

**7.08 VERICIGUAT,
Tablet 2.5 mg, Tablet 5 mg, Tablet 10 mg,
Verquvo[®],
Bayer Australia Ltd.**

1 Purpose

- 1.1 The early re-entry resubmission sought a General Schedule listing for vericiguat for the treatment of symptomatic (NYHA class II, III or IV) chronic heart failure in patients with a reduced ejection fraction (left ventricular ejection fraction less than 45%) and who are stabilised after a recent decompensation heart failure event requiring hospitalisation and/or intravenous diuretic therapy.

2 Background

- 2.1 At the March 2022 meeting, the PBAC considered that the outstanding issues for vericiguat could be resolved in a simple early re-entry resubmission if the following changes were made:
- amend the PBS restriction as outlined in Paragraph 7.6 of the vericiguat PSD, March 2022 PBAC Meeting;
 - an ICER of less than \$35,000 to < \$45,000 per QALY gained with the intention-to-treat (ITT) results of the VICTORIA trial applied in the economic model;
 - revised financial estimates (as outlined in Paragraph 7.16 vericiguat PSD, March 2022 PBAC Meeting) and including the lower price resulting from the aforementioned changes to the economic model; and
 - outline a Risk Share Arrangement (RSA) to manage the risk of use in a broader population (paragraph 7.18, vericiguat PSD, March 2022 PBAC Meeting).
- 2.2 The changes compared with the previous submission are outlined in Table 1.

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Table 1: Summary of key matters to be addressed

	PBAC comments	July 2022 resubmission
Restriction	Various amendments to align more closely with clinical trial	Amendments made as requested by PBAC Grandfather restriction proposed
AEMP (effective)	Previous submission: AEMP: \$ ¹ DPMQ: \$ ²	30% price reduction proposed AEMP: \$ ¹ DPMQ: \$ ²
Economic model	Use ITT results from VICTORIA trial in model	Done as requested
ICER	Less than \$ ¹ /QALY required (versus \$ ² /QALY in previous submission with ITT applied)	\$ ¹ /QALY
Financial estimates: inputs		
- prevalence	Should be increased from 1.5% to 1.85%;	2% applied (noting dapagliflozin used 2.2%), which was higher than requested
- uptake rate	Should be substantially lower Was: ³ % in Year 1, ³ % in Year 2, ³ % in Year 3, ³ % in Year 4, ³ % in Year 5, ³ % in Year 6	Uptake rate: unchanged in Years 1 to 3, ³ % decreases applied in Years 4 to 6 only (i.e. ³ % in Year 4, ³ % in Year 5, ³ % in Year 6).
- % of pts with a worsening HF event	Likely overestimated (was 26.6%) given the narrower restriction (should be around 20%)	20% as requested
- adherence	Adherence (assumed to be 95.3% in the submission) would likely be closer to 86% to 89% (as was reported to be observed with sacubitril/valsartan).	89% as requested.
- Other inputs that PBAC did not request changes to	- % patients stabilised following a worsening event was 77.17% - Grandfathered patients were not specifically included due to use of prevalent population estimates.	- Increased to 86.3% based on trial in the resubmission; amended to 85.3% in pre-PBAC response. - < 500 grandfather patients included in Year 1 in the resubmission; removed from estimates in pre-PBAC response
Financial impact to PBS/RPBS	- Year 1: \$ ³ - Year 6: \$ ⁴ - Over 6 years: \$ ⁵	- Year 1: \$ ³ - Year 6: \$ ⁴ - Over 6 years: \$ ⁶ - Reduced in pre-PBAC response to Year 1: \$ ³ Year 6: \$ ⁴ Over 6 years: \$ ⁶
RSA	Outline an RSA to manage the risk of use in a broader population	- Caps based on financial estimates - ³ % rebate for expenditure beyond caps

Source: Compiled during preparation of Submission Overview

The redacted values correspond to the following ranges:

¹ \$35,000 to < \$45,000

² \$55,000 to < \$75,000

³ \$0 to < \$10 million

⁴ \$10 million to < \$20 million

⁵ \$60 million to < \$70 million

⁶ \$40 million to < \$50 million

3 Requested listing

3.1 The resubmission proposed the following restrictions with amendments advised by PBAC in March 2022 in italics (additions) and strikethrough (deletions).

