Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2428

dapagliflozin 10mg film-coated tablets (Forxiga®)

AstraZeneca UK Ltd

8 April 2022

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

ADVICE: following a full submission

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

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

SMC Restriction:

- in patients with an estimated glomerular filtration rate of ≥25 to ≤75 mL/min/1.73m^2 at treatment initiation, and
- 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 of at least 23mg/mmol, or type 2 diabetes mellitus or both.

In a randomised, double-blind, phase III study in patients with chronic kidney disease, treatment with dapagliflozin added to standard of care significantly reduced the risk of first occurrence of ≥50% sustained decline in estimated glomerular filtration rate, end stage renal disease, cardiovascular death or renal death when compared with standard of care alone.

Chairman
Scottish Medicines Consortium

Indication

In adults for the treatment of chronic kidney disease.[1]

Dosing Information

The recommended dose is 10mg dapagliflozin once daily.

Dapagliflozin can be taken orally once daily at any time of day with or without food. Tablets are to be swallowed whole.

In the DAPA-CKD study, dapagliflozin was administered in conjunction with other chronic kidney disease related therapies.

It is not recommended to initiate treatment with dapagliflozin in patients with an estimated glomerular filtration rate (eGFR) <15mL/min/1.73m^2. Please see Summary of product characteristics (SPC) for further information on special warnings and precautions for use for patients with renal impairment.[1]

Product availability date

9 August 2021

Summary of evidence on comparative efficacy

Dapagliflozin is a sodium-glucose co-transporter 2 (SGLT2) inhibitor. Inhibition of SGLT2 reduces reabsorption of glucose and sodium in the proximal renal tubule, which leads to urinary excretion of glucose and osmotic diuresis. An increase in the delivery of sodium to the distal tubule is believed to increase tubuloglomerular feedback and reduce intraglomerular pressure. These effects lead to a reduction in volume overload, reduced blood pressure and lower preload and afterload, which may have beneficial effects on cardiac remodelling and preserve renal function. The cardiac and renal benefits of dapagliflozin are not solely dependent on the blood glucose-lowering effect and not limited to patients with diabetes mellitus as demonstrated in the DAPA-HF and DAPA-CKD studies.[1]

The submitting company has requested that SMC considers dapagliflozin when positioned for use in patients with chronic kidney disease (CKD) and 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 (ACE) inhibitor or angiotensin receptor blocker (ARB), unless these are not tolerated.

The key evidence supporting the efficacy and safety of dapagliflozin in the indication under review comes from DAPA-CKD, an international, randomised, double-blind, parallel group, phase III study in patients with CKD, with and without type 2 diabetes mellitus**.** This study recruited adult patients with an eGFR ≥25 and ≤75mL/min/1.73m^2 and albuminuria with urine albumin creatinine ratio (uACR) ≥23 and ≤565 mg/mmol at screening. Eligible patients were also receiving a stable and maximum tolerated labelled daily dose of an ACE inhibitor or ARB for at least 4 weeks before screening, if not medically contraindicated (97% of patients were treated with ACE inhibitor or ARB, at randomisation).[2, 3]

Patients were randomised equally to receive dapagliflozin 10mg (n=2,152; dose could be reduced to 5mg if clinically indicated) or placebo (n=2,152), orally once daily. In addition to their treatment with ACE inhibitor or ARB (unless medically contraindicated), patients received background standard of care for CKD complications (such as hyperphosphataemia, hyperparathyroidism, hyperkalaemia, acidosis and renal anaemia), cardiovascular (CV) risk factors (for example blood pressure, lipids, and antithrombotic treatment), and diabetes mellitus. The subset of patients with type-2 diabetes mellitus (T2DM) at randomisation continued their T2DM treatment, based on established clinical guidelines and local laboratory values. Randomisation was stratified according to T2DM status (with or without) and UACR (>113 and ≤113 mg/mmol).[2]

The primary composite outcome was the time to the first occurrence of any of the components of this composite:

- ≥50% sustained decline in eGFR from baseline, based on two consecutive central laboratory values at least 28 days apart,
- reaching end stage renal disease (ESRD; sustained eGFR <15mL/min/1.73m^2 or, chronic dialysis treatment for at least 28 days [or dialysis treatment was stopped before day 28 due to death, futility or patient electing to stop dialysis and the renal deterioration is deemed irreversible] or, receiving a renal transplant),
- CV death,
- renal death.[2,3]

