# NICE Technology Appraisals (TA) briefing paper for local implementation

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| **NICE TA Guidance name and number** | Empagliflozin for treating chronic kidney disease<br>TA 942 | | |
| **Available at** | Overview \| Empagliflozin for treating chronic kidney disease \| Guidance \| NICE | | |
| **Date of issue** | 20 December 2023 | **Implementation deadline** | 20 March 2024 (3 months) |

| **Medicine details[1]** | |
|---|---|
| **Name and brand name** | Empagliflozin (Jardiance) |
| **Manufacturer** | Boehringer Ingelheim Limited |
| **Mode of action** | Sodium-glucose co-transporter 2 (SGLT2) inhibitor |
| **Licenced indication** | Treatment of chronic kidney disease in adults |
| **Formulation** | 10mg and 25mg film-coated tablets |
| **Dosage** | 10mg once a day |
| **Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]** | NICE have made the recommendation in line with dosing as above but have identified more specific patient cohorts for treatment based on access to standard care and estimated glomerular filtration rates<br><br>This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the licence following NICE publication will need to be considered by the Area Prescribing Committee and will not be routinely funded by local commissioners, as the incremental cost per QALY would not have been considered. |

## NICE TA recommendations[2]

**Recommendations**

1.1 Empagliflozin 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 of:
  - 20 ml/min/1.73 $m^2$ to less than 45 ml/min/1.73 $m^2$ 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.

1.2 If people with the condition and their clinicians consider empagliflozin to be 1 of a range of suitable treatments (including dapagliflozin), after discussing the advantages and disadvantages of all the options, use the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements

1.3 This recommendation is not intended to affect treatment with empagliflozin that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop

## Decision making framework (DMF)

### National guidance and priorities

The ICS has a legal obligation to commission this medicine in line with the NICE TA.

- This NICE TA has been assigned an implementation deadline of 3 months
- The implementation deadline is 20th March 2024

### Clinical effectiveness

Management of CKD aims to slow its progression. Standard care is lifestyle and dietary changes, and usually ACE inhibitors or ARBs. Empagliflozin is an oral treatment for CKD. The company proposes that empagliflozin would be used as an add-on to optimised standard care with ACE inhibitors or ARBs. Some people take dapagliflozin as an add-on to standard care. The company proposes that empagliflozin would be used in a similar but slightly broader population to dapagliflozin. This does not include everyone who it is licensed for.

Clinical trial evidence suggests that empagliflozin plus standard care is more effective than standard care alone. But the main clinical trial did not include people with CKD with an estimated glomerular filtration rate of less than 20 ml/min/1.73 $m^2$. And people with an estimated glomerular filtration rate between 45 ml/min/1.73 $m^2$ and 90 ml/min/1.73 $m^2$ were only included if they also had a urine albumin-to-creatinine ratio of 22.6 g/mmol or more.

There are no clinical trials directly comparing empagliflozin with dapagliflozin in people with CKD. Results of an indirect comparison suggest that empagliflozin has a similar effectiveness to dapagliflozin, and it likely has similar safety.

Dapagliflozin differs in its NICE recommendation, being more limited to:

- 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) of 22.6 mg/mmol or more.

### Patient safety

- The product should be used within its product licence.
- Empagliflozin has already been approved by APC for use in diabetes and heart failure
- NICE did not identify any additional safety concerns outside those already recognised and described in BNF / SPC.
- All SGLT2 inhibitors are subject to the following MHRA alerts:
    - Diabetic ketoacidosis 2016
    - Fournier's gangrene 2019
    - Increased risk of lower limb amputation (2017)
- During discussion about use of dapagliflozin, APC members noted the impact that SGLT2 inhibitors could have on patients with type 2 diabetes so PAD includes a statement to consider discussion with the specialist diabetes team before initiation

### Patient factors

- Empagliflozin is an additional option for patients with CKD and optimised standard care. It will cover a slightly broader cohort of patients than dapagliflozin (which was approved for CKD by APC in June 2022)

### Environmental impact

- There is no additional environmental impact over and above the already approved dapagliflozin

### Equality & diversity

NICE did not make any specific mention of the impact on equalities and diversity however they note that CKD can progress more quickly in some ethnic minority groups and, in people with type 2 diabetes, it progresses more quickly in people under 55. This was acknowledged but could not be considered in the decision making.

