# Evidence Review on SGLT2 Inhibitors in Patients with Chronic Kidney Disease and Diabetes

## Overview

SGLT2 inhibitors are antidiabetic medications that provide not only glucose-lowering effects but also significant renal and cardiovascular protection. They are now strongly recommended for patients with type 2 diabetes and chronic kidney disease (CKD), heart failure, or established cardiovascular disease—even independent of HbA1c levels.

## Key SGLT2 Inhibitor Agents

- Empagliflozin
- Dapagliflozin
- Canagliflozin
- Ertugliflozin

## Renal Outcomes

- SGLT2 inhibitors slow CKD progression and **reduce the risk of end-stage kidney disease (ESKD)**.
- Major trials:
    - **DAPA-CKD**: ~39% reduction in composite renal outcomes (eGFR decline, kidney failure, CV/renal death).
    - **CREDENCE**: 30% reduction in kidney outcomes in diabetic patients with albuminuria.
- Dapagliflozin showed benefit even in **non-diabetic CKD patients**.

## Cardiovascular Benefits

- Reduce **hospitalizations for heart failure** (HFrEF and HFpEF) by ~30%.
- **Empagliflozin** and **dapagliflozin** demonstrated **CV mortality reduction** in trials like EMPEROR-Reduced and DAPA-HF.
- Moderate reduction in MACE (major adverse cardiovascular events) in patients with **ASCVD**.

## Clinical Guidelines

- Recommended in patients with T2D and **eGFR ≥20 mL/min/1.73 m²**.
- Can be **initiated early**, even before metformin, if high cardiorenal risk is present.
- **ADA** and **KDIGO** endorse their use in CKD/diabetic patients with or without albuminuria.

## Mechanism of Benefit

- Reduce **intraglomerular pressure** and restore tubuloglomerular feedback.
- Promote **glycosuria** and **natriuresis**, decreasing blood pressure and weight.
- Decrease **albuminuria**, oxidative stress, and inflammation—protecting kidney structure and function.
- Effects are largely **independent of glucose control**.

## Safety Considerations

- Generally **well tolerated** but watch for:
  - **Volume depletion** (especially in older patients or those on diuretics)
  - **Genital infections** (e.g., mycotic infections)
  - Rare **euglycemic diabetic ketoacidosis (DKA)** in insulin-dependent or catabolic states
- Not recommended for:
  - Type 1 diabetes
  - Recurrent UTIs
  - eGFR <20 mL/min/1.73 m² (initiation phase)
- Monitor:
  - **eGFR** and **electrolytes**
  - **Hydration status** and **ketoacidosis symptoms** in at-risk patients

## Clinical Application Summary

| Patient Profile | Recommendation |
|---|---|
| T2D + CKD (eGFR ≥20) | Start SGLT2 inhibitor even if HbA1c at target |
| T2D + Heart Failure (HFrEF or HFpEF) | Preferred over other oral agents |
| ASCVD + CKD | Consider combo with GLP-1 RA for additive effect |

| Patient Profile | Recommendation |
| --- | --- |
| On diuretics/elderly | Monitor volume status |