A hierarchical statistical testing strategy was applied in the study for the primary and three secondary efficacy outcomes with no formal testing of outcomes after the first non-significant outcome in the hierarchy (in the order of presentation in Table 1). With the exception of eGFR outcomes, all primary and secondary outcomes were adjudicated by a blinded independent review committee in the full analysis set (FAS), which included all randomised patients.[2, 3]

DAPA-CKD was an event-driven study that was stopped early, after a median follow-up of 2.4 years, due to clear efficacy. Dapagliflozin was superior to placebo in reducing the incidence of the primary composite and secondary outcomes. See details in Table 1 below.[2, 3]

Table 1: Primary and secondary efficacy outcome results from DAPA-CKD (FAS).[2, 3]

	Dapagliflozin (N=2,152)	Placebo (N=2,152)	Hazard ratio (95% CI)	p-value
Primary efficacy outcome				
Composite of ≥50% eGFR decline, ESRD and renal or CV death, % of patients with event (n/N)	9.2% (197/2152)	14% (312/2152)	0.61 (0.51 to 0.72)	<0.001
Secondary efficacy outcomes				
Composite of ≥50% eGFR decline, ESRD and renal death, % of patients with event (n/N)	6.6% (142/2152)	11% (243/2152)	0.56 (0.45 to 0.68)	<0.001
Composite of CV death and hospitalisation for HF, % of patients with event (n/N)	4.6% (100/2152)	6.4% (138/2152)	0.71 (0.55 to 0.92)	0.0089
Death from any cause, % of patients with event (n/N)	4.7% (101/2152)	6.8% (146/2152)	0.69 (0.53 to 0.88)	0.0035

***Abbreviations**: CI = confidence interval; CV =cardiovascular; eGFR = estimated glomerular filtration rate; ESRD = end stage renal disease; FAS = Full Analysis Set; HF = heart failure.*

Based on the Kaplan-Meier plot for the primary composite outcome, dapagliflozin and placebo curves separated early at around 4 months and continued to do so over the study period. In addition, all four components of the primary outcome (descriptively assessed) favoured the dapagliflozin group; however, the treatment effect was mainly driven by the components ≥50% sustained decline in eGFR (hazard ratio [HR]: 0.53 [0.42 to 0.67]) and ESRD (HR: 0.64 [0.50 to 0.82]). The endpoint ESRD was predominantly driven by decline in eGFR below 15 mL/min/1.73m^2. For the component renal death, only eight events were reported in total. The component CV death was numerically lower in the dapagliflozin group (HR: 0.81 [95% CI: 0.58 to 1.12]).[1]

The treatment benefit of dapagliflozin on the primary efficacy outcome was generally consistent across subgroups (including by T2DM status, uACR, and eGFR at baseline).[2]

Health Related Quality of Life (HRQoL) was assessed using two questionnaires: the Kidney Disease Quality of Life-36 (KDQOL™-36; a self-reported questionnaire that combines generic and disease-specific components to assess the HRQoL of patients with CKD), and the generic EuroQol five-dimensional five-level questionnaire (EQ-5D-5L).[3] No clinically relevant changes were seen at 12, 24 and 36 months compared to baseline for either group with these outcomes.[2]

The submitting company provided additional supportive evidence from two randomised, double-blind, phase III studies that compared dapagliflozin with placebo in different patient populations. DECLARE-TIMI 58 (N=17,160) included patients with T2DM, with or without albuminuria (30% of patients had albuminuria with uACR ≥30mg/g) at risk of CV events or with CV disease; only a small proportion of patients had CKD (7.4% of patients had eGFR <60mL/min/1.73m^2).[1] DAPA-HF

(N=4,744) included patients with heart failure with reduced ejection fraction, with or without T2DM; all patients had an eGFR ≥30mL/min/1.73m^2 (41% of patients had eGFR <60mL/min/1.73m^2).[1] The results of subgroup analyses suggested that dapagliflozin provides a treatment effect in a broader CKD population than the DAPA-CKD study.

