# Review proposal of dapagliflozin for treating chronic kidney disease [TA775]

Dapagliflozin for treating chronic kidney disease (TA775) was published in March 2022.

## Proposal

A review of the guidance should be planned into the appraisal work programme, which will follow the cost comparison process.

## Rationale

Dapagliflozin for chronic kidney disease (CKD) was appraised by NICE in 2022 (TA775). It was recommended for use in a narrower CKD population than the population covered by the marketing authorisation, reflecting the trial inclusion criteria. Dapagliflozin (a sodium-glucose co-transporter 2 [SGLT2] inhibitor) may show similar clinical efficacy and safety to another SGLT2 inhibitor (empagliflozin), which is already recommended in technology appraisal guidance at a similar point in the treatment pathway for a different, slightly broader CKD population (TA942; 2023).

System intelligence has outlined that dapagliflozin and empagliflozin are used at a similar point in the treatment pathway, and if dapagliflozin had the same NICE recommendation as empagliflozin it would avoid unnecessary complexity for prescribers. Dapagliflozin may be an alternative to empagliflozin if the current TA775 recommendations change to include the broader CKD population recommended in TA942 for empagliflozin (which matches the available evidence base for that product).

Supporting evidence for dapagliflozin in the wider population included in TA942 is not yet available publicly. However, the company have indicated that this evidence will be available for use in an appraisal. A full single technology appraisal of dapagliflozin for a broader population than is currently recommended is unlikely to add value. A fast-track appraisal with a cost comparison comparing dapagliflozin to empagliflozin is likely to be appropriate if supporting evidence is provided. Population differences in dapagliflozin and empagliflozin trials and real-world evidence, in terms of renal function, type 2 diabetes status and albumin-to-creatinine ratio (ACR), need to be considered.

### Review remit

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

## The technology

Dapagliflozin (Forxiga, AstraZenica) has a marketing authorisation 'for the treatment of chronic kidney disease' in adults.

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| **Intervention(s)** | Dapagliflozin |
| **Population(s)** | People with chronic kidney disease who have an eGFR of:<br>• 20 ml/min/1.73 $m^2$ to less than 45 ml/min/1.73 $m^2$ or<br>• 45 ml/min/1.73 $m^2$ to 90 ml/min/1.73 $m^2$ and have either:<br>  ○ type 2 diabetes or<br>  ○ a uACR of 22.6 mg/mmol or more |
| **Subgroups** | If the evidence allows the following subgroups will be considered:<br>• people with diabetes<br>• people with cardiovascular disease<br>• people with other causes of CKD |
| **Comparators** | Empagliflozin |
| **Outcomes** | The outcome measures to be considered include:<br>• 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)<br>• mortality<br>• hospitalisation<br>• adverse effects of treatment<br>• health-related quality of life. |

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| **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.<br><br>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.<br><br>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.<br><br>Costs will be considered from an NHS and Personal Social Services perspective.<br><br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account |
| **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:**<br><br>Empagliflozin for treating chronic kidney disease (2023) NICE technology appraisal guidance 942<br><br>Finerenone for treating chronic kidney disease in type 2 diabetes (2023) NICE technology appraisal guidance 877<br><br>**Related NICE guidelines:**<br><br>Type 2 diabetes in adults: management (2015, last updated 2022) NICE guideline NG28<br><br>Chronic kidney disease: assessment and management (2021) NICE guideline NG203<br><br>Renal replacement therapy and conservative management (2018) NICE guideline NG107<br><br>**Related quality standards:**<br><br>Renal replacement therapy services for adults (2014) NICE quality standard QS72 |

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| | Chronic kidney disease in adults (2011, updated 2017) NICE quality standard QS5 |
| **Related National Policy** | The NHS Long Term Plan (2019) NHS Long Term Plan<br>NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 15 – Adult specialist renal services |

