NHS
South West London

Sodium Glucose Co-Transporter 2 Inhibitors (SGLT2i) for Treating Chronic Kidney Disease (CKD) in Adults Information Sheet

Introduction

Dapagliflozin and empagliflozin are currently sodium-glucose co-transporter 2 inhibitor (SGLT2i) licensed for the treatment of CKD. Adding dapagliflozin or empagliflozin to current standard care has been shown to significantly reduce the risk of having declining kidney function, end-stage kidney disease and all cause of mortality in the DAPA-CKD trial and EMPA-Kidney trial.

SGLT2i work by blocking the SGLT2 protein in the renal proximal convoluted tubule to reduce glucose reabsorption and increase urinary glucose and sodium excretion. Blocking this protein alleviates kidney damage by reducing pressure and inflammation in the kidneys independent of the glucose lowering effects.

South West London (SWL) Formulary status

SWL recommends prescribing dapagliflozin in line with NICE Technology appraisal guidance [TA775] or empagliflozin in line with NICE Technology appraisal guidance [TA942] with for patients in primary care as an option for treating CKD.

Initiation criteria

Dapagliflozin

NICE TA775 recommends prescribing dapagliflozin 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/1.73 m^2 to 75 ml/min/1.73 m^2 at the start of treatment and:
    - have type 2 diabetes or
    - have a urine albumin-to-creatinine ratio (uACR) more than or equal to 22.6 mg/mmol.

Empagliflozin

NICE TA942 recommends prescribing empagliflozin 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:
    - 20 ml/min/1.73 m^2 to less than 45 ml/min/1.73m^2 or
    - 45 ml/min/1.73 m^2 to 90 ml/min/1.73 m^2 and either
        - a urine albumin-to-creatinine ratio of 22.6 mg/mmol or more, or
        - type 2 diabetes.

Prescribing Guidance

Dapagliflozin:

- Dosage: 10mg once a day
- Renal function: Avoid initiation if eGFR less than 25ml/min/m^2
- Hepatic Impairment: severe hepatic impairment: start at lower dose 5mg once a day and increase to 10mg if tolerated
- Age: licensed for 18 years and older

Empagliflozin:

- Dosage: 10mg once a day
- Renal function: Avoid initiation if eGFR less than 20ml/min/1.73m^2
- Hepatic Impairment: Mild and moderate (as above): 10 mg once a day. Severe: Not recommended for use due to lack of experience.
- Age: licensed for 18 years and older

Good practice prescribing: Ensure SGLT2i is linked to the indication and a prescription direction is added e.g. “for Chronic Kidney Disease”, as well as the dispensing label in pharmacy. This is to avoid ambiguity and ensure it is not inadvertently stopped as part of a routine diabetes review.

Contra-indications and cautions

Note: this is not an exclusive list- refer to dapagliflozin: BNF/ SPC or empagliflozin: BNF/ SPC for an up-to-date list.

Do not prescribe in the following patients:

- Type 1 diabetes or rapid progression to insulin (within 1 year of diagnosis) - refer to MHRA 2021
- History of diabetic ketoacidosis (DKA)
- Active foot ulceration
- Pregnancy and breastfeeding
- Hypersensitivity to active substance or excipients

Prescribe with caution in patients:

- Who are undergoing a surgical procedure, have a restricted food intake or are dehydrated as there is a risk of DKA. Temporarily withhold and monitor ketone levels – refer to MHRA guidance and reiterate sick day rules.
- With a history of urinary tract infections or recurrent thrush, as urogenital infection or perineal abscess may predispose to necrotising fasciitis.
- With HbA1c (Glycated haemoglobin) above 85mmol/mol due to potentially increased risk of side effects.

Further cautions documented under monitoring requirements section below

Side effects:

Full list of other potential side effects can be accessed: BNF and SPC.
Important side effects that may require cessation of therapy:

- Fournier's gangrene (necrotising fasciitis of the genitalia or perineum): very rare; therapy should be stopped immediately and emergency treatment organised – refer to the MHRA guidance.
  Note: this is usually only seen in Type 1 diabetes
- Diabetic ketoacidosis (DKA): has not yet been reported in patients without diabetes but patients with undiagnosed Type 2 diabetes mellitus (T2DM) may be at risk of DKA. Advise the patient to stop therapy and immediately.
  Note: this is usually only seen in Type 1 diabetes.
- Seek medical advice if signs and symptoms of metabolic acidosis occur -refer to the MHRA guidance.

Interactions

These are related to the potential effects of synergistic hypotension with medications that lower blood pressure, and these parameters should be monitored in patients without diabetes. Documented interactions can be found: (dapagliflozin: BNF and SPC) and (empagliflozin: BNF and SPC).

Monitoring requirements in primary care

Also available as a visual summary: Appendix 1

On Initiation- measure and assess baseline:

Blood Pressure:

Caution: if systolic blood pressure (SBP) less than 95mmHg or if symptomatic hypotension, particularly in patient who are:

- elderly (older than 65 years old) or frail.
- on anti-hypertensive therapy with a history of hypotension.
- prescribed diuretics at risk of hypotension or dehydration.

Renal function:

- If eGFR fall below NICE recommendations, it is not recommended to initiate however, if patient stabilised on treatment refer to dapagliflozin: SPC, empagliflozin: SPC).
- If eGFR falls below 15ml/min/1.73m^2 - consider renal advice and reviewing co-prescribed medications/co-morbidities that may affect eGFR.

Hepatic function:

- Severe hepatic impairment with dapagliflozin reported- manufacturer advises caution with dapagliflozin- see prescribing guidance for dose recommendation.

HbA1c and glucose levels:

- It is good practice to check HbA1c prior to starting therapy to exclude undiagnosed T2DM.