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Add new medicinal product as follows:

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
VERICIGUAT					
vericiguat 2.5 mg, film-coated tablet, 28	NEW	1	28	5	Verquvo®
vericiguat 5.0 mg, film-coated tablet, 28	NEW	1	28	5	
vericiguat 10 mg, film-coated tablet, 28	NEW	1	28	5	

Restriction Summary [new] / Treatment of Concept: [new]
Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)
Severity: Chronic
Condition: Heart failure
Indication: Chronic heart failure
Treatment Phase: Initial treatment
Treatment criteria
Must be initiated under the supervision of a <i>specialist cardiologist treated by a cardiologist OR</i>
<i>Must be treated by a medical practitioner who has been directed to prescribe this medicine by a cardiologist</i>
AND
Clinical criteria:
Patient must be symptomatic with NYHA classes II, III or IV
AND
Clinical criteria:
Patient must have a documented left ventricular ejection fraction (LVEF) of less than 45%
AND
Clinical criteria:
The condition must be stabilised following a decompensation event that required either (i) hospitalisation in the past 6 months (ii) intravenous diuretic therapy in the past three months
AND
Clinical criteria:
Patient must not have clinical signs of fluid overload
AND
Clinical criteria:
Patient must not have received intravenous treatment <i>for fluid overload</i> in the previous 24 hours
AND
Clinical criteria:
Patient must not have a systolic blood pressure less than 100 mmHg
AND
Clinical criteria:
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include a beta-blocker, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated
AND
Clinical criteria:

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The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an ACE inhibitor, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin II antagonist, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin receptor with neprilysin inhibitor combination therapy unless contraindicated according to the TGA-approved Product Information or cannot be tolerated,
Administrative Advice: Special Pricing Arrangements apply
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: The date of the decompensation event and date of initiation of treatment with this drug must be documented in the patient's medical records when PBS-subsidised treatment is initiated.
Treatment Phase: Continuing treatment
Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [new code]
Clinical criteria:
Patient must have previously received PBS-subsidised treatment with this drug for this condition
AND
Clinical criteria:
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include a beta-blocker, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated
AND
Clinical criteria:
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an ACE inhibitor, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin II antagonist, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin receptor with neprilysin inhibitor combination therapy unless contraindicated according to the TGA-approved Product Information or cannot be tolerated,
Administrative Advice: Special Pricing Arrangements apply
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Treatment Phase: Grandfather treatment
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)
Treatment criteria
Must be initiated under the supervision of a specialist treated by a cardiologist OR
Must be treated by a medical practitioner who has been directed to prescribe this medicine by a cardiologist
AND
Clinical criteria:
Patient must have met the PBS Initial treatment and clinical criteria at the time of initiating non-PBS subsidised drug for this PBS indication Patient must have received non-PBS-subsidised treatment with this drug for this this condition prior to [insert listing date]
AND
Clinical criteria:
Patient must have been symptomatic with NYHA classes II, III or IV prior to initiating non-PBS subsidised treatment with this drug for this condition

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AND
Clinical criteria:
<i>Patient must have had a documented left ventricular ejection fraction (LVEF) of less than 45% prior to initiating non-PBS subsidised treatment with this drug for this condition</i>
AND
Clinical criteria:
<i>At the time of initiating non-PBS subsidised treatment with this drug , the condition must have been stabilised following a decompensation event that required either</i>
<i>(i) hospitalisation in the 6 months prior to initiating non-PBS subsidised drug for this PBS indication</i>
<i>(ii) intravenous diuretic therapy in the three months prior to initiating non-PBS subsidised drug for this PBS indication</i>
AND
Clinical criteria:
<i>Patient must not have had clinical signs of fluid overload at the time of initiating non-PBS subsidised treatment with this drug for this condition</i>
AND
Clinical criteria:
<i>Patient must not have received intravenous treatment in the 24 hours prior to initiating non-PBS subsidised treatment with this drug for this condition</i>
AND
Clinical criteria:
<i>Patient must not have a systolic blood pressure less than 100 mmHg</i>
AND
Clinical criteria:
<i>The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include a beta-blocker, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated</i>
AND
Clinical criteria:
<i>The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an ACE inhibitor, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or</i>
<i>The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin II antagonist, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or</i>
<i>The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin receptor with neprilysin inhibitor combination therapy unless contraindicated according to the TGA-approved Product Information or cannot be tolerated,</i>
Administrative Advice: Special Pricing Arrangements apply
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: The date of the decompensation event and date of initiation of treatment with this drug must be documented in the patient's medical records when PBS-subsidised treatment is initiated.
<i>A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the continuing treatment criteria.</i>
<i>This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</i>