***Has there been any change to the price of the technology(ies) since the guidance was published?***

No

***Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?***

No

***Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?***

The evidence supporting dapagliflozin in TA775 came from Heerspink et al. (2020) (DAPA-CKD). This was a randomised, double-blind trial in adults with CKD, with or without type 2 diabetes, comparing dapagliflozin plus standard care (n=2,152) with placebo plus standard care (n=2,152). DAPA-CKD included people with an eGFR of 25 ml/min/1.73 m2 to 75 ml/min/1.73 m2 and a uACR of 22.6 mg/mmol to 565 mg/mmol. The primary outcome was a composite of a sustained decline in eGFR of at least 50%, end-stage kidney disease, or death from renal or cardiovascular causes. Results showed that the dapagliflozin arm had a lower risk of the primary composite outcome (hazard ratio [HR] 0.61, 95% confidence interval [CI] 0.51 to 0.72).

Additional clinical evidence was reviewed for TA775, from 2 randomised controlled trials, Wiviott et al. (2019) (DECLARE-TIMI-58, n=17,160) and McMurray et al. (2019) (DAPA-HF, n=4,744), to provide renal outcome data across a broader population. DECLARE-TIMI-58 included people with a creatinine clearance of 60 ml/min or more and DAPA-HF included people with an eGFR of 30 ml/min/1.73 m2 or more. Results from these trials suggested that dapagliflozin plus standard care is more effective than standard care alone across the broad CKD population, regardless of uACR and eGFR. DECLARE-TIMI-58 showed that the dapagliflozin treatment effect was consistent between people with a uACR of less than 22.6 mg/mmol and those with a uACR of 22.6 mg/mmol or more for some outcomes.

The committee concluded that dapagliflozin was cost effective in the population represented in DAPA-CKD, and a sub-population in DECLARE-TIMI-58; people with CKD with a uACR of less than 22.6 mg/mmol and type 2 diabetes. The committee noted that the evidence was weaker for dapagliflozin outside of the eGFR range in DAPA-CKD, and that it could not be recommended in people with a uACR of less

than 22.6 mg/mmol who do not have type 2 diabetes due to no direct clinical evidence informing this subgroup.

The recommendation for dapagliflozin in TA775 is being reviewed to match the broader CKD population in the recommendation for empagliflozin in TA942. The evidence to support this review is not yet available publicly. However, the company have indicated that it will be available for an appraisal.

### *Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?*

Empagliflozin for treating chronic kidney disease (2023) NICE technology appraisal guidance 942

- Comparator for the suggested appraisal
- No updates required

Finerenone for treating chronic kidney disease in type 2 diabetes (2023) NICE technology appraisal guidance 877

- Add-on to treatment with SGLT2 inhibitors
- No updates required

Type 2 diabetes in adults: management (2015, last updated 2022) NICE guideline NG28

- Includes section on chronic kidney disease
- May need to be updated with new link to dapagliflozin guidance if new criteria are recommended (empagliflozin guidance also to be added)

Chronic kidney disease: assessment and management (2021) NICE guideline NG203

- Relevant NICE guideline for the disease area
- May need to be updated with new link to dapagliflozin guidance if new criteria are recommended (empagliflozin guidance also to be added)

Renal replacement therapy and conservative management (2018) NICE guideline NG107

- Potentially relevant guideline for people with chronic kidney disease
- No updates required

Renal replacement therapy services for adults (2014) NICE quality standard QS72

- Potentially relevant quality standard for people with chronic kidney disease
- No updates required

Chronic kidney disease in adults (2011, updated 2017) NICE quality standard QS5

- Relevant NICE quality standard for the disease area
- To be updated with link to dapagliflozin guidance (empagliflozin guidance also to be added)

***Additional comments***

The search strategy from the original ERG report was adapted for the Cochrane Library, Medline, Medline In-Process and Embase. References from August 2020 to March 2024 were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section above. See Appendix C for further details of ongoing and unpublished studies.

## Equality issues

During the original appraisal (TA775), several potential equality issues were raised:

- CKD disproportionally affects people from Black, Asian, and minority ethnic groups and lower socioeconomic backgrounds.
- People from these groups are also more likely to have chronic kidney disease that progresses quicker to kidney failure and to die earlier.
- Use of ACE inhibitors or ARBs differs by ethnicity and socioeconomic status.

## Proposal paper sign off

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