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IN BRIEF

Empagliflozin *(Jardiance)* for Chronic Kidney Disease

The sodium-glucose cotransporter 2 (SGLT2) inhibitor empagliflozin (*Jardiance* – Boehringer Ingelheim/Lilly) is now FDA-approved to reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular death, and hospitalization in adults with chronic kidney disease (CKD) at risk of progression. It is also approved to improve glycemic control in patients ≥10 years old with type 2 diabetes, to reduce the risk of cardiovascular death and hospitalization for heart failure (HF) in adults with HF, and to reduce the risk of cardiovascular death in adults with type 2 diabetes and established cardiovascular disease.

OTHER SGLT2 INHIBITORS — The SGLT2 inhibitors canagliflozin *(Invokana)* and dapagliflozin *(Farxiga)* are also approved to improve renal outcomes (see Table 1). The SGLT2 inhibitors ertugliflozin *(Steglatro)* and bexagliflozin *(Brenzavvy)* and the SGLT1/2 inhibitor sotagliflozin *(Inpefa)* have not been approved by the FDA for any renal indications.[1-3]

Table 1. Renal Indications for SGLT2 Inhibitors

Canagliflozin *(Invokana)*

- To reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for HF in adults with type 2 diabetes and diabetic nephropathy with albuminuria

Dapagliflozin *(Farxiga)*

- To reduce the risk of sustained eGFR decline, end-stage kidney disease, CV death, and hospitalization for HF in adults with CKD at risk of progression

Empagliflozin *(Jardiance)*

- To reduce the risk of sustained eGFR decline, end-stage kidney disease, CV death, and hospitalization in adults with CKD at risk of progression

CKD = chronic kidney disease; CV = cardiovascular; HF = heart failure

CLINICAL STUDIES — Approval of the new indication for empagliflozin was based on the results of a double-blind trial (EMPA-KIDNEY) in 6609 patients (with or without type 2 diabetes) with CKD (eGFR ≥20-<45 mL/min/1.73 m², or eGFR ≥45-<90 mL/min/1.73 m² with a urine albumin-to-creatinine ratio ≥200 mg/g). Patients were randomized to receive empagliflozin 10 mg or placebo once daily in addition to a renin-angiotensin system inhibitor. Over a median follow-up of 2 years, the incidence of the primary endpoint, a composite of progression

Table 2. EMPA-KIDNEY Clinical Trial Results[1]

Endpoint	Empagliflozin (n=3304)	Placebo (n=3305)
Progression of kidney disease or CV death[2]	13.1%*	16.9%
Hospitalization for HF or CV death	4.0%	4.6%
All-cause hospitalization[3]	24.8 events/100 patient-years*	29.2 events/100 patient-years
All-cause mortality	4.5%	5.1%
Progression of kidney disease	11.6%	15.2%
CV death	1.8%	2.1%
End-stage kidney disease or CV death	4.9%	6.6%

*Statistically significant difference vs placebo; CV = cardiovascular; HF = heart failure

1. Includes patients with or without type 2 diabetes. About 86% of patients were taking a renin-angiotensin system inhibitor. The EMPA-KIDNEY Collaborative Group. N Engl J Med 2023; 388:117.
2. The primary endpoint. Progression of kidney disease was defined as end-stage kidney disease, a sustained decrease in eGFR to <10 mL/min/1.73 m², a sustained decrease in eGFR of ≥40% from baseline, or death from renal causes.
3. Hospitalizations included first and all subsequent events.

Table 3. Dosage and Cost of SGLT2 Inhibitors with Renal Indications

Drug	Usual Adult Dosage[1]	Cost[2]
Canagliflozin – *Invokana* (Janssen)	100 mg PO once/day[3]	$598.60[4]
Dapagliflozin – *Farxiga* (AstraZeneca)	10 mg PO once/day[5]	565.30
Empagliflozin – *Jardiance* (Boehringer Ingelheim/Lilly)	10 mg PO once/day	593.30

1. Dosage for renal indication. Higher doses may be needed for glycemic control. SGLT2 inhibitors should be taken in the morning to avoid nocturia. Dapagliflozin and empagliflozin can be taken with or without food; canagliflozin should be taken before the first meal of the day.
2. Approximate WAC for 30 days' treatment. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. October 5, 2023. Reprinted with permission by First Databank, Inc. All rights reserved. ©2023. www.fdbhealth.com/drug-pricing-policy.
3. Initiation is not recommended in patients with an eGFR <30 mL/min/1.73 m². Patients with albuminuria >300 mg/day may continue taking 100 mg/day to reduce the risk of end-stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure.
4. The cost of a 30-day supply, excluding shipping and handling, from Mark Cuban Cost Plus Drug Company (www.costplusdrugs.com) is $245.92. Accessed October 26, 2023.
5. Initiation is not recommended in patients with an eGFR <25 mL/min/1.73 m².

of kidney disease or cardiovascular death, was statistically significantly lower with empagliflozin than with placebo. The rate of hospitalization for any cause was also statistically significantly lower with empagliflozin than with placebo, but the rates of all-cause mortality and a composite of hospitalization for heart failure or cardiovascular death were not (see Table 2).[4]

No trials directly comparing the renal benefits of empagliflozin with those of canagliflozin or dapagliflozin are available.

ADVERSE EFFECTS — SGLT2 inhibitors, including empagliflozin, can increase the risk of genital mycotic infection, urinary tract infection, volume depletion, hypotension, and ketoacidosis in patients with type 2 diabetes. In EMPA-KIDNEY, lower limb amputations occurred in 28 patients in the empagliflozin group and in 19 of those in the placebo group.

DOSAGE, ADMINISTRATION, AND COST — The recommended dosage of empagliflozin for all indications is 10 mg taken once daily in the morning. The dose can be increased to 25 mg in patients who need additional glycemic control. ■

1. Drugs for type 2 diabetes. Med Lett Drugs Ther 2022; 64:177.
2. Bexagliflozin (Brenzavvy) – a fifth SGLT2 inhibitor for type 2 diabetes. Med Lett Drugs Ther 2023; 65:130.
3. Sotagliflozin (Inpefa) for heart failure. Med Lett Drugs Ther 2023; 65:114.
4. The EMPA-KIDNEY Collaborative Group. Empagliflozin in patients with chronic kidney disease. N Engl J Med 2023; 388:117.