The submitting company also performed an anchored matching-adjusted indirect comparison (MAIC) to compare the efficacy of dapagliflozin versus canagliflozin in patients with CKD who also have T2DM. However, they considered that canagliflozin was not a relevant comparator in Scotland and the results of this MAIC were only used in scenario analysis in the economics.

Summary of evidence on comparative safety

Overall, the safety profile of dapagliflozin in the DAPA-CKD study was considered similar to that previously seen with dapagliflozin for other indications and no new safety concerns have been raised. There is limited experience with initiating treatment with dapagliflozin in patients with eGFR <25mL/min/1.73m^2, and no experience with initiating treatment in patients with eGFR <15mL/min/1.73m^2. [1, 2]

In the DAPA-CKD study, the median duration of exposure in the dapagliflozin group was 27.3 months and in the placebo group was 27.0 months. Adverse events (AEs) were considered possibly related to the investigational product in 13% (275/2149) of patients in the dapagliflozin group and 10% (222/2149) in the placebo group. In the dapagliflozin and placebo groups respectively, patients with a reported serious AE on-treatment were 28% versus 31%, patients with a dose reduction due to treatment emergent AEs were 1.8% versus 1.4%, the proportion of AEs that led to dose interruptions were 13% versus 12%, and patients discontinuing therapy due to an AE were 5.5% versus 5.7%.[2]

The most frequently reported serious AEs on treatment with an incidence ≥1% in the dapagliflozin group versus the placebo group were: acute kidney injury (1.7% versus 2.0%), pneumonia (1.7% versus 2.7%), cardiac failure (1.6% versus 2.2%), acute myocardial infarction (1.3% versus 1.8%), end stage renal disease (1.1% versus 1.3%), ischaemic stroke (1.0% versus 1.0%), chronic kidney disease (0.7% versus 1.3%), and angina unstable (0.6% versus 1.0%). In the dapagliflozin group versus the placebo group, patients with an AE with an outcome of death were 3.1% and 4.0% on-treatment and 4.9% and 7.4% on- and off- treatment. In both treatment groups, most deaths occurred due to cardiac disorders.[2]

Summary of clinical effectiveness issues

Chronic kidney disease (CKD) is a common and serious progressive condition, associated with CV disease and increased risk of heart failure, premature death, ESRD, and the need for renal replacement therapy via dialysis or transplant. CKD is most commonly caused by diabetes (42%), hypertension (18%), and glomerulonephritis of varying aetiologies (18%). Treatment of the risk

factors associated with CKD progression are recommended. Standard of care for CKD patients consists of blood pressure and proteinuria control with renin-angiotensin-aldosterone system blockade (ACE inhibitors or ARBs) combined with management of CV risk (including with antihypertensive medicines, statins and antiplatelet medicines) and/or glycaemic control as necessary. Canagliflozin, another SGLT2 inhibitor, is licensed for the treatment of adults with insufficiently controlled T2DM as an adjunct to diet and exercise, which includes use as an add on to standard of care for the treatment of diabetic kidney disease.[4] UK guidelines recommend SGLT2 use in adults with CKD (if albuminuria exceeds 25 or 30mg/mmol) and with or without T2DM (for patients with eGFR ≥25mL/min/1.73m^2).[6-7] Clinical experts consulted by SMC considered that dapagliflozin fills an unmet need in this therapeutic area, namely by providing an add-on to standard of care that could help slow CKD progression.

The submitting company has requested that SMC consider dapagliflozin when positioned for use in patients with CKD and an eGFR of ≥25 to ≤75 mL/min/1.73m^2 at treatment initiation, who are receiving an ACE inhibitor or ARB, unless these are not tolerated. Compared with the licensed indication, this positioning population more closely reflects the DAPA-CKD study population. However, it includes patients with UACR <23mg/mmol without T2DM, a population in whom there is limited supporting data, and does not explicitly include patients with a contraindication to an ACE inhibitor or ARB.