Note 1: Drugs approved by NICE for adult conditions will be commissioned in children at specialised paediatric centres if the patient meets the NICE criteria and there is evidence to suggest that the drug is safe and clinically appropriate to use in children as per the NHS England Medicines for Children Policy (see https://www.england.nhs.uk/publication/commissioning-medicines-for-children-specialised-services/ and a Blueteq form is available.

## Place in therapy relative to available treatments

A CKD pathway based on London Kidney Network (LKN) was approved by APC in September 2023. 3 steps to medicines optimisation

- The guidance advises use of SGLT2 inhibitor according to license so will cover the use of empagliflozin
- The guidance uses the more limited eGFR range of 25-75 ml/min/1.73m2 as per the dapagliflozin NICE

LKN have confirmed that they will be reviewing their guidance in response to this NICE TA and also finerenone (TA877). It is proposed to the APC that the current version is removed from PAD in the interim and reference instead made on both empagliflozin and dapagliflozin entries to check NICE guidance for recommended patient cohorts regarding eGFR.

## Stakeholder views

The paper was sent out for consultation and comments received will be listed on the front sheet.

## Cost-effectiveness

The drug cost per Place according to NICE resources does not exceed £100,000 in any one year up to 5 years ahead.

NICE states that the cost-effectiveness estimates for empagliflozin compared with standard care are within the range NICE normally considers an acceptable use of NHS resources. Also, a cost comparison suggests that empagliflozin has similar costs to dapagliflozin. So, empagliflozin is recommended.

Empagliflozin covers a slightly broader cohort of patients so there will be additional costs.

Section 1: cost of the technology

a. Annual cost per patient (or complete course if shorter)

   Costs in primary care: £477 pppa
   Costs in secondary care: £358 pppa

b. Availability of CAP/PAS price:
   N/A

c. Price relative to comparable medicines:
   Empagliflozin and dapagliflozin are the same cost per patient per year (as of Drug Tariff January 2024).

Section 2: NICE resource impact statement and template

a. NICE resource impact statement
   Nationally the additional drug cost per 100,000 population is around £27,000, with around £45,000 per 100,000 of savings from resources released by use of all SGLT-2 inhibitors (not just empagliflozin).

b. NICE resource impact template

Drug costs (£000K) for empagliflozin AND dapagliflozin in Surrey Heartlands:

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 |
|---|---|---|---|---|---|
| People who have CKD and T2D | £0 | £0 | £68 | £68 | £69 |
| People who have CKD and who do not have T2D | £0 | £50 | £151 | £177 | £203 |
| Test costs | £0 | £2 | £10 | £11 | £12 |
| **Sub total COSTS** | **£0** | **£52** | **£228** | **£256** | **£284** |
| Resource savings* | -£8 | -£23 | -£268 | -£369 | -£463 |
| **Total including savings** | **-£8** | **£29** | **-£39** | **-£113** | **-£179** |

*From dapagliflozin resource template (TA775)

Commentary:
In June 2022, dapagliflozin was approved by APC with drug costs of £708K at year 5 and resource savings of £463. NICE have updated their resource template to account for costs of both SGLT2 inhibitors but have not updated the savings. With or without the estimated savings from the dapagliflozin TA, drug costs per place for Surrey Heartlands do not exceed the delegated authority threshold.