- 3.2 The resubmission proposed a Special Pricing Arrangement (SPA) with an effective AEMP for vericiguat of \$ (effective DPMQ of \$) and a published AEMP of \$ (published DPMQ \$) across all dose strengths.
- 3.3 In March 2022 (Paragraph 7.6, vericiguat PSD), the PBAC advised the listing for vericiguat should specify:
- vericiguat must be initiated under the supervision of a specialist cardiologist;
 - the initial restriction should be Authority Required (telephone/online), and the continuing restriction should be Authority Required (Streamlined);
 - a time frame for the recent decompensation event consistent with the VICTORIA trial, which required patients to have had a heart failure hospitalisation in the past 6 months or intravenous diuretic therapy for heart failure (without hospitalisation) in the past 3 months;
 - criteria to identify stabilised patients, namely that the patient must be haemodynamically stable and clinically euvolaemic (i.e. the patient must not have: clinical signs of fluid overload; received IV treatment in the previous 24 hours; or have a systolic blood pressure less than 100 mmHg);
 - vericiguat must be an add-on therapy to optimal standard chronic heart failure treatment including a beta-blocker and an ACEi/ARB/ARNi unless contraindicated;
 - that the patient is symptomatic with NYHA class II, III or IV, and has documented LVEF of less than 45% (as proposed in the submission); and
 - a grandfather restriction to ensure that, at initiation of therapy, patients enrolled in the patient access program met the PBS criteria around experiencing a recent decompensation event and being euvolaemic.
- 3.4 The resubmission updated the restriction to accept the PBAC's previous advice, with the only exception being that the resubmission proposed removal of 'specialist' from the following treatment criteria: 'vericiguat must be initiated under the supervision of a specialist cardiologist'. The resubmission stated this was to align with the approved Product Information.
- 3.5 The secretariat has proposed changes to the initial treatment and grandfather restriction to clarify which medical practitioners may prescribe vericiguat. The changes would allow general practitioners to initiate vericiguat under the guidance of a cardiologist. The PBAC considered the secretariat proposed changes appropriate.
- 3.6 A grandfather restriction was proposed to allow patients to transfer from the patient access program to PBS supply, if otherwise eligible.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer comments

4.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

4.3 Clinical data was not presented in this early re-entry resubmission.

Clinical claim

4.4 In March 2022, the PBAC considered that the claim of superior comparative effectiveness was reasonable although the magnitude of the treatment effect was modest and may have been overestimated in the trial.

4.5 In March 2022, the PBAC considered that the claim of comparable safety was likely reasonable but noted that vericiguat was associated with a slight increase in drug-related adverse events compared with placebo (14.6% versus 11.7%, respectively). Overall, the PBAC considered that vericiguat appeared to be reasonably well tolerated.

Economic analysis

4.6 Compared with the previous submission, the only changes to the economic model were:

- use of the ITT population results from the VICTORIA trial; and
- a 30% reduction to the requested AEMP, which resulted in an incremental cost-effectiveness ratio (ICER) of \$35,000 to < \$45,000 per quality adjusted life year (QALY).

These changes were consistent with the PBAC's advice from its March 2022 meeting.

4.7 The results of the economic evaluation are outlined in Table 22.

Table 2: Results of the modelled economic evaluation

Component	Vericiguat + SoC	Placebo + SoC	Increment
Previous submission: VICTORIA ITT at price proposed in previous submission			
Costs	\$	\$	\$
QALYs	3.52	3.35	0.16
Incremental cost/QALY gained			\$¹
Resubmission base case: VICTORIA ITT at price proposed in resubmission			
Costs	\$	\$	\$
QALYs	3.52	3.35	0.16
Incremental cost/QALY gained			\$²

Source: Table 5, p12 of the resubmission

Abbreviations: QALY, quality-adjusted life year; SoC, standard care.

Blue shading indicates results from previous submission

The redacted values correspond to the following ranges:

¹ \$55,000 to < \$75,000

² \$35,000 to < \$45,000

Drug cost/patient

4.8 The drug cost of vericiguat per patient per year of treatment would be \$ [REDACTED] based on the proposed DPMQ of \$ [REDACTED], an 89% adherence rate and [REDACTED] scripts per year.

Estimated PBS usage & financial implications

4.9 In March 2022, the PBAC considered that the financial estimates would need to be revised to ensure PBS expenditure was restricted to a specific, narrowly defined group of high-risk patients (paragraphs 7.1, 7.2 and 7.16, vericiguat PSD, March 2022 PBAC Meeting).

4.10 As requested by the PBAC in March 2022, the resubmission reduced:

- the proportion of patients with a worsening HF event from 26.6% to 20%
- treatment adherence from 95.3% to 89%.

