

Patient Advice

- Risk of Euglycaemic Ketoacidosis (EKA) and symptoms (vomiting, nausea, abdominal pain, a sweet smell to the breath, confusion etc) and seek urgent medical help- A&E, 999.
- Sick day rules – stop temporarily during acute illness, reduced intake food/fluids, vomiting or diarrhoea.
- Common adverse reactions such as polyuria, genital infection UTI, and Balanitis.
- It is important to counsel patients with diabetes on routine preventative foot care.
- Fournier's gangrene: patients should be advised to seek medical attention if they experience a combination of symptoms of pain, tenderness, erythema, or swelling in the genital or perineal area, with fever or malaise. Be aware that either uro-genital infection or perineal abscess may precede necrotising fasciitis.

Checklist (Cautions)

- Prior amputation, severe peripheral neuropathy, severe peripheral vascular disease, or active diabetic foot ulcers.
- History of organ transplantation.
- History of recurrent mycotic genital tract infection.
- At risk of significant volume depletion and hypotension: may add to the diuretic effect of thiazide and loop diuretics, increased risk of dehydration and hypotension (SBP < 95 mmHg).
- History of pancreatitis, Type 3c DM*, LADA.
- History of alcohol abuse.
- Severe dehydration, sudden reduction in insulin, acute illness, surgery, previous episode of DKA.
- Very low carbohydrate/ketogenic diet.

CONTRAINDICATIONS: polycystic kidney disease or on immunological therapy for renal disease, Type 1 diabetes mellitus, previous DKA, pregnancy or breast feeding. SGLT2i should not be used in patients with ESRD or in patients on dialysis.

Disclaimer: information correct at time of publishing. This is not a comprehensive list of contra-indication or adverse reactions: please refer to individual [SPC](#) for more information.

Diabetes (from the relevant SPCs)

SGLT2i	eGFR [ml/min/1.73 m ²] or CrCl [ml/min]	Total daily dose
Empagliflozin	≥60	Initiate with 10 mg empagliflozin. In patients tolerating 10 mg empagliflozin and requiring additional glycaemic control, the dose can be increased to 25 mg empagliflozin.
	45 to <60	Initiate with 10 mg empagliflozin. Continue with 10 mg empagliflozin in patients already taking empagliflozin.
	30 to <45	Initiate with 10 mg empagliflozin. Continue with 10 mg empagliflozin in patients already taking empagliflozin.
	<30	Empagliflozin is not recommended.
Dapagliflozin	The recommended dose is 10 mg dapagliflozin once daily. No dose adjustment is required based on renal function.	
	It is not recommended to initiate treatment with dapagliflozin in patients with an estimated glomerular filtration rate (eGFR) < 15 ml/min/1.73m ² .	
Canagliflozin	≥ 60	Initiate with 100 mg. In patients tolerating 100 mg and requiring additional glycaemic control, the dose can be increased to 300 mg.
	30 to < 60	Use 100 mg.
	< 30	Continue 100 mg for patients already taking Canagliflozin: with urinary albumin/creatinine ratio > 300 mg/g (30 mg/mmol) For new patients should not be initiated.
Ertugliflozin	>60	The recommended starting dose of ertugliflozin is 5 mg once daily. In patients tolerating ertugliflozin 5 mg once daily, the dose can be increased to 15 mg once daily if additional glycaemic control is needed.
	≥ 45 to < 60	Should be initiated at 5 mg and up-titrated to 15 mg as needed for glycaemic control.
	Ertugliflozin should be discontinued when eGFR is persistently less than 30 ml/min/1.73 m ² or CrCl is persistently less than 30 ml/min.	
	Initiation of this medicinal product is not recommended in patients with an estimated glomerular filtration rate (eGFR) less than 45 ml/min/1.73 m ² or CrCl less than 45 ml/min.	

Treatment doses for SGLT2i

Heart failure

Dapagliflozin & Empagliflozin are recommended as an option for treating symptomatic chronic heart failure with reduced ejection fraction in adults, only if used as an add-on to optimised standard care with:

- Angiotensin-converting enzyme (ACE) inhibitors or angiotensin-2 receptor blockers (ARBs), with beta blockers, and, if tolerated, mineralocorticoid receptor antagonists (MRAs), OR
- Sacubitril valsartan, with beta blockers, and, if tolerated, MRAs.

Initiation is on the advice of a heart failure specialist.

Dosage

- **Dapagliflozin:** 10 mg once daily
- **Empagliflozin:** 10 mg once daily. For treatment of heart failure in patients with or without type 2 diabetes mellitus, empagliflozin 10mg may be initiated or continued down to an **eGFR of 20 ml/min/1.73 m² or CrCl of 20 ml/min.**

CKD

Dapagliflozin 10 mg once daily is recommended as an option for treating chronic kidney disease (CKD) in adults. It is recommended only if:

- It is an add-on to optimised standard care including the highest tolerated licensed dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), unless these are contraindicated, AND
- People have an eGFR of 25 ml/min/1.73m² to 75 ml/min/1.73m² at the start of treatment and have type 2 diabetes or have a urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more.

It is not recommended to initiate treatment with dapagliflozin in patients with an eGFR < 25 ml/min/1.73m².

For adults with type 2 diabetes and CKD who are taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate), **consider an SGLT2 inhibitor (in addition to the ARB or ACE inhibitor) if: ACR is over 3 mg/mmol and offer if ACR is over 30mg/mmol**

Canagliflozin for treatment of diabetic kidney disease as add on to standard of care (e.g. ACE-inhibitors or ARBs):

- A dose of **100 mg canagliflozin once daily should be used and titrated if needed to 300 mg for glycaemic control and the eGFR >60 ml/min/1.73m².**
- For **eGFR 30-60 ml/min/1.73m², use 100mg.**
- If **eGFR is below 30 ml/min/1.73m² do not initiate** but continue 100 mg for patients already taking canagliflozin and continue dosing until dialysis or renal transplantation.

References & Acknowledgements

1. Empagliflozin SPC: <https://www.medicines.org.uk/emc/product/5441/smpc>
2. Dapagliflozin SPC: <https://www.medicines.org.uk/emc/product/7607/smpc>
3. Canagliflozin SPC: <https://www.medicines.org.uk/emc/product/8855/smpc>
4. Ertugliflozin SPC: <https://www.medicines.org.uk/emc/product/10099/smpc>
5. UK Kidney Association Clinical Practice Guideline: Sodium-Glucose Co-transporter-2 (SGLT-2) Inhibition in Adults with Kidney Disease
6. *Type 3c diabetes: <https://www.diabetes.org.uk/diabetes-the-basics/type-3c-diabetes>
7. Dapagliflozin for treating chronic kidney disease, Technology appraisal guidance [TA775] Published: 09 March 2022: <https://www.nice.org.uk/guidance/TA775/chapter/1-Recommendations>
8. Dapagliflozin for treating chronic heart failure with reduced ejection fraction
9. Technology appraisal guidance [TA679] Published: 24 February 2021: <https://www.nice.org.uk/guidance/ta679>
10. Empagliflozin for treating chronic heart failure with reduced ejection fraction: Technology appraisal guidance [TA773] Published: 09 March 2022: <https://www.nice.org.uk/guidance/ta773>

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