In DAPA-CKD, treatment with dapagliflozin when added to standard of care (which included an ACE-inhibitor or ARB, unless medically contraindicated) significantly reduced the risk of first occurrence of the primary composite outcome (≥50% sustained decline in eGFR from baseline, reaching ESRD, or CV or renal death) by 39% when compared with standard of care alone; this was considered clinically relevant. The treatment effect was mainly driven by the components ≥50% sustained decline in eGFR and ESRD. Secondary outcomes and subgroups analyses were supportive and consistent with the primary outcome results for the overall population.[2]

However, the licensed indication is wider than DAPA-CKD study population. Specifically, study DAPA-CKD did not include patients with eGFR <25 mL/min/1.73m^2, with uACR <23mg/mmol[7], or not on CKD standard of care (i.e. on stable and maximum tolerated labelled daily dose of ACE inhibitor or ARB [unless medically contraindicated]). To address the lack of data for these subgroups and to justify the extrapolation of DAPA-CKD data to a wider population, some data from supportive studies were presented. These included data from patients with uACR <23mg/mmol from DECLARE-TIMI 58[6], which was conducted in patients with T2DM, who had or were at risk for atherosclerotic CV disease. However, robust data are still limited for some subgroups of patients that were not included within DAPA-CKD and completely lacking for others, such as the subgroup of patients without T2DM and with uACR <23mg/mmol. Thus, uncertainty remains around the generalisability of dapagliflozin effect to certain patient groups not represented in DAPA-CKD.

The submitting company defined the relevant comparator as standard of care, which encompasses a variety of treatment strategies to manage both the CKD itself and any underlying conditions and complications. They noted that canagliflozin has low uptake in Scottish clinical practice and

considered that it is not a relevant comparator. Some uncertainty remains about the relevance of canagliflozin as a comparator in T2DM patients; however, clinical experts consulted by SMC considered that dapagliflozin would not displace any therapies

Clinical experts consulted by SMC considered that dapagliflozin is a therapeutic advancement in the treatment of adults with CKD due to significant efficacy. They suggested that the place in therapy of dapagliflozin is as an add-on to standard of care, which includes an ACE inhibitor or ARB unless not tolerated.

Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis evaluating dapagliflozin for the positioning outlined above. In the model, 10mg daily of dapagliflozin was taken by patients alongside their current standard of care (SOC). SOC could include ACE inhibitors and ARBs for the treatment of CKD and statins and antiplatelet medicines for CV disease risk management. Clinicians consulted by SMC agreed that dapagliflozin would be used as an add-on treatment to current care. Dapagliflozin was assumed to be continued up until the point of kidney transplant or intolerable AEs.

The model structure was a Markov model with monthly cycles and 9 mutually exclusive health states. These included 6 CKD states (stages 1, 2, 3a, 3b, 4 and 5). Additionally there was a dialysis state, a transplant state and an absorbing death state. The model assumed that patients could move between the CKD stages 1 to 5 in a forward and backward direction. Once a patient progressed to the point of renal replacement therapy (RRT) (dialysis or transplant), they could not return to any of the other CKD states. Patients could experience the transient events of heart failure, acute kidney injury (AKI) and a variety of AEs.

The main source of clinical evidence used in the economic case was from a combined dataset that brought together patient level data from the DAPA-CKD study and the DECLARE-TIMI study.[3] For the purposes of modelling, the placebo arm of that study was considered equivalent to SOC. From individual patient level data, transition matrices were derived describing the monthly probability of moving between the CKD stages 1 to 5. There were different probability matrices between the placebo and dapagliflozin arms, and separate matrices for the periods of 0 to 4 months and 5 months onwards. This temporal separation was to capture the initial sharper fall in eGFR and then slower decline seen in the dapagliflozin arm than the placebo arm. The company reported this as typical of SGLT2 inhibitors. Given the low number of transitions from the dialysis state to the transplant state within the DAPA-CKD study, these transition probabilities were sourced from the literature.

The probability of mortality, heart failure and AKI were all similarly derived from the combined dataset of DAPA-CKD and DECLARE-TIMI. However, to provide a better match to the expected outcomes in a Scottish population, each was subject to adjustment via multivariate regression. These regressions contained coefficients including the characteristics of the patient population,

whether they were on treatment and their eGFR status in order to estimate adjusted probabilities across each stage. In the case of mortality, the probability of death within the dialysis and transplant states were taken from the literature.

