5.08 DAPAGLIFLOZIN WITH SITAGLIPTIN, Tablet containing dapagliflozin 10 mg with sitagliptin 100 mg Sidapvia®, AstraZeneca Pty Ltd.

1 Purpose of submission

1.1 The Category 2 submission requested Authority Required (Streamlined) listing for the fixed dose combination (FDC) product containing dapagliflozin 10 mg with sitagliptin 100 mg. The FDC was proposed for triple therapy, in conjunction with metformin, of patients with Type 2 diabetes mellitus (T2DM) with an inadequate response to treatment with dual therapy of metformin and an inhibitor of sodium glucose co-transporter 2 (SGLT2i), including but not only dapagliflozin, or metformin and an inhibitor of dipeptidyl peptidase 4 (DPP4i), including but not only sitagliptin.

1.2 Listing was requested on the basis of a cost-minimisation approach versus the individual components of the FDC, dapagliflozin and sitagliptin.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Treatment of patients with T2DM who are inadequately controlled with a with dual oral combination therapy with metformin (MET) and a dipeptidyl peptidase 4 (DPP4) inhibitor or a sodium-glucose co-transporter 2 (SGLT2) inhibitor
Intervention	DAPA/SITA FDC tablet (DAPA 10 mg/SITA 100 mg)
Comparator	DAPA 10 mg and SITA 100mg given individually
Outcomes	Bioequivalence based on pharmacokinetic parameters (i.e., AUCinf, AUClast and Cmax).
Clinical claim	DAPA/SITA FDC is bioequivalent to the individual components taken concomitantly

Source: Table 1.1.2, p19 of the submission.

Abbreviations: AUCinf = area under the plasma concentration-time curve from zero to infinity; AUClast = area under the plasma concentration-time curve from zero to the last quantifiable concentration; Cmax = maximum serum concentration; DAPA = dapagliflozin; FDC fixed dose combination; MET = metformin; SITA = sitagliptin; T2DM = type 2 diabetes mellitus

2 Background

Registration status

2.1 **TGA status at time of PBAC consideration**: The submission was made under the TGA/PBAC Parallel Process. The submission stated that the Marketing Authorisation Application was submitted in parallel with Singapore under the ACCESS New Active Substance Work Sharing Initiative and that the Singapore Health authority has reviewed the Clinical section of the dossier. Under this agreement, the Sponsor only receives reports for modules evaluated by the TGA and therefore did not have access to the regulatory Clinical Evaluation Report.

2.2 At the time of PBAC consideration, the TGA Delegate's Overview was available. The Delegate's Overview noted that while a decision is yet to be made, the Delegate was

inclined to approve the registration of the product. The Delegate noted that based on the available data, at this stage, the benefit-risk ratio is considered positive for a T2DM indication, subject to updates to indication wording and revisions to the PI.

Previous PBAC consideration

2.3 The PBAC has not previously considered an application for this combination product. However, other FDCs containing a DPP4i and a SGLT2i are listed on the PBS following recommendations made by the committee in 2017. These are dapagliflozin/saxagliptin (Qtern), empagliflozin/linagliptin (Glyxambi) and ertugliflozin/sitagliptin (Steglujan). Steglujan was delisted from the PBS on 1 February 2024.

2.4 Currently listed oral FDCs for T2DM are listed in Table 2.

Table 2: Current PBS-listed FDCs for treatment of T2DM

Metformin + DPP4i	Metformin + SGLT2i	DPP4i + SGLT2i
Linagliptin + metformin Trajentamet 2.5/500, 2.5/850, 2.5/1000	**Dapagliflozin + metformin** Xigduo XR 5/1000, 10/500, 10/1000	**Dapagliflozin + saxagliptin** Qtern 5/10
Saxagliptin + metformin Kombiglyze XR 2.5/1000, 5/1000, 5/500	**Empagliflozin + metformin** Jardiamet 5/500, 5/1000, 12.5/500, 12.5/1000	**Empagliflozin+ linagliptin** Glyxambi 10/5, 25/5
Alogliptin + metformin Nesina Met 12.5/1000, 12.5/500, 12.5/850		
Sitagliptin + metformin Janumet / Sitagliptin/metformin Sandoz / Velmetia 50/500, 50/850, 50/1000 Janumet XR / Sitagliptin/metformin Sandoa XR 50/1000, 100/1000, Sitagliptin/metformin Sandoz, Sitagliptin/metformin Sandoz Xr,		
Vildagliptin + metformin Galvumet 50/1000, 50/500, 50/850		

Source: Constructed during the evaluation.
Abbreviations: DPP4i = dipeptidyl peptidase 4 inhibitor; SGLT2i = sodium-glucose co-transporter 2 inhibitor.
Ertugliflozin + sitagliptin FDC (Steglujan). was removed from the PBS on 1 February 2024.

2.5 The PBAC has previously determined that all of the above FDCs are interchangeable on an individual patient basis within its respective class (section 12, metformin with saxagliptin Public Summary Document (PSD), November 2013 PBAC meeting; paragraph 7.6, empagliflozin with metformin PSD, November 2015 PBAC meeting, paragraph 7.8, ertugliflozin with sitagliptin PSD, July 2018 PBAC meeting).

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Requested listing

3.1 Suggestions and additions proposed by the Secretariat are added in italics and suggested deletions are crossed out with strikethrough.

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**No. of repeats**	**Available brands**
DAPAGLIFLOZIN + SITAGLIPTIN					
dapagliflozin 10 mg + sitagliptin 100 mg tablet, *28*	NEW	1	28	5	Sidapvia 10/100

Restriction Summary [new] / Treatment of Concept: [new]	
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (GE)
	Prescriber type: ☒Medical Practitioners
	Restriction type: ☒Authority Required (Streamlined) [new]
Prescribing rule level	***Administrative Advice:*** *This fixed dose combination is not PBS-subsidised for use as a sole therapy or in combination with a thiazolidinedione (glitazone), a glucagon-like peptide-1 analogue, an insulin, another dipeptidyl peptidase 4 inhibitor (gliptin), or another SGLT2 inhibitor.*
	Indication: Diabetes mellitus type 2
	Treatment Phase: Initial treatment
	Clinical criteria:
	The treatment must be in combination with metformin.
	AND
	Clinical criteria:
	Patient must have an HbA1c measurement greater than 7% despite treatment with dual oral combination therapy with metformin and a dipeptidyl peptidase 4 inhibitor (gliptin) or a sodium-glucose co-transporter 2 (SGLT2) inhibitor; or
	Patient must have, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period prior to initiation of triple oral therapy with a sodium-glucose co-transporter 2 (SGLT2) inhibitor, metformin and a gliptin.
	~~**Treatment criteria**~~ ***Prescribing Instructions*:**
	The date and level of the qualifying HbA1c measurement must be documented in the patient's medical records at the time triple oral therapy with an SGLT2 inhibitor, metformin and a gliptin is initiated.
	The HbA1c must be no more than 4 months old at the time triple oral therapy with an SGLT2 inhibitor, metformin and a gliptin is initiated.
	Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances: (a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or (b) Had red cell transfusion within the previous 3 months.
	The results of the blood glucose monitoring, which must be no more than 4 months old at the time of initiation of triple oral therapy with an SGLT2 inhibitor, metformin and a gliptin, must be documented in the patient's medical records.

