

Description	VERTIS-CV	CREDENCE	DAPA-CKD	DAPA-HF	EMPEROR-Reduced
Drug	Ertugliflozin	Canagliflozin	Dapagliflozin	Dapagliflozin	Empagliflozin
N	8,238	4,401	4,304	4,744	3,730
Study Dose	5mg, 15mg	100mg	10mg	10mg	10mg
% with diabetes	100%	100%	67.5%	42%	49.8%
Median follow up	3.5 years	2.6 years	2.4 years	1.5 years	1.3 years
ACEI/ARB (%)	6705 (81.4)	4395 (100)	4174(97)	3,968 (84)	2600 (70)
MRA (%)	6705 (81.4)	--	229 (5)	3,370 (71)	2661 (71)
ARNi	675 (8.2%)	--	3 (0.1)	508 (11)	727 (19)
Metformin	6285 (76.3)	2545 (58)	1250 (29)	1,016 (51)	
Entry eGFR (lower limit)	30ml/1.73m ²	eGFR 30ml/1.73m ²	eGFR ≥25 and ≤75 mL/min/1.73m ²	eGFR 30ml/1.73m ²	eGFR <20 mL/min/1.73m ² or requiring dialysis
eGFR threshold/ criteria for drug discontinuation	eGFR <15 mL/min/1.73m ²	Initiation of dialysis or kidney transplantation	Initiation of dialysis or kidney transplantation	No specific GFR cut-off for drug discontinuation	Initiation of dialysis or kidney transplantation
Baseline urine ACR (mg/g)(%)	≥300: 754 (9.2) 30-300: 2486 (30.2)	>300: 3874 (88) 30-300: 496 (11)	>300: 3859 (90) 30-300: 444 (10)	--	
Baseline(%) established CVD	8236 (99.9)	2220 (50)	1610 (37)	4744 (100) HF	3730 (100) HF

OUTCOMES	VERTIS-CV	CREDESCENCE	DAPA-CKD	DAPA-HF	EMPEROR-Reduced
CV death, nonfatal myocardial infarction, or nonfatal stroke	HR 0.97, 95% (0.85-1.11)	HR 0.80, 95% (0.67-0.95)	-	--	-
CV death	HR 0.92, 95% (0.77-1.11)	HR 0.78, 95% (0.61-1.00)	HR 0.81, 95% (0.58-1.13)	HR 0.82, 95% (0.69 to 0.98)	HR 0.92, 95% (0.75-1.12)
Hospitalization for heart failure	HR 0.70, 95% (0.54-0.90)	HR 0.61, 95% (0.47-0.80)	-	HR 0.70, 95% (0.59-0.83)	HR 0.70, 95% (0.58-0.85)
CV death or hospitalization for heart failure	HR 0.88, 95% (0.75-1.03)	HR 0.69, 95% (0.57-0.83)	HR 0.71, 95% (0.55-0.92)	HR 0.75, 95% (0.65-0.85)	HR 0.75, 95% (0.65-0.86)
All cause mortality	--	HR 0.83, 95% (0.68-1.02)	HR 0.69, 95% (0.53-0.88)	HR 0.83, 95% (0.71-0.97)	HR 0.92, 95% (0.77-1.10)
Kidney composite outcome Definition	Renal death, dialysis/transplant or doubling of serum creatinine	end stage kidney disease, doubling of serum creatinine, death due to kidney disease	>sustained decline in the eGFR of 50% or greater, end-stage , or death due to kidney failure	sustained decline in the eGFR of 50% or greater, end-stage kidney disease, dialysis, or kidney transplantation	chronic dialysis or renal transplantation sustained reduction of ≥40% in estimated GFR; sustained estimated GFR <15 mL (baseline ≥30) or <10 mL (baseline <20) mL
Kidney composite outcome hazard ratio	HR 0.81, 95% (0.63-1.04)	HR 0.70, 95% (0.59-0.82)	HR 0.56, 95% (0.45–0.68)	HR 0.71, 95% (0.44 to 1.16)	HR 0.50, 95% (0.32 to 0.77)

Indication	Canagliflozin	Empagliflozin	Dapagliflozin	Ertugliflozin
Antidiabetic indication	Adjunct to diet and exercise for improved glycemic control in T2DM	Adjunct to diet and exercise for improved glycemic control in T2DM	Adjunct to diet and exercise for improved glycemic control in T2DM	Adjunct to diet and exercise for improved glycemic control in T2DM
Cardiovascular indication	Reduction in CV death, nonfatal MI, and nonfatal stroke in T2DM with established CVD	Reduction in CV death risk in T2DM with established CVD	Reduction in risk of heart failure hospitalization in patients with T2DM and established CVD/multiple CV risk factors	---
Renal indication	To reduce risk of ESKD, doubling of serum creatinine, cardiovascular death and hospitalization for heart failure in T2DM and diabetic nephropathy with albuminuria	---	---	---

Composite evidence suggests that SGLT-2 inhibitors appear safe down to eGFR 30 cc/min/1.73m²

SGLT2i have not been adequately studied in dialysis and should be discontinued at dialysis initiation

Individual eGFR-specific thresholds differ by therapy and therapeutic label (please see updated FDA drug labels)

**The manuscript reviewed data up to March 31, 2020. This table lists FDA approved indications for various SGLT2 inhibitors as of September 1, 2020. The FDA has also eliminated the black box warning for foot and leg amputations for canagliflozin on August 26, 2020.*

Abbreviation list:

- VERTIS-CV - Evaluation of Ertugliflozin Efficacy and Safety Cardiovascular Outcomes Trial
- CREDENCE - Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy
- DAPA-CKD - Dapagliflozin and Prevention of Adverse outcomes in Chronic Kidney Disease
- DAPA-HF - Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction
- EMPEROR-Reduced - Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure
- ACEI/ARB – angiotensin converting enzyme inhibitors/angiotensin receptor blockers
- MRA- mineralocorticoid receptor antagonists
- ARNi-angiotensin receptor neprilysin inhibitors
- eGFR – estimated glomerular filtration rate
- ACR – albumin creatinine ratio
- CV/CVD – cardiovascular/cardiovascular disease
- FDA: Food and Drug Administration
- SGLT2: Sodium glucose co-transporter 2