Sodium Glucose Co-Transporters-2 Inhibitors (SGLT-2i) Comparison Chart

Diabetes Specialist Nurse Forum UK

	Empagliflozin (Jardiance)	Dapagliflozin (Forxiga)	Canagliflozin (Invokana)	Ertugliflozin (Steglatro)
Distributer	Boehringer-Ingelheim & Eli-Lilly	AstraZeneca	A. Menarini Farmaceutica Internazionale SRL	Merck Sharp & Dohme (UK) Limited
Randomised controlled trials (CVOT, Renal and HF)	EMPA-REG OUTCOME, EMPEROR-Reduced, EMPEROR-Preserved, EMPA-KIDNEY	DECLARE-TIMI 58, DAPA-HF, DAPA-CKD, DELIVER	CANVAS AND CANVAS-R, CREDENCE	VERTIS CV
Licenced in T2D under the age of 18 years	No	Yes - Aged 10 years old and above.	No	No
Licenced dose for glucose lowering in T2D	Initiate 10mg OD & continue Can titrate to 25mg OD (see page 3)	Initiate 10mg OD & continue	Initiate 100mg OD & continue Can titrate to 300mg OD (see page 3)	Initiate 5mg OD & continue Can titrate to 15mg OD (see page 3)
Licenced dose for chronic kidney disease	Initiate 10 mg OD & continue	Initiate 10mg OD & continue	In T2D with diabetic kidney disease as add on to standard of care. Initiate 100mg OD.	Not licenced
Licenced dose for symptomatic chronic heart failure	Initiate 10 mg OD & continue	Initiate 10mg OD & continue	Not licenced	Not licenced
eGFR for initiation	> 20 mL/min/1.73m2	>15 mL/min/1.73m2	> 30 mL/min/1.73m2	> 45 ml/min/1.73m2
Glucose lowering efficacy based on eGFR	Glucose lowering efficacy is reduced in people with eGFR < 45ml/min & likely absent when eGFR < 30 ml/min. Additional glucose lowering therapies should be considered in people with T2D when eGFR is persistently < 45 ml/min & HbA1c is above the individualised target.			
Hypoglycaemia risk	Low risk unless used as add-on therapy with insulin or an insulin secretagogue (SU). Dose reduction of concomitant insulin and/or SU may be required in a step wise approach when starting an SGLT2i to avoid hypoglycaemia			
Contraindications	Hypersensitivity to the active substance or to any of the excipients (tablets contain lactose). Type 1 diabetes .Pregnancy and breast feeding			
Common side effects	Mycotic genital infections (vulvovaginal candidiasis, balanitis, balanoposthitis). Urinary tract infection			
When to pause or interrupt treatment in people with T2D	Acute illness including nausea/vomiting/dehydration, prior to surgery or procedure requiring starvation (as per local guidance), acute admission to hospital, ketoacidosis, urinary tract infections. Pre-conception care			
Advice to give when initiating and reviewing therapy	Maintain adequate hydration and fluid intake. Illness management advice and when to pause treatment. Good personal/genital hygiene. Seek treatment for any mycotic genital infections			

CVOT= cardiovascular outcome trials OD= once daily, T2D= type 2 diabetes, DKA= diabetic ketoacidosis, HF = heart failure, CKD= chronic kidney disease, DKA = diabetic ketoacidosis, LLA = lower limb amputations
Please refer to the individual SmPC for full details