Restriction Summary [new] / Treatment of Concept: [new]	
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (GE)
	Prescriber type: ☒Medical Practitioners ☒*Nurse practitioners*
	Restriction type: ☒Authority Required (STREAMLINED) [new]

Prescribing rule level		***Administrative Advice:*** *This fixed dose combination is not PBS-subsidised for use as a sole therapy or in combination with a thiazolidinedione (glitazone), a glucagon-like peptide-1 analogue, an insulin, another dipeptidyl peptidase 4 inhibitor (gliptin), or another SGLT2 inhibitor.*
		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.*
		Indication: Diabetes mellitus type 2
		Treatment Phase: Continuing treatment
		Clinical criteria:
		The treatment must be in combination with metformin.
		AND
		Clinical criteria:
		Patient must have previously received a PBS-subsidised regimen of oral diabetic medicines which included a sodium-glucose co-transporter 2 (SGLT2) inhibitor, metformin and a gliptin for this condition.

3.2 The DPMQ requested was $88.38. The AEMP requested was $70.12, which is the sum of the AEMPs of the currently listed sitagliptin ($28.43) and dapagliflozin ($41.69).

3.3 The PBAC noted restrictions should be aligned with the recent recommendations made by the PBAC at the July 2023 PBAC meeting (item 10.06 PBS Restrictions for Type 2 diabetes mellitus medicines, July 2023 PBAC meeting). The principle changes relevant to the submission were:

- gliptins and flozins must be used with at least one of metformin, insulin, or a sulfonylurea, and the patient must have responded inadequately to at least one of those;
- use of the FDCs gliptins + metformin and flozins + metformin require an inadequate response to metformin, and the FDCs gliptin + flozin require an inadequate response to metformin + gliptin or flozin;
- for GLP-1RA use, (1) patients must be using at least one of metformin, insulin or a sulfonylurea, and "must not have achieved a clinically meaningful glycaemic response with an SGLT2 inhibitor" (no level of HbA1c is specified) or have a contraindication or intolerance to SGLT2 inhibitor therapy requiring treatment discontinuation, and (2) although concomitant use for T2DM of an SGLT2i and GLP-1RA is not subsidised, patients can use a PBS-subsidised SGLT2i for an indication other than T2DM and PBS-subsidised GLP-1RA for T2DM if they have not achieved a clinically meaningful glycaemic response to the SGLT2i.

3.4 In addition, the PBAC suggested that "it may be appropriate to expand the PBS listings for GLP-1 RAs to include people with T2DM who have a body mass index (BMI) greater than 35 kg/m^2 for use in combination with metformin, sulfonylurea or insulin, and without a requirement for contraindication, intolerance or lack of a clinically meaningful glycaemic response to an SGLT2 inhibitor", and noted the following recommendation from March 2022 was not yet implemented: "to expand the PBS-listings for SGLT2 inhibitors to include T2DM patients with established cardiovascular disease or high cardiovascular risk without a glycaemic requirement".

3.5 The Pre-Sub-Committee Response (PSCR) disagreed with the Secretariat proposal to include the following administrative note "This fixed dose combination is not PBS-subsidised for use as a sole therapy or in combination with a thiazolidinedione (glitazone), a glucagon-like peptide-1 analogue, an insulin, another dipeptidyl peptidase 4 inhibitor (gliptin), or another SGLT2 inhibitor." However, the ESC noted this proposal aligned with the current listing for saxagliptin + dapagliflozin and empagliflozin + linagliptin.

3.6 Additionally, the PSCR argued the current restriction of dapagliflozin and dapagliflozin + metformin does not exclude insulin use. The ESC noted that removing "an insulin" from the proposed administrative note aligns with treatment guidelines. However, the ESC noted that while the PBAC in its July 2023 consideration of the PBS restrictions for T2DM medicines recommended a number of changes, it chose to retain this note that excludes combination use with insulin. The PBAC discussed that allowing insulin to be used with DPP4i + SGLT2i FDCs would be reasonable as it is consistent with treatment guidelines and that it would prevent increased use of insulin which in turn would reduce the risk of hypoglycaemia and weight gain. The PBAC agreed with ESC's suggestion to remove insulin from the administrative note to allow insulin to be used in combination with metformin and FDCs containing a DPP4i and a SGLT2i. The PBAC advised the removal of insulin from this administrative note should be added to the July 2023 recommended restriction changes for SGLT2i + DPP4i FDCs.

3.7 The submission stated that 60-day dispensing would not apply to the DAPA/SITA FDC. However, the PBAC noted that alternative product combinations that could be used to achieve triple therapy are included in the 60-day prescription measure and were implemented on 1 March 2024. The PBAC also noted including DAPA/SITA FDC in the 60-day prescription measure would likely reduce patient costs and increase PBS costs to Government, consistently with other similar products on the PBS. The PBAC considered it would be reasonable to include the DAPA/SITA FDC in the 60-day prescription measure.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 T2DM is a common condition associated with substantial risks of serious morbidity and of mortality.

4.2 Glucose homeostasis is a complex process; several aspects of the process can be targeted to control hyperglycaemia, and combinations of treatments targeting different aspects of the homeostatic process are commonly employed.

4.3 Dapagliflozin is an inhibitor of SGLT2. SGLT2 is present in the epithelial cells of the proximal tubule of the kidney, and inhibition reduces tubular reabsorption of filtered glucose and sodium. Treatment with SGLT2i is associated with reductions in:

- cardiovascular morbidity and mortality in patients with T2DM and manifest cardiovascular disease

- hospitalisation for heart failure in patients with T2DM and high cardiovascular risk
- progression of diabetic nephropathy
- body weight
- all-cause mortality.