4.11 However, other changes were made to the financial estimates that did not appear to be consistent with the PBAC's previous advice, as outlined in Table 23.

Table 2: Changes to the financial estimates that did not appear consistent with the PBAC’s March 2022 PSD

PBAC comments	July 2022 resubmission
The PBAC considered that overall the financial estimates were overestimated.	The total financial impact was reduced due to the lower AEMP, however the script numbers increased in Years 1 to 3 (and were relatively unchanged in Years 4 to 6) compared with the previous submission.
<p>Prevalence The PBAC considered prevalence should be increased from 1.5% to 1.85%; to be the mid-point between the March 2022 submission’s estimate of 1.5% and the alternate estimate discussed in the DUSC advice of 2.2% which was reported in the SHAPE study, a retrospective analysis of HF patients in Australian primary care (Liew 2020).</p>	2% applied. The resubmission noted “the PBAC’s decision to recommend dapagliflozin at the September 2021 PBAC Meeting, was based on 2.2% (Liew 2020) estimate of prevalence of HF in the dapagliflozin financial estimates”. The PBAC accepted the proposed prevalence of 2%.
<p>Uptake rate The PBAC considered that a substantially lower uptake rate would be required. Rates applied were: █% in Year 1, █% in Year 2, █% in Year 3, █% in Year 4, █% in Year 5, █% in Year 6</p>	<p>No substantial reduction was applied to the uptake rate. Reduced by █% in Years 4 to 6 only. Rates applied were: █% in Year 1, █% in Year 2, █% in Year 3, █% in Year 4, █% in Year 5, █% in Year 6 The PBAC considered the uptake rates remained uncertain.</p>
<p>Proportion of patients stabilised following a worsening event - was 77.17% - No change requested by PBAC</p>	Increased to 86.3% which was stated to be based on the rate of non-randomised patients who did not specifically meet the clinically stable inclusion criteria in the VICTORIA trial. This was amended to 85.3% in the pre-PBAC response. The PBAC accepted the amended figure.
<p>Grandfathered patients Were not specifically included in the financial estimates as they were assumed to already be included in the prevalent population estimates.</p>	< 500 grandfather patients were included in Year 1 Each grandfather patient was assumed to use 12.43 scripts. This likely resulted in double-counting. These patients were removed in the pre-PBAC response estimates.

Source: Compiled during preparation of the Submission Overview

Uptake rate

- 4.12 At its March 2022 meeting, the PBAC “considered vericiguat would be used after sodium-glucose cotransporter-2 (SGLT2) inhibitors in the treatment algorithm, and noted that the submission had not accounted for this place in therapy given the estimates only included the proportion of patients treated with an ACEi/ARB/ARNi (90%). Overall, the PBAC considered that vericiguat would have a very small, niche place in therapy with the restriction limiting initiation to cardiologists. Further, the target population will comprise patients receiving multiple other cardiovascular medicines who may be reluctant to add another therapy. The PBAC considered that a substantially lower uptake rate would be required.” (paragraph 7.16, vericiguat PSD, March 2022 PBAC Meeting).
- 4.13 The resubmission stated that, based on consultation with three Australian clinicians, it was estimated that there would be “█% initial uptake in general for those cardiologists treating HF patients but for those that work in HF specialist units, the

uptake can reach as high as 100% as the HF specialist units see most of the high-risk patients”. The resubmission also argued that limiting use to the high-risk patients was already accounted for through application of the proportion of patients with a recent worsening heart failure event (20%) and the proportion who are clinically stable (85.3% in the pre-PBAC response).

- 4.14 Based on this consultation, the resubmission maintained the same uptake rates as were applied in the previous submission in Years 1 to 3, but decreased the rates in Years 4 to 6 by 10% each year. This does not align with the PBAC’s previous advice that a “substantially lower uptake rate would be required” (paragraph 7.16, vericiguat PSD, March 2022 PBAC Meeting).
- 4.15 The resubmission stated that, based on consultation with three Australian clinicians, vericiguat would be used after SGLT2 inhibitors (in patients who are suited for SGLT2i therapy), which was consistent with the March 2022 PBAC consideration. However, the financial estimates (in the previous submission and the resubmission) only included the proportion of patients treated with an ACEi/ARB/ARNi (90%), and were not adjusted to specifically account for this later line place in therapy (refer to Paragraph 4.12). No estimates were provided for the proportion of patients requiring further treatment despite being treated with an SGLT2 inhibitor.

