

Invokana® (canagliflozin) – New indication

- On September 27, 2019, [Janssen announced](#) the FDA approval of [Invokana \(canagliflozin\)](#), to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus (T2DM) and diabetic nephropathy with albuminuria > 300 mg/day.
- Invokana is also approved:
 - As an adjunct to diet and exercise to improve glycemic control in adults with T2DM
 - To reduce the risk of major adverse CV events (CV death, nonfatal myocardial infarction and nonfatal stroke) in adults with T2DM and established CV disease.
- In the U.S., one in three people with T2DM has diabetic nephropathy, which multiplies the risk of CV complications including heart failure and CV death, and puts patients on a trajectory to dialysis and kidney transplant. Additionally, heart failure is one of the leading causes of hospitalization.
- The approval of Invokana for the new indication was based on CREDENCE, a randomized, double-blind study in 4,401 patients with T2DM, an estimated glomerular filtration rate (eGFR) ≥ 30 to < 90 mL/min/1.73 m² and albuminuria who were receiving standard of care. Patients received Invokana or placebo. The primary composite endpoint was the time to first occurrence of ESKD (defined as an eGFR < 15 mL/min/1.73 m², initiation of chronic dialysis or renal transplant), doubling of serum creatinine, and renal or CV death.
 - Invokana significantly reduced the risk of the primary composite endpoint based on a time-to-event analysis (hazard ratio [HR]: 0.70; 95% CI: 0.59, 0.82; $p < 0.0001$). The treatment effect reflected a reduction in progression to ESKD, doubling of serum creatinine, and CV death.
 - Invokana also significantly reduced the risk of hospitalization for heart failure (HR: 0.61; 95% CI: 0.47, 0.80; $p < 0.001$).
- In addition to the approval of this new indication, the warning for increases in low-density lipoprotein was removed from the *Warnings and Precautions* section of the Invokana label.
- Invokana carries a boxed warning for lower limb amputation.
- The recommended dose of Invokana for all indications is based on eGFR. In patients with eGFR ≥ 60 mL/min/1.73 m², the recommended initial dose is 100 mg orally once daily, taken before the first meal of the day. The dose can be increased to 300 mg once daily for additional glycemic control. In patients with eGFR 30 to < 60 mL/min/1.73 m², the recommended dose is 100 mg once daily.