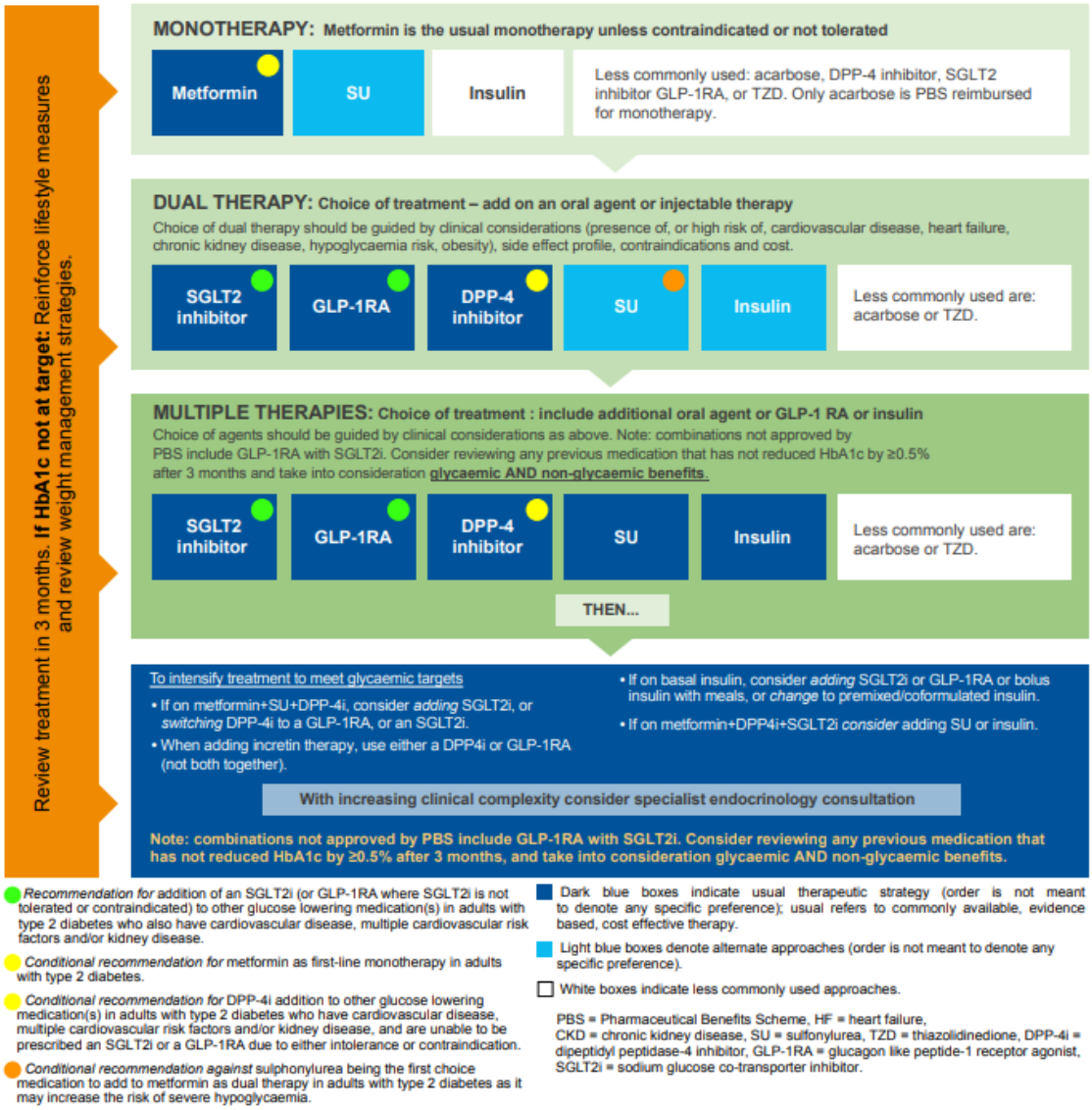
4.4 Sitagliptin is an inhibitor of DPP4. DPP4 is present on the surface of most cells, where it degrades glucagon-like peptide 1 (GLP-1) and some other peptide mediators. However, the effects of DPP4i on GLP-1 activity are less than and not additive to those of GLP-1 receptor agonists (GLP-1RA), and co-administration of DPP4i and GLP-1RA is inappropriate.

4.5 DPP4i treatment is not associated with reduced risk of major cardiovascular or cerebrovascular events, progression of renal impairment, or all-cause mortality, or with weight loss.

4.6 Both SGLT2i and DPP4i are associated with a low risk of symptomatic hypoglycaemia. SGLT2i are associated with genito-urinary infections due to glycosuria, hypotension due to volume contraction, and lower limb amputations, and are contra-indicated in Stage 4 or 5 kidney disease (estimated glomerular filtration rate < 30 mL/min/1.73 m^2) and by a history of diabetic ketoacidosis. DPP4i are contra-indicated by a history of pancreatitis.

4.7 The current Australian treatment recommendations, as presented in the submission, are shown in Figure 1.

Figure 1: Current Australian T2DM glycaemic management algorithm



Source: Figure1.2.1, of the submission

4.8 It is notable that it is recommended that: (1) the choice of second and third-line medications should consider both glycaemic and non-glycaemic effects, and for this reason, (2) a SGLT2i or a GLP-1RA is preferable as second-line treatment to a DPP4i, and (3) in third line treatment, a GLP-1RA is generally preferable to a DPP4i.

4.9 This suggested sequence is partially reflected in the recent changes to PBS restrictions for T2DM treatments, notably the requirement for a trial of a SGLT2i (or contraindication) as a condition of eligibility for a GLP-1RA (paragraph 3.3-4, above).

4.10 When the PBAC considered dapagliflozin as add-on treatment for patients inadequately controlled on metformin + DPP4i, it expressed concern that the listings for T2DM treatments may be consistent with guidelines but nevertheless inappropriate. In that case, there was concern that although guidelines suggested both SGLT2i and DPP4i as second- and/or third-line treatments, the proposed

restriction "inappropriately restricts the initiation of triple therapy to a fixed sequence of dapagliflozin add-on to metformin and a DPP4 inhibitor, this is narrower than published guidelines and clinical practice which recommend multiple options for add-on therapy across a range of glucose-lowering drugs at each line of therapy" (paragraph 4.2, dapagliflozin PSD, July 2017 PBAC Meeting; see also paragraphs 2.5-6). Similar concerns were noted by the PBAC when recommending changes to simplify the restrictions for a range of T2DM medicines in July 2023 (PBS Restrictions for Type 2 diabetes mellitus medicines, PBAC outcomes, July 2023 PBAC meeting).

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Comparator

5.1 The submission nominated dapagliflozin and sitagliptin individual components as the comparator.

5.2 The submission stated that "the additive effectiveness of dapagliflozin + sitagliptin + metformin" was established by data considered by the PBAC in July and November 2017; this data was re-presented in the submission (see Table 7 below). The trial presented compared the addition of dapagliflozin or placebo to metformin + sitagliptin; the results established that the addition of dapagliflozin to metformin + sitagliptin was effective but did not address the gap in evidence noted by the PBAC. This is especially important because the guidelines presented in the submission, and the recent changes to PBS restrictions for T2DM treatments, do not support the treatment sequence used in the trial, being metformin, then metformin + DPP4i, then metformin + DPP4i + SGLT2i.