A similar regression based approach was taken to model quality of life. EQ-5D scores were collected as part of the DAPA-CKD study. Estimates, adjusted for patient characteristics, were presented for each stage of CKD as well as the transient events and AEs, with the values being common to the dapagliflozin and SOC arms of the model. Again, the values for transplant and dialysis were derived from the literature. Further where some of the AE probabilities lacked face validity these were also taken from the literature.

Medicine costs covered the acquisition costs for all treatments, including ACE inhibitors, ARBs, antiplatelet medicines and statins, as well as the treatment of AEs. There were no administration costs and no additional monitoring was assumed for those treated with dapagliflozin.

Each of the health states was attributed a cost that covered all aspects of care, excluding the medicines costs that were accounted for separately. These costs were taken from the literature and increased in value from £1,211 per year for CKD stages 1 to 3b [9] to £32,360 per year for those receiving dialysis [10]. Transplant was associated with an initial cost of £25,472 [11] and a subsequent annual maintenance cost of £5,949 [12]. Transient events were costed separately.

The base case economic results are presented in the table below:

Table 2: Base case economic results.

		Incremental cost	Incremental QALYS	Incremental cost effectiveness ratio
1	**Broad population (weighted average based on the three populations presented below)**	£1,296	0.209	£6,209
2	DAPA-CKD like population with uACR ≥22.6 mg/mmol (sub-analysis 1)	-£2,348	0.361	Dominant
3	CKD patients with uACR <23 mg/mmol and T2DM (sub-analysis 2)	£2,209	0.274	£8,071
4	CKD patients with uACR <22.6 mg/mmol, without T2DM (sub-analysis 3)	£1,187	0.033	£35,644

Abbreviations: ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blockers; CKD: chronic kidney disease; QALYs: quality-adjusted life years; uACR: urinary albumin creatinine ratio; T2DM: type 2 diabetes mellitus; dominant result is dapagliflozin being cheaper and more effective than the comparator. All populations are based on patients with an eGFR ≥25 to ≤75 ml/min/1.73 m^2 treated with ACE inhibitors/ARBs, as per the revised target population for this submission

The disaggregation of these values showed that in the model dapagliflozin increased the time spent in the earlier disease stages (Stages 1 to 3b) and reduced the time spent in the later stages (Stages 4 & 5 and RRT) relative to SOC. In particular, the occupancy of Stage 3b was higher in the

dapagliflozin arm. This disease profile was associated with lower maintenance costs and higher health outcomes in the dapagliflozin group that offset the higher treatment costs.

As part of the economic case, the company submitted a variety of sensitivity and scenario analyses. A key selection of these is presented below, structured around the 'broad population' result presented in table 2 above.

Table 3: Summary of selected scenario analyses.

#	Base case description	Scenario description	ICER
1	Population matched on key criteria to Scottish CKD patients	Population matched to subgroup of Scottish CKD patients with comorbid T2DM	Dominant (dapagliflozin cheaper and more effective)
2	Patients continue dapagliflozin to transplant	Patients discontinue dapagliflozin following initiation of dialysis	£8,037
3	Patients exit model at death	Patients exit model at RRT	£13,207
4	Cohort starting age 76.8 (time horizon of 23.2 years)	Cohort starting age 60 (time horizon of 40 years)	£4,559
5		Cohort starting age 65 (time horizon 35 years)	£4,990

Abbreviations: RRT- renal replacement therapy (dialysis or transplant), ICER= incremental cost effectiveness ratio

The strengths of the economic case were:

- The design of the economic model was appropriate and suitable to represent the clinical area.
- The company reported having validated the model and approach with a variety of experts and clinicians.

The limitations of the analysis were identified as:

- There are issues with the clinical data that have been used in the economic model, as noted in the clinical effectiveness section above. As a result, the cost-effectiveness result in the uACR<23 without T2DM group remains the most uncertain and, as shown in table 2, has the highest ICER. Further, there were key differences in terms of age, sex, smoking and treatment status between the study population and the population of people with CKD in Scotland. This introduces important generalisability issues into the analysis.
- Transition probabilities in the model were uncertain due to data limitations and the employed estimation approach. While the company reported these were endorsed by clinical experts, they had questionable face validity and were not extensively explored in sensitivity analysis.
- To try and correct for the differences between the study and Scottish licensed populations, the company used multivariate analysis to adjust several inputs such as mortality and the frequency of transient health events. The approaches taken towards these adjustment may have introduced bias.

