



Introduction, Purpose and Scope of Document

- SGLT2 inhibitors are an established class of medications for the treatment of type 2 diabetes and act by preventing the absorption of glucose and sodium, mainly from the proximal renal tubule in the kidney
- Glucose and sodium are, lost in urine resulting in a fall in blood glucose level, an osmotic diuresis, reduction in blood pressure and weight loss
- These drugs have been licensed and used widely in people with T2DM and have shown significant cardiovascular and renal benefits in different subsets of this group of patients
- These benefits are thought to be independent of blood glucose lowering
- Dapagliflozin has a NICE TA and is licensed for use in CKD in the UK. It is also licensed for HFrEF and T2DM – these indications are outside the scope of this document

Aims of this document:

- To guide prescribing of dapagliflozin within its current licence for the treatment of CKD
- To ensure that, where dapagliflozin is prescribed in a person for CKD, it is undertaken safely
- To ensure dapagliflozin is only prescribed for the appropriate patients and that the relevant information is given to patients to ensure safety

It is important to note this is only a guide and not exhaustive, appropriate clinical judgement and referral to other reference sources may be appropriate in individual patient cases.

Prescribing Dapagliflozin in CKD

When to consider dapagliflozin in CKD

NICE TA states dapagliflozin is recommended as an option for treating chronic kidney disease (CKD) in adults 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 estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73m² to 75 ml/min/1.73 m² 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



CONTRAINDICATIONS - AVOID in the following situations:

- **Patient Characteristics**
 - Age <18 years
 - Pregnant, breastfeeding, female in their child-bearing years and sexually active without contraception
 - Person with excess alcohol consumption or IVDU
 - History of allergic reaction to dapagliflozin or empagliflozin or any of their excipients
- **Current Medical History**
 - Acutely unwell person (acute medical illness including COVID-19, surgery or planned medical procedure)
 - Inpatient with acute vascular event who is not stable
 - Eating disorder
 - eGFR outside that allowed in the up-to-date licensing of the medication being considered
 - Already on SGLT2 for other co-morbidity
 - Organ transplant
 - Patients receiving dialysis
 - Polycystic kidney disease
- **Diabetes History**
 - Suspected or possible T1DM
 - Any diagnosis or suspicion of latent autoimmune diabetes (LADA), other genetic causes of diabetes, known pancreatic disease or injury, or people who rapidly progressed to needing insulin within 1 year of diagnosis
 - Past history of diabetic ketoacidosis



Use with CAUTION in the following situations:

- **Patient Characteristics**
 - People at risk of hypotension/hypovolaemia (e.g. on diuretic and/or multiple antihypertensive therapies, elderly)
 - Body mass index <25 kg/m² (<23 kg/m² in South Asian patients)
 - Person adhering to a ketogenic/low calorie/low carbohydrate diet (20-50g/day of carbohydrate or less than 10% of a 2000 kcal/day diet)
 - Recent weight loss
 - Potential for pregnancy
 - People diagnosed with or at risk of frailty
 - Cognitive impairment or use of medication compliance aid (as this *may* imply inadequate understanding required to follow sick day guidance and take action to prevent and identify DKA)
- **Other Past Medical History**
 - On long term or recurrent courses of steroids
 - Raised haematocrit
 - Severe hepatic impairment
 - Recurrent urinary or genital tract infections
 - Glomerulonephritis with flares (ANCA associated vasculitis or lupus nephritis) – consider discussion with nephrologist
 - Ongoing or recent requirements of cytotoxic, immunosuppressive or other immunomodulating renal therapy – consider discussion with nephrologist
- **Diabetes History**
 - Long duration of diabetes (generally over 10 years from diagnosis)
 - Person with very high level of HbA1c >86 mmol/mol
 - Person considered at high risk of acute effects of hyperglycaemia (e.g. dehydration due to non-adherence to medication)
 - Active foot disease and past history of active foot disease/foot ulceration – consider discussion with specialist, ensure regular preventative footcare
 - Existing diabetic foot ulcers
 - Previous lower limb amputation
 - History of peripheral arterial disease (PAD)
 - **Taking sulphonylureas and/or insulin – increased risk of hypoglycaemia if commenced on dapagliflozin**



Dapagliflozin in CKD Dosing

SGLT2 Inhibitors	Dose (When using in CKD)	Dose Adjustments (When using CKD)		
		eGFR 25-75 ml/min/1.73m ²	eGFR <25 ml/min/1.73m ²	Hepatic Impairment
Dapagliflozin PIL/SPC	10mg once daily. With or without food.	Initiate 10mg once daily.	Do not initiate. For those already on dapagliflozin can continue down to eGFR of 15ml/min, dialysis or transplantation.	No dose adjustment is necessary for patients with mild or moderate hepatic impairment. Use with caution in severe impairment (risk of increased exposure). See SPC for further information.