5.3 Medications whose use is very likely to be affected are other FDCs combining an SGLT2i and a DPP4i, and FDCs of metformin plus a DPP4i (metformin + alogliptin, linagliptin, saxagliptin, vildagliptin and sitagliptin) or metformin + SGLT2i (metformin + empagliflozin, and metformin + dapagliflozin). FDCs of metformin + SGLT2i or DPP4i are especially relevant, because a patient taking, for example, an FDC of metformin + SGLT2i for whom the addition of a DPP4i inhibitor is considered appropriate can either add the DPP4i alone or switch to metformin alone and an FDC of SGLT2i + DPP4i. (A triple combination FDC of metformin + empagliflozin + linagliptin is registered in the USA but not Australia). This is acknowledged in the submission and included in the financial estimates, but it is not aligned with the submission's clinical rationale of reducing pill burden for listing of the dapagliflozin/sitagliptin FDC. The sponsor presented a "rationale for listing", which was the benefits of "reduc[ing] the medication burden on some patients, by reducing the number of tablets required to be taken by one [tablet] (metformin + dapagliflozin + sitagliptin to metformin + dapagliflozin/sitagliptin FDC)" (of the submission main body) i.e. two tablets rather than three.

5.4 In the context of the cost-minimisation approach taken by the submission, a further consideration for PBAC is that, under Section 101(3B) of the *National Health Act 1953*, when the proposed medicine is substantially more costly than an alternative therapy,

the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy.

5.5 For the requested population, the following PBS-listed medicines may also be considered alternative therapies because they could be replaced in practice: sulphonylureas (glimepiride, gliclazide, glibenclamide, glipizide), insulin, and GLP-1RA (exenatide, semaglutide, dulaglutide) as well as FDCs of a SGLT2i + DPP4i that are currently listed: empagliflozin + linagliptin and ertugliflozin + sitagliptin. Some of these alternative therapies may be less costly than dapagliflozin/sitagliptin. The ESC advised it would be reasonable to compare dapagliflozin/sitagliptin FDC with other SGLT2i + DPP4i FDCs.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer comments

6.2 The PBAC noted and welcomed the input from a consumer group/organisation (1) via the Consumer Comments facility on the PBS website. The PBAC noted the advice received from the National Aboriginal Community Controlled Health Organisation (NACCHO). The comment supported the listing of dapagliflozin/sitagliptin FDC as it would reduce pill burden and provide an alternative FDC in this treatment space to ensure adequate supply in the event of product shortages. The PBAC noted NACCHO's feedback regarding metformin, in particular the burden on treatment of using metformin in combination with SGLT2i and a DPP4i. NACCHO noted the large size of metformin tablets results in patient non-compliance and difficulties when packing it into dose administration aids (e.g. Webster packs). Therefore, NACCHO suggested that the restrictions for dapagliflozin/sitagliptin FDC should not include the requirement to combine treatment with metformin as it is superfluous and risks creating a barrier to effective treatment for patients who may have issues with metformin. The PBAC noted NACCHO's feedback on metformin and would be willing to discuss this matter further with NACCHO.

Clinical study

6.3 The submission was based on one bioequivalence study comparing the FDC of dapagliflozin + sitagliptin to the components, referred to as Study 14.

6.4 Details of the study are provided in Table 3.

Table 3: Bioequivalence study presented in the submission

Trial ID	Protocol title	Publication citation
EudraCT Number 2021-005104-35	A Randomized, 2-period, 2-treatment, Single-dose, Crossover Study to Assess the Bioequivalence of the Fixed Dose Combination (FDC) of Dapagliflozin 10 mg and Sitagliptin 100 mg, and Dapagliflozin 10 mg and Sitagliptin 100 mg Administered as Individual Tablets in Healthy Subjects.	NR

Source: Study 0014 Clinical Study Report,. NR = not reported.

6.5 The key features of Study 14 are summarised in Table 4.

Table 4: Key features of the bioequivalence study

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
FDC DAPA/SITA vs DAPA and SITA					
Study 14	46	R, OL	*Low*	Healthy, 18-55 years, male or female, BMI 18.5 to 30 kg/m^2 and weight 50-100 kg	AUCinf, AUClast, Cmax; adverse events

Source: CSR,.

Abbreviations: AUCinf = area under curve at infinite time; AUClast = area under curve to last observation; BMI = body mass index; Cmax = maximum concentration; DAPA = dapagliflozin; OL = open label; R = randomised; SITA = sitagliptin.

6.6 The dapagliflozin/sitagliptin FDC was referred to as Treatment A, and the components separately was referred to as Treatment B. Subjects were randomised to receive the treatment in the order A then B, or B then A. Administration of treatments was unblinded, but data collection and analysis were strictly protocol-driven and the open-label nature of the study does not elevate the risk of bias.

6.7 Results of the pharmacokinetic outcomes are shown in Table 5. There were no differences in the pharmacokinetic parameters between the FDC and the components.

Table 5: Summary of pharmacokinetic results

Parameter (unit)	Treatment	n	Geometric LSM (95% CI)	Pairwise comparison A/B Ratio (%) (90% CI)
DAPA in FDC (A) vs. DAPA individual (B)				
AUCinf (h·ng/mL)	A	42	429.8 (399.8, 462.1)	98.77 (96.87, 100.71)
	B	42	435.2 (404.7, 467.9)	Reference
AUClast (h·ng/mL)	A	43	424.3 (394.4, 456.5)	99.49 (97.50, 101.51)
	B	43	426.5 (396.5, 458.9)	Reference
Cmax (ng/mL)	A	43	112.9 (103.5, 123.1)	96.96 (90.57, 103.81)
	B	43	116.4 (106.7, 127.0)	Reference
SITA in FDC (A) vs. SITA individual (B)				
AUCinf (h·ng/mL)	A	43	3313 (3113, 3526)	99.74 (98.25, 101.26)
	B	43	3322 (3121, 3535)	Reference
AUClast (h·ng/mL)	A	43	3271 (3074, 3481)	99.85 (98.33, 101.40)
	B	43	3276 (3078, 3486)	Reference
Cmax (ng/mL)	A	43	362.2 (329.8, 397.9)	100.12 (94.51, 106.07)
	B	43	361.8 (329.4, 397.4)	Reference

Source: Table ES2, of the submission.

Abbreviations: AUCinf = Area under plasma concentration-time curve from zero to infinity; AUClast = Area under the plasma concentration-time curve from zero to the last quantifiable concentration; Cmax = Maximum observed plasma drug concentration; CI = confidence interval; LSM = least-squares mean; n = number of subjects included in the statistical comparison analysis.