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Generic (brand) name	Empagliflozin (Jardiance)	Dapagliflozin (Forxiga)	Canagliflozin (Invokana)	Ertugliflozin (Steglatro)
Special considerations/cautions (Euglycaemic DKA)	Euglycaemic DKA is a rare complication (1 in 10,000 people) associated with the use of SGLT-2 inhibitors in people with T2D. People who may be at higher risk of ketoacidosis include those with low beta-cell function reserve (e.g., T2D with low C-peptide or latent autoimmune diabetes in adults (LADA) or patients with a history of pancreatitis). Those with conditions that lead to restricted food intake or severe dehydration (e.g., Ketogenic diet, alcohol abuse, eating disorders, fasting prior to elective surgery or procedures requiring NBM). Those with increased insulin requirements due to acute medical illness and/or admission to hospital. Restarting SGLT2 inhibitor treatment in patients with previous ketoacidosis while on SGLT2 inhibitor treatment is not recommended, unless another clear precipitating factor is identified and resolved. Refer to individual SmPC for detailed information.			
Special considerations/cautions (Lower Limb Amputations)	It is important to counsel patients on routine preventative foot-care.	It is important to counsel patients on routine preventative foot-care.	The CANVAS trial showed a higher incidence of LLA (mainly toes) in people with T2D who had established CVD or had 2 or more CVD risk factors. Regardless of treatment with canagliflozin or placebo, the risk of amputation was highest in patients with a history of prior amputation, peripheral vascular disease, and neuropathy. The risk of lower limb amputation was not dose-dependent. The CREDENCE trial did not replicate these findings.	It is important to counsel patients on routine preventative foot-care.
Special considerations/cautions (Fournier's Gangrene)	Necrotising fasciitis of the perineum, (Fournier's gangrene), has been reported in female and male patients with T2D taking SGLT2 inhibitors, but is very rare. It is difficult to know if it is directly related to SGLT2 inhibitors as people with T2D are already predisposed to Fournier's gangrene (FG). Other risk factors include obesity, atherosclerosis and peripheral vascular disease, which are highly prevalent in people with T2D. FG is a rare but serious and potentially life-threatening event that requires urgent surgical intervention and antibiotic treatment. SGLT2 inhibitor treatment should be stopped if FG is suspected or diagnosed.			
Dose adjustment in hepatic impairment	No dose adjustment is required for patients with hepatic impairment. Avoid in severe hepatic impairment	No dose adjustment in mild or moderate. In severe hepatic impairment, initiate 5 mg OD & if well tolerated, the dose may be increased to 10 mg.	No dose adjustment in mild or moderate. Avoid in severe hepatic impairment.	No dose adjustment in mild or moderate. Avoid in severe hepatic impairment.
Use in the elderly	Elderly patients may be at a greater risk for volume depletion and are more likely to be treated with diuretics. Elderly patients are more likely to have impaired renal function, and/or to be treated with anti-hypertensive medicinal products that may cause changes in renal function such as angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin II type 1 receptor blockers (ARB).			

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Licence indications and dose adjustments based on eGFR

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SGLT-2 inhibitor	Licence indication	eGFR (ml/min/1.73 m2)					
		≥ 60	59-45	44-30 *	< 30 *	< 20 *	< 15 *
Canagliflozin (Invokana)	Glucose lowering in T2D	Start 100mg OD & can increase to 300mg	Start & continue 100mg		Continue until dialysis or renal transplantation, if ACR is > 30 mg/mmol. No new initiations if eGFR < 30		
Dapagliflozin (Forxiga)	Glucose lowering in T2D	Start 10mg OD & continue					Continue 10mg OD No new initiations if eGFR < 15
	Symptomatic chronic HF						
	CKD						
Empagliflozin (Jardiance)	Glucose lowering in T2D	Start 10mg OD & can increase to 25mg	Start 10mg OD & continue			Continue 10mg OD No new initiations if eGFR < 20	
	Symptomatic chronic HF	Start 10mg OD & continue					
	CKD						
Ertugliflozin (Steglatro)	Glucose lowering in T2D	Start 5mg OD & can increase to 15mg		Continue 5mg OD or 15mg if already initiated No new initiations	Not recommended if eGFR < 30		

*** The glucose lowering efficacy is dependent on renal function & is reduced in people with eGFR < 45ml/min & likely absent when eGFR < 30 ml/min.**
Additional glucose lowering therapies should be considered in people with T2D when eGFR is persistently < 45 ml/min & HbA1c is above the individualised target.

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