NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Dapagliflozin for treating chronic kidney disease.

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dapagliflozin 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.[1] 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 end-stage kidney disease (ESKD) 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 3-5 in England.[3] High blood pressure and diabetes are associated with around 25% and 40% of CKD cases, respectively.[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 3-5 CKD.[3] Estimates suggest that antihypertensive medicines are taken in about half of all CKD cases.[5]

For people with CKD, NICE clinical guideline 182 '[chronic kidney disease in adults: assessment and management]' (currently being updated) recommends:

- keeping systolic blood pressure below 140 mmHg (target range 120–139 mmHg) and the diastolic blood pressure below 90 mmHg. For people with diabetes or an ACR of 70 mg/mmol or more, systolic blood pressure should be below 130 mmHg (target range 120–129 mmHg) and diastolic blood pressure below 80 mmHg.

- a drug that blocks or inhibits the renin-angiotensin system including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs) and direct renin inhibitors to manage blood pressure in people with: a) concurrent diabetes and an ACR of 3 mg/mmol or more, b) hypertension and an ACR of 30 mg/mmol or more, or c) an ACR of 70 mg/mmol or more.

- Atorvastatin (a steroid) for primary or secondary prevention of cardiovascular disease

- Antiplatelet drugs (e.g. apixaban) for the secondary prevention of cardiovascular disease.

The technology

Dapagliflozin (Forxiga, AstraZeneca) is a sodium-glucose co-transporter 2 (SGLT-2) inhibitor. The mechanism of action in CKD is not yet fully understood. It is administered orally.

Dapagliflozin does not currently have a marketing authorisation in the UK for CKD. It is being studied in combination with individually optimised standard care in a randomised controlled trial compared with placebo with individually optimised standard care, in adults with an eGFR between 25 and 75 mL/min/1.73m^2 and increased albuminuria for 3 months or more who are stable on optimised standard care with the maximum tolerated dose of ACE inhibitor or ARBs.

Intervention(s)	Dapagliflozin in combination with optimised standard care (including treatment with an ACE inhibitor or ARB).
Population(s)	Adults with chronic kidney disease who are stable on individually optimised standard care
Comparators	Established clinical management without dapagliflozin
Outcomes	The outcome measures to be considered include: • morbidity including cardiovascular outcomes, disease progression (such as renal replacement, ESKD) and markers of disease progression (such as serum creatinine, albuminuria) • mortality • 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. 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	If the evidence allows the following subgroups will be considered: • people with diabetes • people with cardiovascular disease • people with other causes of CKD The availability and cost of biosimilar and generic products should be taken into account. 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 and NICE Pathways	**Related Technology Appraisals:** Dapagliflozin with insulin for treating type 1 diabetes (2019, updated 2020) NICE technology appraisal 597. Review date 2022. Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes (2016) NICE technology appraisal 390. Review date 2019. Dapagliflozin in triple therapy for treating type 2 diabetes (2016) NICE technology appraisal 418. Review date 2019. Dapagliflozin in combination therapy for treating type 2 diabetes (2013, update 2016) NICE technology appraisal 288. Review date 2017. **Technology Appraisals in development:** Dapagliflozin for treating heart failure with reduced ejection fraction [ID1656]. NICE technology appraisal guidance. Publication expected February 2021. **Related Guidelines:** Renal replacement therapy and conservative management (2018). NICE guideline 107. Chronic kidney disease in adults: assessment and management (2014, updated 2015). NICE clinical guideline 182. Type 2 diabetes in adults: management (2015, updated 2019). NICE guideline 28. Chronic kidney disease: managing anaemia (2015). NICE guideline 8.

	Guidelines in development Chronic kidney disease: assessment and management (update) NICE guideline. Publication expected July 2021. **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 NICE Pathways:** Chronic kidney disease (last updated 2019). NICE pathway.
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 steroids and antiplatelet drugs given in this population?

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

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

Are the outcomes listed appropriate?

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

Where do you consider dapagliflozin will fit into the existing NICE pathway, chronic kidney disease?

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 dapagliflozin 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.

Do you consider dapagliflozin to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of dapagliflozin can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. NHS choices (2019) Chronic kidney disease. Accessed December 2020.

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

3. Public Health England (2014) Chronic kidney disease prevalence model. Accessed December 2020.

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

5. NHS Kidney Care (2012) Chronic Kidney Disease in England: The Human and Financial Cost. Accessed January 2021