Patient Education – Sick Day Guidance

All patients should be counselled on initiation of dapagliflozin for CKD (by the initiating clinician) about sick day guidance and when to stop taking their dapagliflozin due to associated risks with dehydration and development of DKA:

- If ill with diarrhoea, UTI, vomiting, fever or unusual drowsiness, patient's should be advised to STOP dapagliflozin and not to restart until feeling better and eating/drinking fluids normally
 - Restart only AFTER eating normally for AT LEAST 24 HOURS AND no longer acutely unwell
 - Encourage patient to avoid dehydration with appropriate fluid intake
 - ALL patients must be counselled on the risk of ketoacidosis and signs and symptoms of this (nausea, vomiting, abdominal pain, stupor, fatigue, difficulty breathing) and to STOP SGLT2 inhibitor if any symptoms develop
 - To seek urgent medical attention if symptoms of Fournier's gangrene (e.g. severe pain, tenderness, erythema, swelling in genital or perineal area)
 - Seek medical advice if particularly unwell with infection or illness
 - Stop dapagliflozin prior to surgery—as advised by pre-op team
- Ensure patient has copy of patient information leaflet

Side Effects

Common:

- Increased risk of UTI
- Polydipsia
- Polyuria
- Fungal genital infections,
- Volume depletion effects (thirst, postural dizziness, hypotension, dehydration)
- Hypoglycaemia (increased risk if on sulphonylureas and/or insulin)
- Decreased eGFR

Uncommon but **serious**: (see MHRA alerts below)

- DKA
- Fournier's Gangrene
- Lower limb amputation – encourage regular preventative footcare

Please see individual drug monograph in BNF/SPC for a complete side-effect profile – see hyperlink in table overleaf.

Monitoring Requirements and Documentation

Monitoring – Additional monitoring after starting SGLT2 inhibitors is NOT recommended.

Routine monitoring of kidney function should continue as part of routine care, frequency based upon CKD stage, as per NICE CKD guidance, and in line with person's other co-morbidities as appropriate, **but additional routine tests are not recommended after starting dapagliflozin.**

People with T2DM

- Patients with T2DM who are commenced on dapagliflozin for CKD may require adjustment to their other glucose lowering medication and closer monitoring of HbA1c/capillary blood glucose following initiation of dapagliflozin due to the potential for hypoglycaemia.
 - For patients with a HbA1c on initiation of dapagliflozin of <48mmol/mol or if HbA1c falls to <48mmol/mol during treatment with dapagliflozin concurrent diabetes medication should be promptly reviewed to prevent risk of hypoglycaemia
 - **There is an increased risk of hypoglycaemia when dapagliflozin is used alongside sulphonylureas and/or insulin**
- It is worth noting that due to its mechanism of action patients on dapagliflozin will test positive for glucose in their urine

Documentation

It must be clearly documented on the patient's medical record that the primary indication for dapagliflozin is CKD and not T2DM or HF to ensure follow up and monitoring is appropriate. Though it should be noted some patients may have multiple conditions for dapagliflozin will confer benefit.

Contacts and Communication Links

- For CCGs served by South Tees Renal Service, advice can be sought via: stees.renal@nhs.net
- For CCGs served by Newcastle upon Tyne Renal Service advice can be sought via electronic referral, 'Advice and Guidance' to Nephrology
- For CCGs served by Sunderland Renal Service, advice can be sought via electronic referral, 'Advice and Guidance' to Nephrology
- For CCGs served by North Cumbria Integrated Care/Renal Service, advice can be sought via usual referral process

Additional Important Safety Information

Additional Important safety information – Please see hyperlinks for more detailed advice:

- [MHRA/CHM advice \(updated April 2016\): SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis \(DKA\)](#)
 - People should be informed on the signs and symptoms of DKA, discontinue treatment with the SGLT2 inhibitor immediately if DKA is suspected or diagnosed
 - Test for raised ketones in patients with ketoacidosis symptoms, even if plasma glucose levels are near-normal
- [MHRA/CHM advice \(MHRA/CHM advice March 2017\): SGLT2 inhibitors: updated advice on increased risk of lower-limb amputation \(mainly toes\)](#)
 - SGLT2i's may increase the risk of lower-limb amputation (mainly toes). All people taking an SGLT2i should be counselled on good preventive foot care. Review if lower limb complications develop (e.g. skin ulcer, osteomyelitis, or gangrene). Monitor people with risk factors for amputation.
- [MHRA/CHM advice: SGLT2 inhibitors: reports of Fournier's gangrene \(necrotising fasciitis of the genitalia or perineum\) \(February 2019\)](#)
 - If Fournier's gangrene is suspected, stop the SGLT2 inhibitor and urgently start treatment (including antibiotics and surgical debridement as required)
 - Fournier's gangrene is a rare but potentially life-threatening infection that requires urgent medical attention
- [MHRA/CHM advice: SGLT2 inhibitors: monitor ketones in blood during treatment interruption for surgical procedures or acute serious medical illness \(March 2020\)](#)
 - SGLT2 inhibitor treatment should be interrupted in people who are hospitalised for major surgical procedures or acute serious medical illnesses and ketone levels measured, preferably in blood rather than urine. Treatment may be restarted when the ketone values are normal and the person's condition has stabilised
- [MHRA/CHM advice: Dapagliflozin \(Forxiga\): no longer authorised for treatment of type 1 diabetes mellitus](#)
 - The authorisation holder for dapagliflozin has withdrawn the indication for type 1 diabetes mellitus. The removal of the type 1 diabetes indication is not due to any new safety concerns and the other indications of dapagliflozin are unchanged

Further Information and References

- Summary of Product Characteristics (SPC) for dapagliflozin available at: www.medicines.org.uk
- NICE Dapagliflozin for treating chronic kidney disease Technology appraisal guidance [TA775] available at: <https://www.nice.org.uk/guidance/ta775>

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