Notes:

Treatment A = 1 × dapagliflozin/sitagliptin 10 mg/100 mg FDC tablet (test formulation).

Treatment B = 1 × dapagliflozin 10 mg tablet + 1 × sitagliptin 100 mg tablet co-administered as individual tablets (reference formulation).

Only the subjects with valid PK parameter in both treatments were included for statistical analysis.

Result based on linear mixed effect ANOVA of log-transformed PK parameter with sequence, period, treatment as fixed effect, and subject nested within sequence as random effect.

Geometric mean ratio and corresponding 90% CI were back transformed and presented as percentages. Geometric LS mean and corresponding 95% CI were also back transformed.

6.8 Results of the safety assessment are shown in Table 6. No differences were apparent, although with a total of 46 participants, only very large differences in the rate of adverse events would be detectable.

Table 6: Summary of adverse events

	Treatment A DAPA/SITA FDC N=44 n (%)	Treatment B DAPA + SITA N=45 n (%)	Total N=46 n (%)
Any AE	12 (27.3)	12 (26.7)	20 (43.5)
Any SAE	0	0	0
Any SAE with outcome of death	0	0	0
Any AE leading to discontinuation of IMP	1 (2.3)	2 (4.4)	3 (6.5)
Any possibly related AE[a]	11 (25.0)	5 (11.1)	15 (32.6)
Any possibly related SAE[a]	0	0	0

Source: Table 2.5.6, of the submission.

Abbreviations: AE = Adverse event; DAPA = dapagliflozin; FDC = fixed dose combination; IMP = investigational medicinal product; n =number of subjects per category; N = number of subjects per treatment group; SAE = serious adverse event; SITA = sitagliptin.

[a] judged by the investigator to be possibly or probably related to the treatment.

6.9 The submission also presented a brief summary of the results from Study 10/Stratum 2, which was considered by the PBAC in July and November 2017. The results for mean change in HbA1c are presented in Table 7.

Table 7: Results of mean change in HbA1c from baseline across randomised trials assessing the addition of DAPA to SITA + MET

Treatment group	Baseline HbA1c Mean (SD)	Week 24 HbA1c Mean (SD)	Adj change from baseline Mean (SD)	Difference in adj change Mean (95 % CI)
Intervention – Study 10 [Stratum 2 only]				
DAPA+SITA+MET (n=113)	7.80 (0.81)	7.38 (0.73)	-0.43 (0.64)	-0.40 (-0.58, -0.23)
PBO+SITA+MET (n=113)	7.87 (0.75)	7.84 (1.05)	-0.02 (0.64)	Reference

Source: Table 2.5.5, of the submission. Abbreviations: Adj = adjusted; CI = confidence interval; DAPA = dapagliflozin; HbA1c = glycosylated haemoglobin; MET = metformin; PBO = placebo; SD = standard deviation; SITA = sitagliptin

Comparative harms

6.10 No extended assessment of comparative harms was presented by the submission; the submission stated that the safety of dapagliflozin and sitagliptin are already well established. This was reasonable, since sitagliptin has been in use since 2006 and dapagliflozin since 2012.

Clinical claim

6.11 The submission described the FDC as bioequivalent to the components taken separately. The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonable. The TGA Delegate's Overview (p23) stated the efficacy and safety of dapagliflozin and sitagliptin for the use in T2DM was established. Additionally, the PBAC noted the overview stated the bioequivalence of dapagliflozin and sitagliptin between dapagliflozin/sitagliptin 10mg/100mg FDC tablet and co-administered dapagliflozin 10mg tablet and sitagliptin 100mg tablet was demonstrated.

Economic analysis

6.12 The submission presented a cost-minimisation approach comparing the cost of the FDC to its components. The key components are summarised in Table 8.

Table 8: Key components and assumptions of the cost-minimisation approach

Component	Claim or assumption
Therapeutic claim: effectiveness	Based on evidence presented in Section 2, FDC of dapagliflozin/sitagliptin added to metformin is assumed to be therapeutically bioequivalent compared with taking each treatment individually.
Evidence base	Bioequivalence between the FDC and individual formulations was demonstrated in healthy individuals in a 2-period, 2-treatment, single-dose crossover study (Study 14). Bioequivalence was based on: • Area under plasma concentration-time curve from zero to infinity (AUCinf) for dapagliflozin and sitagliptin, • Area under the plasma concentration-time curve from zero to the last quantifiable concentration (AUClast) for dapagliflozin and sitagliptin, and • Maximum observed plasma (peak) drug concentration (Cmax) for dapagliflozin and sitagliptin.
Equi-effective doses	Comparison of doses of dapagliflozin+sitagliptin FDC with dapagliflozin and sitagliptin are based on the dosage recommendations in the product information and Study 14. The proposed equi-effective dose is dapagliflozin / sitagliptin FDC (10 mg/100 mg) = dapagliflozin 10 mg + sitagliptin 100 mg **Dapagliflozin:** The recommended dose of dapagliflozin in the PI is 10 mg per day. Dapagliflozin 10 mg is the only available marketed strength. The dose of dapagliflozin 10 mg per day is aligned with the dose in the Study 14 trial protocol. At the time of the submission, dapagliflozin 10mg is currently listed on the PBS with a DPMQ of $57.82 (AEMP $41.69) for a pack of 28 tablets. **Sitagliptin:** The recommended target dose of sitagliptin in the PI is 100 mg per day. The dose of sitagliptin 100 mg per day is aligned with the dose in the Study 14 trial. At the time of the submission, sitagliptin 100 mg is currently listed on the PBS with a DPMQ of $43.56 (AEMP $28.43) for a pack of 28 tablets.
Direct medicine costs	The proposed AEMP for dapagliflozin/sitagliptin FDC (10 mg/100 mg) is based on the sum of component products approach, i.e., adding the cost per day (AEMP) of 10 mg dapagliflozin to 100 mg sitagliptin. Thus, the proposed ex-manufacturer price for a 28-day supply of dapagliflozin/sitagliptin FDC (10 mg/100 mg) for the management of T2DM in patients who are treated with metformin is $70.12 (DPMQ $88.38).
Other costs or cost offsets	None.

Source: Table 3.1.1, of the submission.
Abbreviations: dapagliflozin = dapagliflozin; FDC = fixed dose combination; MET = metformin; PBO = placebo; SITA = sitagliptin

6.13 The equi-effective doses were estimated as dapagliflozin/sitagliptin FDC (10 mg/100 mg) = dapagliflozin 10 mg + sitagliptin 100 mg.

