NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Empagliflozin for treating chronic kidney disease ID6131

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of empagliflozin within its marketing authorisation for treating chronic kidney disease.

Background

Chronic kidney disease (CKD) is a condition where the kidneys do not work as well as they should and it is linked with adverse outcomes including cardiovascular disease.

People with CKD do not usually have symptoms during the early stages of the disease but symptoms including weight loss and poor appetite, swollen ankles, feet or hands, shortness of breath, tiredness, feeling sick and blood in the urine can develop as the disease progresses.[1] The severity of CKD is determined by the estimated glomerular filtration rate (eGFR), with 6 categories ranging from normal to kidney failure, and the albumin to creatinine ratio (ACR), with 3 categories (normal to mild increase, moderate increase and severe increase).[2] An ACR of more than 3 mg/mmol (a moderate or severe increase) is an indicator for albuminuria, when albumin, a protein that is normally found in the blood, is found in the urine.[2] CKD can progress to kidney failure in a small but significant percentage of people, which may require dialysis or a kidney transplant.[1,2]

In 2014, approximately 2.6 million people aged 16 years and over had CKD stage 3 to 5 in England.[3] High blood pressure is a common cause of kidney failure, whilst diabetes has been established as a cause in around a quarter of all CKD cases.[4] CKD occurs more frequently in women than in men.[3] Prevalence also increases with age, and around 30% of people aged 75 and over will have stage 3 to 5 CKD.[3] Estimates suggest that antihypertensive medicines are taken in about half of all CKD cases.[5] In 2009, there were an estimated 40,000 to 45,000 premature deaths in people with CKD.[6]

Treatment aims to prevent or delay progression of CKD, reduce or prevent complications, and reduce the risk of cardiovascular disease. The current treatment options recommended for adults by NICE NG203 are:

- antihypertensive therapy in adults with hypertension and an ACR of 30 mg/mmol or less. In adults with CKD and an ACR under 70 mg/mmol, the guidelines recommend keeping systolic blood pressure below 140 mmHg (target range 120 to139 mmHg) and the diastolic blood pressure below 90 mmHg. For people with an ACR of 70 mg/mmol or more, systolic blood pressure should be below 130 mmHg (target range 120 to 129 mmHg) and diastolic blood pressure below 80 mmHg

- angiotensin-receptor blockers (ARB) or an angiotensin-converting enzyme (ACE) inhibitor (titrated to the highest licensed dose that the person can tolerate) in adults with either:

  - hypertension and an ACR of 30 mg/mmol or more
  - concurrent diabetes and an ACR of 3 mg/mmol or more
  - an ACR of 70 mg/mmol or more.

- a sodium glucose co-transporter 2 (SGLT2) inhibitor for adults with concurrent type 2 diabetes who are taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate) if:

  - ACR is over 30 mg/mmol (can be considered if ACR is between 3 to 30 mg/mmol) and
  - they meet the criteria in the marketing authorisation (including relevant eGFR thresholds).

- dapagliflozin (SGLT2 inhibitor) for adults with type 2 diabetes or a urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more, if:

  - it is an add-on to optimised standard care including the highest tolerated licensed dose of ACE inhibitors or ARBs, unless these are contraindicated, and
  - people have an eGFR of 25 ml/min/1.73 m^2 to 75 ml/min/1.73 m^2 at the start of treatment

- have a statin for primary or secondary prevention of cardiovascular disease

- antiplatelets and anticoagulants (e.g. apixaban) for the secondary prevention of cardiovascular disease.

The technology

Empagliflozin (Jardiance, Boehringer-Ingelheim) does not currently have a marketing authorisation in the UK for treating adults with chronic kidney disease. It has been studied in a clinical trial in combination with standard care compared with placebo.

Empagliflozin does have a marketing authorisation for:

- the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise

  - as monotherapy when metformin is considered inappropriate due to intolerance
  - in addition to other medicinal products for the treatment of diabetes

- the treatment of symptomatic chronic heart failure with reduced ejection fraction in adults.

Intervention	Empagliflozin
Population	Adults with chronic kidney disease having individually optimised standard care

Subgroups	If the evidence allows the following subgroups will be considered: • people with diabetes • people with cardiovascular disease • people with other causes of CKD
Comparators	Established clinical management with or without dapagliflozin
Outcomes	The outcome measures to be considered include: • morbidity including cardiovascular outcomes, disease progression (such as kidney replacement, kidney failure) and markers of disease progression (such as estimated glomerular filtration rate (eGFR), albuminuria) • mortality • hospitalisation • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related Technology Appraisals:** Dapagliflozin for treating chronic kidney disease (2022) NICE technology appraisal 775. Review date 2022 **Related appraisals in development:**

	Finerenone for treating chronic kidney disease in people with type 2 diabetes NICE technology appraisal guidance [ID3773]. Publication date to be confirmed. **Related Guidelines:** Renal replacement therapy and conservative management (2018). NICE guideline 107. Chronic kidney disease: assessment and management (2021). NICE guideline 203. Type 2 diabetes in adults: management (2015, updated 2022). NICE guideline 28. Chronic kidney disease: managing anaemia (2015). NICE guideline 8 Hypertension in adults: diagnosis and management (2019, updated 2022). NICE guideline 136. Cardiovascular disease: risk assessment and reduction, including lipid modification (2014, updated 2016) NICE guideline 181 Atrial fibrillation: diagnosis and management (2021). NICE guideline 196 Venous thromboembolic diseases: diagnosis, management and thrombophilia testing (2020), NICE guideline 158 **Related Quality Standards:** Chronic kidney disease in adults (2011, updated 2017). NICE quality standard 5. Renal replacement therapy services for adults (2014, updated 2018). NICE quality standard 72. Diabetes in adults (2011, updated 2016) NICE quality standard 6
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 15 'Adult specialists renal services' page 65. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2.

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for chronic kidney disease? How often are statins, antiplatelets/anticoagulants, SGLT2 inhibitors given in this population?

In clinical practice, would people always be stable on the maximum tolerated dose of ACE inhibitors or ARBs before empagliflozin would be considered?

Where do you consider empagliflozin will fit into the existing care pathway for chronic kidney disease?

In what circumstances would empagliflozin be added to standard care? Would it ever be used to treat people whose CKD is responding to treatment with standard care?

Would empagliflozin be a candidate for managed access?

Are the outcomes listed appropriate?

Are the subgroups suggested appropriate? Are there any other subgroups of people in whom empagliflozin is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Do you consider that the use of empagliflozin can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which empagliflozin will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost-comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. NHS choices (2019) Chronic kidney disease. Accessed October 2022.

2. Kidney Research UK (2020) Stages of kidney disease. Accessed October 2022.

3. Public Health England (2014) Chronic kidney disease prevalence model. Accessed October 2022.

4. NHS Inform (2020) Causes of chronic kidney disease. Accessed October 2022.

5. NHS Kidney Care (2012) Chronic Kidney Disease in England: The Human and Financial Cost. Accessed October 2022

6. Insight Health Economics for NHS Kidney Care (2017). Chronic Kidney Disease in England: The Human and Financial Cost. Accessed October 2022