7.13 DAPAGLIFLOZIN, Tablet 10 mg, Forxiga®, AstraZeneca Pty Ltd

1 Purpose of Submission

1.1 The Early Re-Entry submission requested an Authority Required (STREAMLINED) general schedule listing for dapagliflozin for the treatment of chronic kidney disease (CKD).

2 Background

Registration status

2.1 Dapagliflozin (Forxiga) is registered on the Australian Register of Therapeutic Goods (ARTG) for chronic kidney disease, indicated to reduce the risk of progressive decline in kidney function in adults with proteinuric chronic kidney disease (CKD Stage 2, 3 or 4 and urine ACR greater than or equal to 30 mg/g).

Previous PBAC consideration

2.2 This is the fourth submission to the PBAC for CKD. Prior submissions were considered by PBAC in July 2021, September 2021 and November 2021. At its November 2021 meeting, the PBAC considered that the listing would be cost-effective at the price proposed in the pre-PBAC response from July 2021 (the [redacted] PBS price for dapagliflozin for [redacted]). However, PBAC considered that the revised financial estimates were high and uncertain, and did not form a reliable basis for a risk sharing arrangement (RSA) with the Australian Government.

3 Requested listing

3.1 An Authority Required (STREAMLINED) general schedule listing for dapagliflozin for the treatment of chronic kidney disease.

MEDICINAL PRODUCT medicinal product pack	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DAPAGLIFLOZIN				
dapagliflozin 10 mg tablet, 28	1	28	5	Forxiga
Restriction Summary [new] / Treatment of Concept: [new]				
	Category / Program: GENERAL – General Schedule (Code GE)			
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners			
	Restriction type: ☒Authority Required – Streamlined [new code]			

	Indication: Chronic kidney disease
	Clinical criteria:
	Patient must have an estimated glomerular filtration rate of between 25 and 75 mL/min/1.73 m^2 inclusive, to substantiate the diagnosis of kidney disease, prior to initiating treatment with this drug,
	AND
	Clinical criteria:
	Patient must have a urinary albumin to creatinine ratio of between 200 and 5000 mg/g inclusive, to substantiate the diagnosis of kidney disease, prior to initiating treatment with this drug,
	AND
	Clinical criteria:
	Patient must not progress to end-stage renal disease defined as an estimated glomerular filtration rate (eGFR) of less than 15 mL/min/1.73 m^2 while on this drug.
	AND
	Clinical criteria:
	Patient must receive treatment in combination with the maximum tolerated dose of an ACE inhibitor; or
	Patient must receive treatment in combination with the maximum tolerated dose of an angiotensin II antagonist
	AND
	Clinical criteria:
	Patient must not be receiving treatment with another sodium-glucose co-transporter 2 (SGLT2) inhibitor.
	Prescribing Instructions: Patient must be stabilised on either (i) an ACE inhibitor or (ii) an angiotensin II antagonist for a period of 4 weeks prior to initiation of combination therapy with this drug.
	Administrative Advice: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.

3.2 For the July 2021 submission the PBAC was asked to consider whether ACEI/ARB-intolerant or contraindicated patients should still be eligible for dapagliflozin. The Secretariat had suggested removing elements of the proposed criteria that permitted use of dapagliflozin where ACEI/ARB use was "medically contraindicated".

For more detail on PBAC's view, see section 6 PBAC outcome.

4 Comparator

4.1 Unchanged from standard care as the main comparator. This was previously considered to be appropriate (Public Summary Document [PSD] item 6.03, July 2021 PBAC, paragraph 7.1).

For more details on PBAC's view, see section 6 PBAC outcome.

5 Consideration of the evidence

Consumer comments

5.1 The PBAC noted and welcomed the input from organisations (2) via the Consumer

Comments facility on the PBS website. The PBAC noted the comments from Kidney Health Australia which considered that the listing would be of significant benefit for people living with CKD. The PBAC noted the comments from Diabetes Australia supporting the listing of dapagliflozin for CKD and highlighting the importance of treating diabetes-related complications such as CKD.

Clinical claim

5.2 The Early Re-Entry submission did not present new clinical evidence. The PBAC was previously satisfied that dapagliflozin added to standard care and provides, for some patients, a significant improvement in efficacy over standard care alone (PSD for item 6.03, July 2021 PBAC, paragraph 7.1).

Pricing

5.3 The Early Re-Entry submission did not propose a new price. The PBAC previously considered that the listing would be cost effective at the [redacted] PBS price for dapagliflozin for [redacted] (PSD, July 2021 PBAC, paragraph 7.1).

Estimated PBS utilisation and financial implications

5.4 As an Early Re-Entry submission, the financial estimates analysis and Risk Sharing Arrangement (RSA) proposal have not been independently evaluated.

5.5 The Early Re-Entry submission presented revised financial estimates for CKD with inputs and assumptions as recommended by PBAC in November 2021. The PBAC noted that the revised financial estimates were validated by the Drug Utilisation Sub-Committee (DUSC) Secretariat.

Financial Management – Risk Sharing Arrangements

5.6 An RSA was proposed by the sponsor in the context of the CKD population, combined with the agreed-upon utilisation caps for heart failure with reduced ejection fraction (HFrEF) and incorporating estimated utilisation for the currently listed T2DM indication. A [redacted]% rebate of expenditure exceeding the cap was proposed by the sponsor.

5.7 The T2DM estimates were revised since the previous submission (September 2021). The T2DM component of the base-case combined estimates included dapagliflozin and other SGLT2-Is.