6.14 The submission stated that the proposed cost per day (AEMP) for the FDC was based on the PBAC guidelines which state "generally, the combination product will have the same cost as its components". Thus, the proposed AEMP per 28-day supply was $70.12 ($41.69 + $28.43). The proposed dispensed price using October 2023 markups for a 28-day supply of dapagliflozin/sitagliptin FDC (10 mg/100 mg) for the management of T2DM in patients who are treated with metformin was $88.38. The ESC noted that some diabetes medicines are subject to price reductions on 1 April 2024, i.e. Anniversary price reduction of 5% for dapagliflozin (SGLT2i) and alogliptin (DPP4i) and Price Disclosure for metformin (reduction between 14.91% to 14.96%) and sitagliptin (reduction of 19.35%). These price reductions will flow on to the relevant FDC diabetes medicines, therefore, the price for these diabetes medicines

and the relevant FDCs (refer Table 2) will be lower than the current AEMPs from 1 April 2024.

6.15 The submission quoted the PBAC as accepting the approach of using the costs of the individual components for the cost-minimisation approach in its consideration of dapagliflozin + saxagliptin FDC in July 2017. The evaluation noted that this is not correct. The PBAC accepted the use of the components as the comparator for the FDC, but not the cost-minimisation against the sum of the component costs. The PBAC noted that there was no evidence that adding a third drug – whether that was a SGLT2i added to metformin + DPP4i or a DPP4i added to metformin + SGLT2i – provided the same incremental benefit as adding either to metformin, and, therefore, "the PBAC was of the view that it would not be cost-effective for dapagliflozin + a DPP4i + metformin treatment to be at the same price as the sum of the component parts" (para 7.3, dapagliflozin + saxagliptin PSD, July 2017 PBAC Meeting).

6.16 The PSCR presented a weighted approved ex-manufacturer's price (AEMP) across the treatments that would likely be substituted by dapagliflozin/sitagliptin FDC, resulting in an AEMP of $ down from the AEMP of $70.12 proposed in the submission. The ESC considered the sponsor's market share assumptions to derive the weighted price were complex and unclear in parts and may not reflect Australian practice. Of note, the ESC noted the high proportion of services (21%) for continuing treatment with empagliflozin + linagliptin, noting that this included services for empagliflozin + sitagliptin. Additionally, the ESC noted the initiating and continuing proportion of services for dapagliflozin monotherapy was equal to the services for sitagliptin 100 mg but it was unclear why this was the case. The ESC also considered the substitution rates to determine pricing was complicated by the rise of both SGLT2i and GLP-1RA usage as well as potential off label use of GLP-1RA and medicine shortages in this space, resulting in assumptions which are not reflective of the current treatment landscape. The pre-PBAC response agreed with the ESC that that sum of individual components approach would be appropriate if dapagliflozin/sitagliptin FDC would only replace saxagliptin + dapagliflozin FDC (lowest price combination of the PBS listed components of the DPP4i + SGLT2i FDCs), however, the pre-PBAC response maintained that dapagliflozin/sitagliptin FDC is expected to substitute the market across four different scenarios.

6.17 The ESC noted the two DPP4i + SGLT2i FDCs currently listed on the PBS, dapagliflozin+saxagliptin and empagliflozin+linagliptin are cost-minimised to each other; with equi-effective doses = empagliflozin 10 mg or 25 mg plus linagliptin 5 mg compared to dapagliflozin 10 mg plus saxagliptin 5 mg. The PBAC noted that given the TGA Delegate Overview stated that bioequivalence was demonstrated between dapagliflozin/sitagliptin 10 mg/100 mg FDC tablet and co-administered dapagliflozin 10 mg tablet and sitagliptin 100 mg tablet, that the cost of dapagliflozin/sitagliptin should be no greater than the lowest price of the PBS listed DPP4i + SGLT2i FDCs that are available for T2DM.

Estimated PBS usage & financial implications

6.18 This submission was not considered by DUSC. DUSC last reviewed the utilisation of medicines for Type 2 diabetes in September 2022.

6.19 The submission used a market share approach to estimate the number of prescriptions and total cost of listing the FDC.

6.20 The market share approach included four scenarios as shown in Table 9, noting that all use of the proposed FDC would be in combination with metformin:

- The dapagliflozin/sitagliptin FDC substituting for the single components;
- The dapagliflozin/sitagliptin FDC substituting for one of the 3 other FDCS containing a SGLT2i + a DPP4i (the submission (p69) noted that ertugliflozin + sitagliptin will be delisted by the time dapagliflozin/sitagliptin FDC is listed);
- The dapagliflozin/sitagliptin FDC substituting for metformin/dapagliflozin FDC given in combination with sitagliptin mono-component;
- The dapagliflozin/sitagliptin FDC substituting for a metformin/sitagliptin FDC given in combination with dapagliflozin mono-component.

Table 9: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Market size	PBS Utilisation data June 2022-June 2023; projected to grow by 2.2% based on ABS population growth	Evaluation noted growth rate proposed is higher than average population growth rate of 1.6% used in the Utilisation and Cost Model Workbook for PBAC Submissions User Manual (v1.4). The pre-PBAC response presented revised utilisation including 1.6% population growth rate and PBS Utilisation data from January -December 2023.
Uptake rate	<table><tr><th>Scenario</th><th>2025</th><th>2026</th><th>2027</th><th>2028</th><th>2029</th><th>2030</th></tr><tr><td>1 – Individual mono-components</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td></tr><tr><td>2 – SGLT2/DPP4 FDCs</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td></tr><tr><td>3 – DAPA/MET FDCs plus SITA</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td></tr><tr><td>4 – SITA/MET plus DAPA</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td><td>[redacted]%</td></tr></table>	Uptake rate estimated by the Sponsor. May be overestimated as a proportion of total market due to increase in prescription of GLP-1RA. May be underestimated as a proportion of DPP4i/SGLT2i market.

Source: Table 4.2.2, of the submission.

6.21 The most recent DUSC review of medicines for Type 2 diabetes (September 2022) found that from 2021 there had been a marked increase in the numbers of patients initiating T2DM therapy with a GLP-1 RA or SGLT2i, while the number of new patients initiating therapy with DPP4i has been stable. Given the favourable clinical outcome data for the GLP-1RA and SGLT2i, it is likely that the treatment pathway will

increasingly favour these classes of drugs. However, it is difficult to predict the magnitude of this change with respect to the estimates over 6 years, because several new agents, including small-molecule GLP-1RA, dual agonists of GLP-1 + glucose-dependent insulinotropic polypeptide (GIP), and triple agonists of GLP-1 + GIP + glucagon, are undergoing clinical trials, and may affect utilisation of currently available medications for T2DM.

6.22 The estimated number of prescriptions and therefore total cost of listing dapagliflozin/sitagliptin FDC is shown in Table 10.