The Surrey Heartlands Director of Pharmacy and Medicines Optimisation has delegated authority to enable the Committee to be a decision-making committee providing the impact of any single decision does not exceed £100,000 within an individual Place per annum. Decisions with a cost impact of over £100,000 within an individual Place per annum require authorisation from Surrey Heartlands Health & Care Professionals Committee at their next meeting. Exception to this will be for any decision made in relation to a NICE Technology Appraisal (which are subject to requiring mandatory funding by commissioners) and other urgent items. The exceptions will be taken to the next Executive Meeting (which meets weekly) for authorisation.

**Traffic light recommendation to APC**

NHS Payment Scheme (NHSPS) excluded high-cost drug: see NHS England » 2023-25 NHS Payment Scheme
No

Recommended traffic light status and rationale:
**GREEN** – as per decision already made for dapagliflozin. There is no requirement for specialist assessment to diagnosis CKD or select, initiate and monitor treatment.
The majority of patients to which this applies are not under the care of Nephrology and would not normally be referred to Nephrology and so BLUE traffic light status would not be appropriate
The accessibility of renal consultants to primary care physicians through *Advice and Guidance* (*A&G*) will allow any concerns and queries (including reassurance) to be addressed promptly. Any A&G can be converted to a referral if the Nephrologist feels this is required

PAD definitions, available at:

FINAL April 2023
Colour classification g

**Implementation**

NICE TA implementation must be within 90 days of publication.

Actions to implement:

**a. Primary care**
- No additional monitoring needed except standard CKD review which will include U+E's, eGFR, BP and ACR at diagnosis
- Already prescribed in primary care for other indications so GPs have experience with using it.
- Alternative SGLT2 inhibitor already prescribed for this indication

**b. Secondary care**
- Will be initiated in primary care so no significant increase in demand to secondary care
- No additional prescribing or monitoring in secondary care necessary beyond pre-existing CKD specialist care.

**c. ICS**
- Liaison with London Kidney Network to update the 3 steps to medicines optimisation as necessary

**d. PAD**
- Suggested PAD narrative for agreement:
  *The Surrey Heartlands Integrated Care System Area Prescribing Committee recommends empagliflozin for treating chronic kidney disease in line with NICE TA 942.* Check NICE guidance for recommended patient cohorts regarding eGFR

*Empagliflozin will be considered GREEN on the traffic light system.*

*Key considerations:*
- *If a patient with diabetes were on insulin and on multiple other treatments, a discussion with the specialist diabetes team may be prudent prior to empagliflozin initiation*

- Remove the current steps to medicines optimisation in CKD guidance on the PAD

**e. Joint Formulary**
- Empagliflozin and dapagliflozin to be GREEN
- No restrictions or preferred product on either empagliflozin or dapagliflozin
- Link to safety alerts and relevant NICE on both
- Comment to include, check NICE guidance for recommended patient cohorts regarding eGFR.

| **Proposed tick box forms** |
|---|
| N/A |

**References:**


1 Summary of Product Characteristics. emc. Available at: Jardiance 10 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed 24th January 2024

2 NICE Technology Appraisal Guidance: . Available at: Overview | Empagliflozin for treating chronic kidney disease | Guidance | NICE Accessed 24th January 2024

3 NICE Resource Impact Report and template: . Available at: Tools and resources | Empagliflozin for treating chronic kidney disease | Guidance | NICE Accessed 24th January 2024

4 MHRA Drug Safety Updates:
SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis - GOV.UK (www.gov.uk) published 18 April 2016
SGLT2 inhibitors: updated advice on increased risk of lower-limb amputation (mainly toes) - GOV.UK (www.gov.uk) published 22 March 2017
SGLT2 inhibitors: reports of Fournier's gangrene (necrotising fasciitis of the genitalia or perineum) - GOV.UK (www.gov.uk) published 18 February 2019

5 NICE Resource Impact Report and template: Available at: Tools and resources | Dapagliflozin for treating chronic kidney disease | Guidance | NICE Accessed 24th January 2024


Declaration of interest:

| | Name | Role | Date | Declaration of interests (please give details below) |
|---|---|---|---|---|
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