Table 1: Base-case combined estimates across CKD + HFrEF + T2DM current listing for the total SGLT2-I market

	2022	2023	2024	2025	2026	2027
CKD: Net cost to R/PBS ($)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][4]
HFrEF: Net cost to R/PBS ($)	[redacted][1]	[redacted][4]	[redacted][6]	[redacted][7]	[redacted][9]	[redacted]*[11]
T2DM: Net cost to R/PBS ($)	[redacted][2]	[redacted][2]	[redacted][5]	[redacted][5]	[redacted][8]	[redacted][10]
Combined: Net cost to R/PBS ($)	[redacted][2]	[redacted][5]	[redacted][5]	[redacted][8]	[redacted][10]	[redacted][10]
Comparison with November 2021 estimates						
Combined: Net cost to R/PBS ($)	[redacted][2]	[redacted][5]	[redacted][5]	[redacted][8]	[redacted][10]	[redacted][12]
Difference ($)	[redacted][3]	[redacted][3]	[redacted][1]	[redacted][4]	[redacted][4]	[redacted][6]

Source: Table 5 of the main submission, Attachment 4 Sheet 'Base case combined SGLT2-I'.

Note: *2027 estimates not included in Executed Deed for HFrEF.

The redacted values correspond to the following ranges:

[1] *$10 million to < $20 million*
[2] *$200 million to < $300 million*
[3] *$0 to < $10 million*
[4] *$20 million to < $30 million*
[5] *$300 million to < $400 million*
[6] *$30 million to < $40 million*
[7] *$40 million to < $50 million*
[8] *$400 million to < $500 million*
[9] *$50 million to < $60 million*
[10] *$500 million to < $600 million*
[11] *$60 million to < $70 million*
[12] *$600 million to < $700 million*

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

6.1 The PBAC recommended the listing of dapagliflozin for the treatment of chronic kidney disease (CKD), noting that the resubmission provided revised financial estimates for CKD consistent with the inputs and assumptions advised by the PBAC in November 2021.

6.2 The PBAC noted standard care as the main comparator.

6.3 The PBAC reiterated that the listing for chronic kidney disease would be cost-effective at the price proposed, i.e. at the [redacted] PBS price for dapagliflozin for [redacted].

6.4 The PBAC did not accept the sponsor's proposed RSA consisting of a combined expenditure cap for the three SGLT2-I indications, including the agreed financial estimates for CKD, the agreed utilisation caps for HFrEF and incorporating estimated utilisation for the currently listed T2DM indication, and a [redacted]% rebate of expenditure exceeding the combined expenditure cap. The PBAC noted the outcomes of the cost-effectiveness review of SGLT2-I inhibitor medicines also considered at the March 2022 PBAC meeting. The PBAC noted that the projected utilisation of SGLT2-I medicines for

T2DM presented in the cost-effectiveness review was substantially less than the T2DM forecast proposed for the expenditure caps for the CKD listing. The PBAC considered that the resubmission's T2DM estimates remained likely substantially overestimated and did not provide a robust basis for setting RSA caps. As such, the PBAC recommended that the expenditure caps for the RSA should only be based on the agreed financial estimates for CKD and the agreed utilisation caps for HFrEF. The PBAC considered that T2DM should be excluded from the expenditure caps until appropriate financial estimates for this indication to inform the RSA are resolved.

6.5 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

7 Recommended listing

7.1 Add new indication (13188 – Chronic kidney disease) as follows:

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
DAPAGLIFLOZIN					
dapagliflozin 10 mg tablet, 28	NEW	1	28	5	Forxiga
Add restriction Summary [new] / Treatment of Concept: [new]					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners				
	Restriction type: ☒Authority Required – Streamlined [new code]				
	Indication: Chronic kidney disease				
	Treatment Phase:				
	Clinical criteria:				
	Patient must have a diagnosis of chronic kidney disease, defined as abnormalities of kidney structure or function present for 3 months or more, prior to initiating treatment with this drug,				
	AND				
	Clinical criteria:				
	Patient must have an estimated glomerular filtration rate of between 25 and 75 mL/min/1.73 m^2 inclusive prior to initiating treatment with this drug,				
	AND				
	Clinical criteria:				
	Patient must have a urinary albumin to creatinine ratio of between 200 and 5000 mg/g (22.6–565 mg/mmol) inclusive prior to initiating treatment with this drug,				
	AND				
	Clinical criteria:				
	Patient must discontinue treatment with this drug prior to initiating renal replacement therapy, defined as dialysis or kidney transplant,				
	AND				

	Clinical criteria:
	Patient must receive treatment in combination with the maximum tolerated dose of an ACE inhibitor; or
	Patient must receive treatment in combination with the maximum tolerated dose of an angiotensin II receptor antagonist unless medically contraindicated to these classes of drug,
	AND
	Clinical criteria:
	Patient must not be receiving treatment with another sodium-glucose co-transporter 2 (SGLT2) inhibitor.
	Prescribing instructions: Patient must be stabilised on either (i) an ACE inhibitor or (ii) an angiotensin II receptor antagonist for a period of 4 weeks, unless medically contraindicated, prior to initiation of combination therapy with this drug.
	Prescribing instructions: Patients with polycystic kidney disease, lupus nephritis or ANCA-associated vasculitis; patients requiring or with a recent history of cytotoxic or immunosuppressive therapy for kidney disease; and patients with an organ transplant are not eligible for treatment with this drug.
	Administrative advice: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.

This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.