- The maintenance costs used across the early stages of CKD 1 to 3b were consistent, possibly underestimating the costs for the higher stages of that range. Dapagliflozin was modelled as having increased the time spent in stages 3a and 3b over SOC, and so underestimates of the costs in those stages would artificially lower the ICER.

Given these issues, dapagliflozin is accepted for restricted use in patients with chronic kidney disease (CKD) and

- an estimated glomerular filtration rate (eGFR) of ≥25 to ≤75 mL/min/1.73m^2 at treatment initiation, and
- are receiving an ACE inhibitor or ARB, unless these are not tolerated or contraindicated and
- have a uACR of at least 23 mg/mmol, or type 2 diabetes mellitus or both.

Summary of patient and carer involvement

No patient group submission was received.

Additional information: guidelines and protocols

The National Institute for Health and Care Excellence (NICE) published in August 2021 'Chronic Kidney Disease: Assessment and Management' [NG203].[5] These defined the levels of estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (UACR) used to classify CKD into stages with varying risk of adverse outcomes. An eGFR <15ml/min/1.73m^2 indicates kidney failure, or end-stage kidney disease [ESKD]). Recommendations are made in regards to the treatment of risk factors associated with CKD progression; such as cardiovascular disease, diabetes, hypertension and proteinuria. For adults with CKD and diabetes (type 1 or 2) an angiotensin receptor blocker (ARB) or an angiotensin converting enzyme (ACE) inhibitor are recommended (titrated to the highest licensed dose that the person can tolerate) if albumin: creatinine ratio (ACR) is 3mg/mmol or more. If patients have CKD without diabetes, an ARB or an ACE inhibitor are also recommended (titrated to the highest licensed dose that they can tolerate), if ACR is 70mg/mmol or more. If patients have hypertension or cardiovascular disease, recommendations include antihypertensive medicines, statins and antiplatelet medicines, respectively.

NICE guideline [NG28][6] on "Type 2 diabetes in adults: management" recommends that for adults with type 2 diabetes and CKD who are taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate), an SGLT2 inhibitor (in addition to the ARB or ACE inhibitor) should be offered if ACR is over 30mg/mmol and they meet the criteria in the marketing authorisation (including relevant estimated glomerular filtration rate [eGFR] thresholds) and it should be considered if ACR is between 3 and 30mg/mmol and they meet the criteria in the marketing authorisation (including relevant eGFR thresholds). These guidelines predate the availability of dapagliflozin.

The UK Kidney Association published in October 2021 “Clinical Practice Guideline : Sodium-Glucose Co-transporter-2 (SGLT-2) Inhibition in Adults with Kidney Disease”.[7] This guideline recommends the initiation of SGLT-2 inhibitors in people with kidney disease caused both by type 2 diabetes and other causes down to an eGFR of 25mL/min/1.73m^2, if albuminuria exceeds 25mg/mmol. The guideline highlights that the evidence for this is strongest in people with type 2 diabetes. In addition, the guideline recommends initiation of SGLT-2 inhibitors in people with CKD and a history of heart failure. Once initiated, this guideline recommends that the SGLT-2 inhibitor can be continued until the individual reaches end-stage kidney disease.

Additional information: comparators

Standard of care.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost year (£)
Dapagliflozin	**10mg once daily**	**476**

Costs from BNF online on 28 January 2022.

Additional information: budget impact

The submitting company estimated there would be 1,053 patients estimated to receive treatment in year 1 rising to 13,163 patients in year 5.

The gross impact on the medicines budget was estimated to be £511k in year 1 rising to £6.4m in year 5. As other medicines were assumed to be displaced, the net total medicines budget impact was estimated to be £480k in year 1 and £6m in year 5. Given there is no expected displacement of medicine likely to take place, this may be a slight underestimate expenses in year 1 and overestimate savings in year 5.

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This assessment is based on data submitted by the applicant company up to and including 11 March 2022.

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 represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. 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.