



Pharmacy Pearls

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SGLT-2 Inhibitors: A refresher on indications

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Sodium-Glucose Cotransporter-2 (SGLT-2) Inhibitors

- Reduce HbA1c up to 1% in patients with T2DM and preserved renal function, primarily by blocking reabsorption of glucose in the proximal convoluted tubule
 - Glucose-lowering is attenuated in patients with eGFR <60 mL/min/1.73 m², and minimal <30 mL/min/1.73 m²
- Reduce BP approximately 3-6 mmHg (SBP) and 1-2 mmHg (DBP) through several mechanisms
 - BP reduction is generally observed regardless of HTN status and eGFR
- Reduce weight by an average of 2-3 kg, through several mechanisms including urinary glucose excretion and diuresis

Monitor kidney function and volume status during treatment- initial decrease in eGFR (up to 30%) may be seen but generally stabilizes and does not warrant discontinuation

Indications for US-Approved SGLT-2 Inhibitors

Medication	Indications	Off-Label Uses
Canagliflozin (Invokana®)	<ul style="list-style-type: none"> • Improve glycemic control in adults with T2DM • ↓risk of MACE in adults with T2DM and established CVD • ↓risk of ESRD, doubling of SCr, CV death, and HF hospitalization in adults with T2DM and urinary albumin excretion >300 mg/day 	--
Dapagliflozin (Farxiga®)	<ul style="list-style-type: none"> • Improve glycemic control in adults with T2DM • ↓risk of HF hospitalization in pts with T2DM and established CVD or multiple risk factors • ↓risk of CVD death and HF hospitalization in adults with HF rEF class II-IV • ↓risk of sustained eGFR decline, ESRD, CV death, and HF hospitalization in adults with CKD 	• HFpEF
Empagliflozin (Jardiance®)	<ul style="list-style-type: none"> • Improve glycemic control in adults with T2DM • ↓risk of CV mortality in pts with T2DM and established CVD • ↓risk of CV mortality and HF hospitalization in adults with HF 	--
Ertugliflozin (Steglatro®)	<ul style="list-style-type: none"> • Improve glycemic control in adults with T2DM 	--

MACE: major cardiovascular events (CV death, nonfatal MI, and nonfatal stroke)

A Review of Evidence

- Jardiance® and Invokana® reached superiority in 3-point MACE in EMPA-REG and CANVAS studies, respectively.
- Invokana® and Farxiga® reached superiority in the reduction of poor renal outcomes in CANVAS-R and DECLARE-TIMI 58 studies, respectively.
- All SGLT2 inhibitors reached superiority in the reduction of heart failure hospitalization

Cost Savings Opportunity

For patients prescribed a DPP-4 inhibitor (Januvia®, Tradjenta®, Onglyza®, Nesina) as well as a SGLT-2 inhibitor, consider one of the combination products listed below instead. This offers patients cost savings at the pharmacy (2 copays instead of 1).

Combination Product Available

Dapagliflozin + saxagliptin (Qtern®)
Dapagliflozin + saxagliptin + metformin (Qternmet® XR)
Empagliflozin + linagliptin (Glyxambi®)
Empagliflozin + linagliptin + metformin (Trijardy® XR)
Ertugliflozin + sitagliptin (Steglujan®)