- If HbA1c is above 48mmol/mol -manage according to NICE guidance for T2DM and SGLT2i in T2DM guideline and/or seek specialist diabetic advice on how best to adjust existing diabetic medication and management prior to initiation/ during treatment.

Ongoing Monitoring and review

- Annual CKD review unless clinical condition or medication changes in which case more frequent monitoring may be required.
- Blood pressure within the first 3 months and then annually.
- Renal function check as clinically indicated and at least annually thereafter.
- HBA1c and glucose levels if clinically indicated.
- Liver function tests if clinically indicated.
- Side effects and adherence review within the first 3 months, as indicated and at least annually thereafter.
- Other: If patient presents with intercurrent conditions that may lead to volume depletion (e.g. gastrointestinal illness) monitor volume status (this includes physical examination, BP measurements) and laboratory tests including haematocrit and electrolytes, urea.

Counselling

Patients should be counselled on the adverse side effect associated with SGLT2i - refer to side effects section above

Sick day rules should be discussed on initiation and reiterated at every opportunity.

- SGLT2i should be temporarily withheld in the following circumstances:
    - If hospitalised for major surgery or acute serious illnesses (see MHRA 2020). Blood ketone levels should be monitored (and be normal before restarting).
    - Pre-surgery: 24 hours prior to surgery and not restarted until the patient is eating and drinking normally, is not dehydrated, is not receiving variable rate intravenous insulin infusion, ketone levels are normal, and the patient's condition has stabilised. Advise patient to seek advice from hospital teams.
    - Consider stopping in any other hospital admission, if acutely unwell, until patient well/stable. If unsure withhold and seek advice from named healthcare practitioner.
    - If patient develops volume depletion, not eating or drinking or has inter-current conditions that may lead to volume depletion (e.g. vomiting/diarrhoea).
    - If patient has a severe infection.

  Treatment may be restarted once the patient's condition has stabilised, and they are eating normally for at least 24 hours (providing no new contra-indications exist).

Patient information:

- Patients should also be advised to read the Patient Information Leaflet (PIL).

- UKKA patient information sheet for patients with diabetes.
- UKKA patient information sheet for patients without diabetes should be provided to patients as currently all product information refers to SGLT2i in diabetes which may cause confusion.

Reference:

1. Jardiance 10 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc)
2. Forxiga 10 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc)
3. Overview | Dapagliflozin for treating chronic kidney disease | Guidance | NICE, Published: 09 March 2022
4. Overview | Empagliflozin for treating chronic kidney disease | Guidance | NICE, Published: 20 December 2024

Document History

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Author: **SWL Renal Network**

Approved by: **Integrated medicines committee (IMOC)**

Approval date: **29/01/2025**

Review Date: **29/01/2027 or sooner where appropriate**

Appendix 1:

Summary Table of Initiation and Monitoring Requirements in primary care

<table>
<tr><th>Parameter</th><th>Initiation requirement</th><th>Ongoing monitoring requirement</th></tr>
<tr><td rowspan="2">Blood pressure</td><td>Baseline assessment</td><td>Within the first 3 months and then at least annually</td></tr>
<tr><td colspan="2">Caution if systolic blood pressure (SBP) <95mmHg or if symptomatic hypotension, particularly in:
elderly (older than 65 years old) or frail
on anti-hypertensive therapy with a history of hypotension
prescribed diuretics at risk of hypotension or dehydration</td></tr>
<tr><td rowspan="2">Renal function</td><td>Baseline assessment</td><td>Check as clinically indicated and at least annually thereafter.</td></tr>
<tr><td colspan="2">Cautions if eGFR falls below 15ml/min/m^2 for dapagliflozin and 20ml/min/m^2 empagliflozin consider specialist/renal advice and co-prescribed medications/co-morbidities that may affect eGFR.</td></tr>
<tr><td>HbA1c & glucose levels</td><td>It is good practice to check HbA1c prior to starting therapy to exclude undiagnosed type 2 diabetes mellitus (T2DM). Refer to DM team if HbA1c is above 48 mmol/mol. See NICE guidance for T2DM and SGLT2i in T2DM</td><td>If clinically indicated</td></tr>
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<table>
<tr><td rowspan="2">Liver function tests</td><td>Baseline assessment</td><td>If clinically indicated</td></tr>
<tr><td colspan="2">Cautions:
Dapagliflozin
• For severe hepatic impairment initiate dapagliflozin at 5mg daily; increase to 10mg if well-tolerated.
Empagliflozin
• Mild and moderate (as above): No dose adjustment required. Severe: Not recommended for use due to lack of experience.</td></tr>
<tr><td rowspan="2">Counsel on side effects & adherence</td><td>Counsel upon initiation</td><td>Review tolerance to therapy within the first 3 months, as indicated and at least annually</td></tr>
<tr><td colspan="2">Issue:
• Patient Information Leaflet (PIL)
• UKKA patient information sheet for patients with diabetes or UKKA patient information sheet for patients without diabetes
• If patient presents with intercurrent conditions that may lead to volume depletion (e.g. gastrointestinal illness) monitor volume status (this includes physical examination, BP measurements) and laboratory tests including haematocrit and electrolytes, urea.</td></tr>
<tr><td rowspan="2">Counsel on sick day rules</td><td>Baseline checks</td><td>Ongoing basis</td></tr>
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○ Consider stopping in any other hospital admission, if acutely unwell, until patient well/stable. If unsure withhold and seek advice from named healthcare practitioner.
○ If patient develops volume depletion, not eating or drinking or has inter-current conditions that may lead to volume depletion (e.g. vomiting/diarrhoea).
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