Table 10: Estimated use and financial implications

	Year 1 2025	Year 2 2026	Year 3 2027	Year 4 2028	Year 5 2029	Year 6 2030
Estimated extent of use						
Number of scripts dispensed	[redacted]1	[redacted]2	[redacted]2	[redacted]3	[redacted]3	[redacted]3
Estimated financial implications of DAPA/SITA FDC						
Cost to PBS/RPBS less copayments	[redacted]4	[redacted]4	[redacted]4	[redacted]4	[redacted]4	[redacted]4
Estimated financial implications for other DPP4i and SGLT2i						
Number of scripts (initial)	-[redacted]5	-[redacted]2	-[redacted]2	-[redacted]2	-[redacted]3	-[redacted]3
Number of scripts (continuing)	-[redacted]2	-[redacted]2	-[redacted]2	-[redacted]2	-[redacted]3	-[redacted]3
Cost to PBS/RPBS less copayments	[redacted]6	[redacted]6	[redacted]6	[redacted]6	[redacted]6	[redacted]6
Net financial implications *(base case)*[a]						
Net cost to PBS/RPBS	[redacted]4	[redacted]4	[redacted]4	[redacted]4	[redacted]4	[redacted]4
Net financial implications presented in PSCR (with updated co-payments from 1 January 2024)						
Update base case using submitted price of $70.12	[redacted]4	[redacted]4	[redacted]4	[redacted]4	[redacted]4	[redacted]4
Updated base case using weighted price ($[redacted])	[redacted]6	[redacted]6	[redacted]6	[redacted]6	[redacted]6	[redacted]6

Source: Tables 4.2.3, 4.2.4, 4.3.1, 4.4.1, of the submission.

[a] Patient co-payments were updated from 1 January 2024. However, the evaluation noted the patient co-payments from 2023 were used in the submission.

The redacted values correspond to the following ranges:

[1] 5,000 to < 10,000

[2] 10,000 to < 20,000

[3] 20,000 to < 30,000

[4] $0 to < $10 million

[5] 500 to < 5,000

[6] net cost saving

6.23 The total cost to the PBS/RPBS of listing DAPA/sitagliptin FDC presented in the submission was estimated to be $0 to < $10 million in Year 6, and a total of $0 to < $10 million in the first 6 years of listing. However, the net cost allowing for substitution of other products as proposed in the submission was $0 to < $10 million over 6 years. The PSCR presented estimates with updates to patient co-payments and using the proposed weighted price of $[redacted], which resulted in a net cost saving of $0 to < $10 million over 6 years. The pre-PBAC response presented revised utilisation including 1.6% population growth rate and PBS Utilisation data from January -December 2023, increasing the weighted price slightly to $[redacted].

6.24 The submission provided a sensitivity analysis varying population growth and the uptake across the 4 scenarios. The total financial impact remained less than $$0 to < $10 million at year 6.

6.25 The estimates may be an underestimate if the proposed FDC is substituted more broadly than the four scenarios presented in the submission, but they may be an overestimate if prescribers switch to GLP-1RA, as noted in paragraph 6.21. The PSCR presented a multivariate sensitivity analysis incorporating the weighted AEMP ($) with the assumption that the market is substituted by 5% to account for GLP-1RA switching. This scenario also results in a cost saving to the PBS, with the estimated net cost to Government resulting in savings of $0 to < $10 million over the first 6 years of PBS listing. The ESC noted the analysis could not be validated as the data was hard coded in the revised UCM workbook.

Quality Use of Medicines

6.26 The submission provided brief information about the proposed activities to support quality use of medicines, focussing on prescriber education to ensure that the FDC would be used in the appropriate population.

6.27 At its July 2023 meeting, the PBAC noted the comments received from a range of T2DM stakeholders on the proposed changes to the PBS restrictions for T2DM medicines. The PBAC noted that stakeholders generally supported the simplification of the restrictions and clarification of combinations of medicines that are not PBS-subsidised. The PBAC considered that it would be useful to review the utilisation of T2DM medicines again in 24 months to monitor the effectiveness of the restriction changes and any unintended consequences. If recommended for listing, the restrictions for dapagliflozin/sitagliptin FDC should also align with the recommended T2DM restriction changes.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC recommended that dapagliflozin (DAPA) 10 mg with sitagliptin (SITA) 100 mg (Sidapvia) fixed dose combination (FDC) be listed on the PBS as an Authority Required (Streamlined) listing for use in conjunction with metformin (MET), for patients with type 2 diabetes mellitus (T2DM) with an inadequate response to treatment with dual therapy of MET and an inhibitor of sodium glucose co-transporter 2 (SGLT2i), or dipeptidyl peptidase 4 (DPP4i). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of dapagliflozin + sitagliptin FDC would be acceptable if it were cost-minimised to the lowest cost PBS-listed SGLT2i + DPP4i FDC. The PBAC advised the equi-effective doses to be dapagliflozin + sitagliptin FDC (10 mg/100 mg) = empagliflozin+linagliptin (10 mg or 25 mg/5 mg) FDC = dapagliflozin+saxagliptin (10 mg/5 mg) FDC.

7.2 The PBAC considered there was a clinical place for SGLT2i + DPP4i FDC products in the management of T2DM. The PBAC noted the consumer comments, particularly from

the National Aboriginal Community Controlled Health Organisation (NACCHO), that a dapagliflozin/sitagliptin FDC would reduce pill burden and provide an alternative FDC in this treatment space to ensure adequate supply in the event of product shortages.

7.3 The PBAC noted the TGA Delegate's Overview stated bioequivalence was demonstrated between dapagliflozin/sitagliptin FDC (10 mg/100 mg) and dapagliflozin 10 mg and sitagliptin 100 mg.

7.4 The PBAC considered that the nominated comparator of the dapagliflozin and sitagliptin individual components was reasonable. The PBAC agreed with the ESC's advice that other SGLT2i + DPP4i FDCs could also be considered alternative therapies to dapagliflozin/sitagliptin FDC.

7.5 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonable. The PBAC considered that Study 14 comparing the FDC of dapagliflozin + sitagliptin to the FDC's individual components provided reasonable evidence that the FDC and the individual components are bioequivalent which was supported by the TGA Delegate's Overview. Additionally, the TGA Delegate's Overview stated the efficacy and safety of dapagliflozin and sitagliptin for the use in T2DM was established.

7.6 The PBAC noted the submission presented a cost-minimisation approach comparing the cost of the FDC to its components. The PBAC considered the weighted price approach proposed in the PSCR was not appropriate. Based on TGA advice regarding bioequivalence and that there is no evidence that dapagliflozin/sitagliptin offers greater incremental benefits than the two listed DPP4i + SGLT2i FDCs, the PBAC agreed with the ESC that the cost of dapagliflozin/sitagliptin should be no greater than the lowest price combination of the PBS listed individual components of the DPP4i + SGLT2i FDCs that are available for T2DM. The PBAC assessed that the cost-effectiveness of dapagliflozin + sitagliptin FDC would be acceptable if it were cost-minimised to the lowest cost PBS-listed SGLT2i + DPP4i FDC.

