Healthcare Improvement Scotland | SMC Advice on new medicines

Advice document
SMC2763

dapagliflozin film-coated tablets (Forxiga®)

AstraZeneca UK Ltd

07 March 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following an abbreviated submission

dapagliflozin (Forxiga®) is accepted for restricted use within NHSScotland.

Indication under review: in adults for the treatment of chronic kidney disease (CKD).

SMC restriction: in patients having individually optimised standard care (including angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, unless these are contraindicated or not tolerated), and either, at the start of treatment:

- an estimated glomerular filtration rate (eGFR) of 20 mL/min/1.73m^2 up to 45 mL/min/1.73m^2, or
- an eGFR of 45 mL/min/1.73m^2 up to 90 mL/min/1.73m^2 and either:
    - A urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more, or
    - Type 2 Diabetes Mellitus (T2DM).

Dapagliflozin offers an additional treatment choice in the therapeutic class of sodium-glucose co-transporter 2 (SGLT2) inhibitor.

This advice incorporates the previous SMC advice for dapagliflozin in the treatment of CKD (SMC2428).

Chair, Scottish Medicines Consortium

1.1. Medicine background

Dapagliflozin is a sodium-glucose co-transporter 2 (SGLT2) inhibitor. It is licensed for the treatment of chronic kidney disease and was previously accepted for restricted use by SMC (SMC2428), restricted for use in patients with an estimated glomerular filtration rate (eGFR) of ≥25 to ≤75 mL/min/1.73m^2 at treatment initiation, who are receiving an angiotensin converting enzyme inhibitor or angiotensin receptor blocker (unless these are not tolerated or contraindicated), and have a urine albumin creatinine ratio (uACR) of at least 23mg/mmol, or type 2 diabetes mellitus (T2DM), or both. This abbreviated submission supports use of dapagliflozin in an extended patient population, in line with the current SMC advice for empagloflozin.

The recommended dose of dapagliflozin in CKD is 10 mg orally once daily. [1]

1.2. Relevant comparator

Empagliflozin (SMC2642) is another SGLT2 inhibitor licensed for the treatment of CKD that has been accepted for restricted use in NHSScotland with the following restrictions: in patients having individually optimised standard care (including angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, unless these are contraindicated or not tolerated), and either, at the start of treatment:

- an eGFR of 20 mL/min/1.73m^2 up to 45 mL/min/1.73m^2, or
- an eGFR of 45 mL/min/1.73m^2 up to 90 mL/min/1.73m^2 and either:
    - A urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more, or
    - Type 2 Diabetes Mellitus (T2DM)

2. Summary of Clinical Evidence

2.1. Evidence to support comparable efficacy with relevant comparators

There is no direct evidence comparing dapagliflozin with empagliflozin in patients with CKD and the submitting company included real world evidence (RWE), data from previous clinical studies of dapagliflozin and an indirect treatment comparison with empagliflozin and to support the abbreviated submission.

OPTIMISE-CKD was an observational study using data from a large claims database in the USA and Japan. This demonstrated efficacy of dapagliflozin in patients with CKD across a range of uACR levels in patients without T2DM, and in patients with lower uACR levels both with and without T2DM.[2, 3] The company presented subgroup analyses in patients without T2DM and uACR <22.6mg/mmol from the DAPA-CKD and DAPA-HF studies as supportive evidence of the effectiveness of dapagliflozin in patients without T2DM at lower levels of albuminuria.[4, 5]

DAPA-advKD was a randomised, open label study comparing dapagliflozin plus integrated CKD care with integrated CKD care only in patients with CKD stages 4 and 5 (eGFR ≥ 10 to < 30 mL/min/1.73m2).[6] There was no restriction on uACR level. Patients randomised to receive

dapagliflozin had improvements in the key outcome of eGFR slope as well as renal and cardiovascular outcomes compared with integrated CKD care alone.

Subgroup analysis from the DECLARE-TIMI 58 study in patients with T2DM, who had or were at risk of cardiovascular disease demonstrated improvements in renal specific outcomes in patients with an eGFR of ≥ 60 mL/min/1.73m.[7].

The company performed an indirect treatment comparison using propensity score analysis to estimate the relative treatment effect of dapagliflozin and empagliflozin in patients with CKD using RWE from a large US-based database. The inclusion criteria aligned with the EMPA-KIDNEY population: baseline eGFR ≥20 and <45 mL/min/1.73m^2 and any level of uACR; or baseline eGFR ≥ 45 and <90 mL/min/1.73m^2 and uACR ≥200mg/g and outcomes included eGFR slope; time to first hospitalisation for CKD; time to first hospitalisation for heart failure and time to death within hospital from any cause. No statistically significant difference was observed for any of the outcomes analysed.[8]

Overall, the evidence presented by the submitting company supported similar efficacy of dapagliflozin and empagliflozin in patients with CKD.

3. Company Estimate of Budget Impact

3.1. Company's estimate of budget impact

The company has indicated that there is no expected budget impact with dapagliflozin.

3.2. Budget Impact assumption

Medicines reviewed under the abbreviated submissions process are estimated to have a limited net budget impact and resource allocation across NHS Scotland.

References

1. Forxiga 10mg film-coated tablets. SmPC. Available from: https://www.medicines.org.uk/emc/product/7607/smpc#about-medicine. [Last accessed: 28/03/2024]. 2021.
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5. Jhund PS, Solomon SD, Docherty KF, Heerspink HJL, Anand IS, Bohm M*, et al.* Efficacy of Dapagliflozin on Renal Function and Outcomes in Patients With Heart Failure With Reduced Ejection Fraction: Results of DAPA-HF. Circulation. 2021;143(4):298-309. Epub 20201012.
6. Hung C-C, Chiu Y-W, Hwang S-J. Efficacy and Safety of Dapagliflozin in Patients with CKD Stages 4-5: SA-OR96. Journal of the American Society of Nephrology. 2024;35(10S):10.1681/ASN.2024aa8zcvkv.
7. Mosenzon O, Wiviott SD, Cahn A, Rozenberg A, Yanuv I, Goodrich EL*, et al.* Effects of dapagliflozin on development and progression of kidney disease in patients with type 2 diabetes: an analysis from the DECLARE-TIMI 58 randomised trial. Lancet Diabetes Endocrinol. 2019;7(8):606-17. Epub 20190610.
8. Staplin N, Haynes R, Judge PK, Wanner C, Green JB, Emberson J*, et al.* Effects of empagliflozin on progression of chronic kidney disease: a prespecified secondary analysis from the empa-kidney trial. The Lancet Diabetes & Endocrinology. 2024;12(1):39-50.

This assessment is based on data submitted by the applicant company up to and including 27 February 2025.

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice is based on the estimation of at least similar comparative efficacy and limited net budget impact compared with other medicinal products, within the same therapeutic class, that are in routine use within NHSScotland.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after evaluation of the evidence submitted by the company. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.