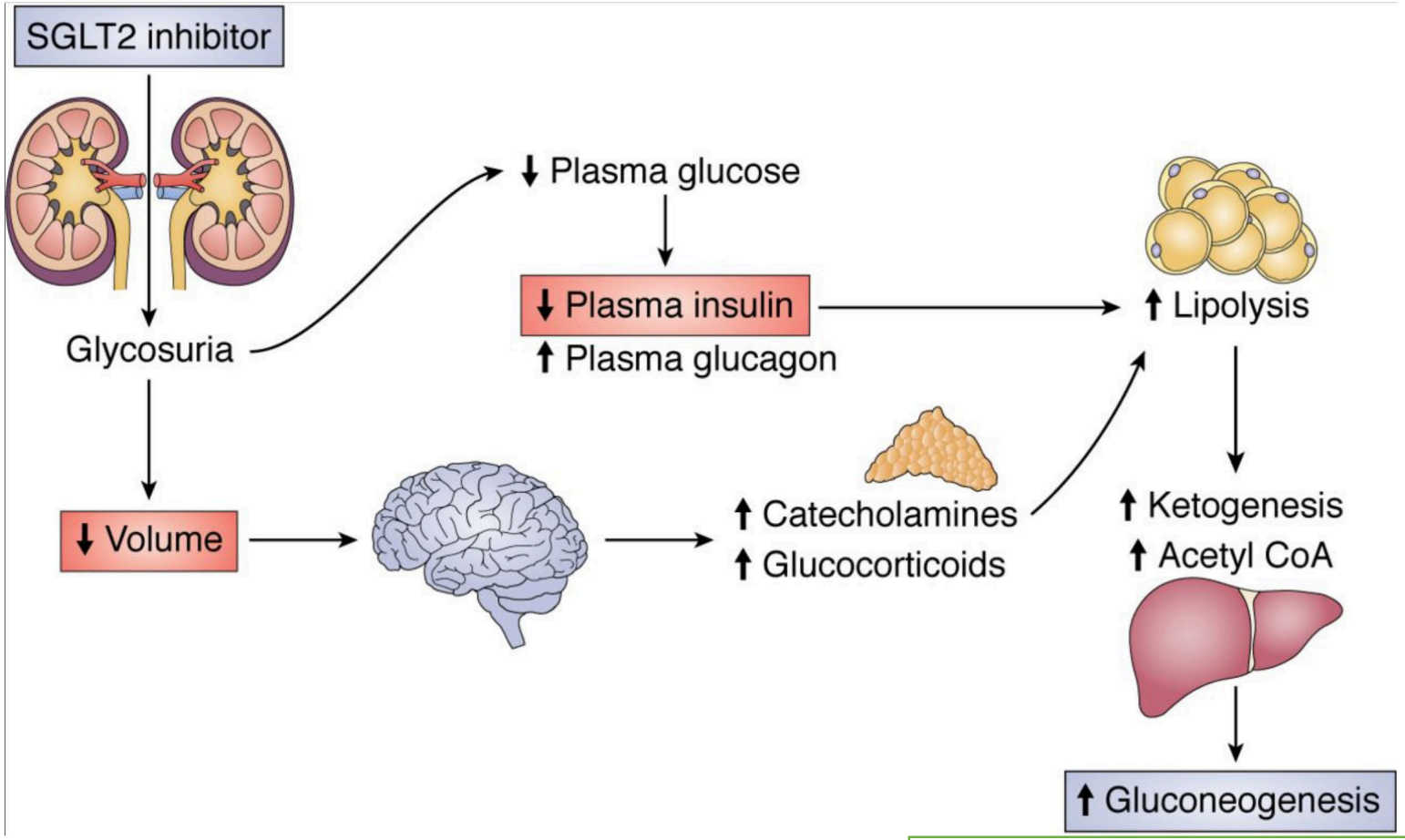
- Lower extremity amputation

Should be used with caution in patients with risk factors for foot ulceration (eg, neuropathy, foot deformity, vascular disease, and/or history of previous foot ulceration).

Monitor for signs and symptoms of foot ulceration.

Shi Q et al BMJ. 2023;381:e074068. Epub 2023 Apr 6.

DKA with SGLT2i



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Diabetic Ketoacidosis

- Euglycemic - plasma glucose <250 mg/dL
- Absence of substantial hyperglycemia delays the diagnosis
- Off-label use in type 1 diabetes is NOT recommended.
- Counsel about symptoms (eg, fatigue, myalgias, nausea, and emesis) -> perform urine ketone monitoring.
- SGLT2 inhibitors should be withheld during times of increased DKA risk (eg, infection, hospitalization, or surgery).

Marilly E et al Diabetologia. 2022;65(12):2000. Epub 2022 Aug 4

Clinical Factors to consider

- DKA risk in individuals with insulin deficiency
- Diminish the risk with sick day rule
- Discontinue before scheduled surgery (3-4 days), during critical illness, or during prolonged fasting
- Genital mycotic infections - Diminish the risk with genital hygiene
- Intravascular volume depletion – Adjust other volume-contracting agents as applicable.
- Monitor kidney function and blood pressure on initiation.

Resource Links

- Please share your resources here!
  Please make sure the links work!

Questions?

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