7.7 The PBAC considered the revised utilisation estimates presented in the pre-PBAC response were reasonable, noting the standard 1.6% population growth rate and PBS utilisation data from January-December 2023 were included.

7.8 The PBAC noted the restrictions aligned overall with the current restrictions of other DPP4i and a SGLT2i FDCs.

7.9 As raised in the PSCR, the PBAC recommended that insulin be removed from the current administrative note which prevents this combination use with metformin and other DPP4i + SGLT2i FDCs. The PBAC advised that the change to the administrative note be flowed on to other SGLT2i + DPP4i FDCs. The PBAC considered this was reasonable as it was consistent with treatment guidelines.

7.10 The PBAC also noted that SGLT2i and DPP4i were PBS-listed based on a series of cost-minimisation comparisons going back to insulin. As a result of price reductions to DPP4i in 2014 and SGLT2i in 2015 to account for use outside of the PBS restrictions, both DPP4i and SGLT2i are now priced below equi-effective doses of insulin.

Therefore, the PBAC considered that allowing use of SGLT2i + DPP4i FDCs in combination with insulin and metformin was likely to be cost saving to the PBS, as it would reduce the dosage of insulin used by patients. The PBAC considered that the other options for treatment escalation in patients inadequately controlled on metformin + SGLT2i + DPP4i were likely to be more costly and included use of metformin with DPP4i or SGLT2i and higher doses of insulin, or switching of patients to metformin with GLP-1RA and insulin.

7.11 The PBAC noted that the recommended listing should align with all other recommendations for item 10.06 PBS Restrictions for Type 2 diabetes mellitus medicines from the July 2023 PBAC meeting.

7.12 The PBAC considered it would be reasonable to include the dapagliflozin/sitagliptin FDC in the 60-day prescription measure as the alternative product combinations that could be used to achieve triple therapy are included, with implementation to the PBS effective on 1 March 2024. The PBAC advised the standard clinical criteria for 60-day PBS items as recommended at the December 2022 PBAC meeting, should be included in the restriction i.e. "The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient."

7.13 The PBAC advised that dapagliflozin with sitagliptin FDC is suitable for inclusion in the PBS medicines for prescribing by nurse practitioners within collaborative arrangements as continuing therapy only, as per other medicines for T2DM.

7.14 The PBAC recommended that the Early Supply Rule of 50 days should apply to 60 day dispensing items for dapagliflozin with sitagliptin FDC products, as the Early Supply Rule applies to the current 60 day dispensing PBS listings for other SGLT2i with DPP4i FDCs in the continuing treatment phase.

7.15 The PBAC advised that, under subsection 101(3BA) of the *National Health Act 1953,* dapagliflozin with sitagliptin FDC should be treated as interchangeable on an individual patient basis with dapagliflozin with saxagliptin FDC and empagliflozin with linagliptin FDC.

7.16 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because dapagliflozin with sitagliptin FDC is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over dapagliflozin and sitagliptin individual medicines the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.

7.17 The PBAC noted that this submission is not eligible for an Independent Review as this item was recommended.

Outcome:
Recommended

8 Recommended listing

8.1 Add new items:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of repeats	Available brands
DAPAGLIFLOZIN + SITAGLIPTIN					
dapagliflozin 10 mg + sitagliptin 100 mg tablet, *28*	NEW	1	28	5	Sidapvia 10/100

Restriction Summary [new] / Treatment of Concept: [new]	
Concept ID	**Category / Program:** GENERAL – General Schedule (GE)
	Prescriber type: ☒Medical Practitioners
	Restriction type: ☒Authority Required (Streamlined) [new]
	Administrative Advice: This fixed dose combination is not PBS-subsidised for use as a sole therapy or in combination with a thiazolidinedione (glitazone), a glucagon-like peptide-1 analogue, another dipeptidyl peptidase 4 inhibitor (gliptin), or another SGLT2 inhibitor.
	Indication: Diabetes mellitus type 2
	Treatment Phase: Initial treatment
	Clinical criteria:
	The treatment must be in combination with metformin.
	AND
	Clinical criteria:
	Patient must have an HbA1c measurement greater than 7% despite treatment with dual oral combination therapy with metformin and a dipeptidyl peptidase 4 inhibitor (gliptin) or a sodium-glucose co-transporter 2 (SGLT2) inhibitor; or
	Patient must have, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period prior to initiation of triple oral therapy with a sodium-glucose co-transporter 2 (SGLT2) inhibitor, metformin and a gliptin.
	Prescribing Instructions:
	The date and level of the qualifying HbA1c measurement must be documented in the patient's medical records at the time triple oral therapy with an SGLT2 inhibitor, metformin and a gliptin is initiated.
	The HbA1c must be no more than 4 months old at the time triple oral therapy with an SGLT2 inhibitor, metformin and a gliptin is initiated.
	Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances: (a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or (b) Had red cell transfusion within the previous 3 months.
	The results of the blood glucose monitoring, which must be no more than 4 months old at the time of initiation of triple oral therapy with an SGLT2 inhibitor, metformin and a gliptin, must be documented in the patient's medical records.

MEDICINAL PRODUCT medicinal product pack		PBS item code	Max. qty packs	Max. qty units	No. of repeats	Available brands
DAPAGLIFLOZIN + SITAGLIPTIN						
dapagliflozin 10 mg + sitagliptin 100 mg tablet, *28*		NEW	2	56	5	Sidapvia 10/100
Restriction Summary [new] / Treatment of Concept: [new]						
Concept ID (	**Category / Program:** GENERAL – General Schedule (GE)					
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners					
	Restriction type: ☒Authority Required (STREAMLINED) [new]					
	Administrative Advice: This fixed dose combination is not PBS-subsidised for use as a sole therapy or in combination with a thiazolidinedione (glitazone), a glucagon-like peptide-1 analogue, another dipeptidyl peptidase 4 inhibitor (gliptin), or another SGLT2 inhibitor.					
	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.					
	Indication: Diabetes mellitus type 2					
	Treatment Phase: Continuing treatment					
	Clinical criteria:					
	The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient.					
	Clinical criteria:					
	The treatment must be in combination with metformin.					
	AND					
	Clinical criteria:					
	Patient must have previously received a PBS-subsidised regimen of oral diabetic medicines which included a sodium-glucose co-transporter 2 (SGLT2) inhibitor, metformin and a gliptin for this condition.					

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

9 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.

10 Sponsor's Comment

The sponsor had no comment.