Other inputs

- 4.16 The financial estimates included < 500 grandfather patients who are expected to transfer from the patient access program onto the PBS in Year 1. These grandfather patients were each assumed to require 12 months of PBS-subsidised treatment (versus 14 months for other patients, as it was assumed that patients would receive approximately 3 months of therapy through the patient access program). The resubmission added grandfather patients onto the prevalent population, which was likely to result in double-counting. While the previous submission stated there would be < 500 grandfather patients, these patients were assumed to already be included in the prevalent population estimates (and thus were not explicitly added onto the prevalent population), which the previous commentary considered to be appropriate. The pre-PBAC response removed the < 500 grandfather patients from the financial estimates.
- 4.17 The resubmission increased the proportion of patients stabilised following a worsening event from 77.17% (which was based on an analysis of NT-proBNP quartiles where 77.17% of patients were in quartiles 1-3) to 86.30% (amended to 85.3% in the pre-PBAC response) which was stated to be based on the rate of non-randomised patients who did not specifically meet the clinically stable inclusion criteria in the VICTORIA trial. The resubmission stated this was to align with the PBS criteria of identifying stabilised patients namely that the patient must be haemodynamically stable and clinically euvolaemic. However, it was unclear whether the proportion of patients with ‘screen failure’ (i.e. who were screened but not randomised due to not

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meeting the inclusion criteria or meeting the exclusion criteria) would be relevant or applicable to the PBS population (e.g. patients may already be more likely to be stable if they are being screened for inclusion in a trial where this is known to be required).

4.18 Table 34 outlines the estimated PBS usage and financial impact.

Table 3: Estimated number of treated patients and prescriptions

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Eligible population						
Australian population age ≥18 years	21,082,471	21,411,852	21,744,502	22,073,220	22,393,101	22,714,178
Heart failure prevalence (2%)	¹	¹	¹	¹	¹	¹
LVEF <45% (59.9%)	²	²	²	²	²	²
NYHA class II-IV (88%)	²	²	²	²	²	²
Worsening HF event (20%)	³	³	³	³	³	³
Treated with ACEi/ARB/ARNi (90%)	⁴	³	³	³	³	³
Stabilised after HF event (86.3%)	⁴	⁴	⁴	⁴	⁴	⁴
Utilisation estimates						
Treatment uptake	%	%	%	%	%	%
Initiating patients	⁵	⁶	⁶	⁶	⁷	⁷
Initial year scripts (12.43/patient)	⁷	⁸	⁹	¹⁰	¹¹	¹¹
Surviving patients who continued treatment (57.1% from prior year)	-	⁵	⁵	⁵	⁵	⁶
Continuing year scripts (2.06/patient)	-	⁵	⁶	⁶	⁶	⁷
Grandfathered patients	¹²	-	-	-	-	-
Grandfathered scripts (12.43/patient)	⁵	-	-	-	-	-
Total scripts	⁷	⁸	⁹	¹¹	¹¹	¹¹
Net PBS/RPBS cost	\$ ¹³	\$ ¹³	\$ ¹³	\$ ¹³	\$ ¹⁴	\$ ¹⁴
Pre-PBAC response						
Total scripts	⁷	⁸	⁹	¹¹	¹¹	¹¹
Net PBS/RPBS cost	\$ ¹³	\$ ¹³	\$ ¹³	\$ ¹³	\$ ¹⁴	\$ ¹⁴
Previous submission						
Total scripts	⁷	¹⁵	⁹	¹¹	¹¹	¹¹
Net PBS/RPBS cost	\$ ¹³	\$ ¹³	\$ ¹⁴	\$ ¹⁴	\$ ¹⁴	\$ ¹⁴

Source: Table 7 of the resubmission

Abbreviations: ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; HF, heart failure; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association

Blue shading indicates results from previous submission

The redacted values correspond to the following ranges:

- ¹ 400,000 to < 500,000
- ² 200,000 to < 300,000
- ³ 40,000 to < 50,000
- ⁴ 30,000 to < 40,000
- ⁵ 500 to < 5,000
- ⁶ 5,000 to < 10,000
- ⁷ 10,000 to < 20,000
- ⁸ 60,000 to < 70,000
- ⁹ 80,000 to < 90,000
- ¹⁰ 90,000 to < 100,000
- ¹¹ 100,000 to < 200,000
- ¹² < 500
- ¹³ \$0 to < \$10 million
- ¹⁴ \$10 million to < \$20 million
- ¹⁵ 50,000 to < 60,000

- 4.19 The resubmission estimated a net cost to the PBS/RPBS of \$0 to < \$10 million in Year 1, increasing to \$10 million to < \$20 million in Year 6, a total of \$40 million to < \$50 million over 6 years. This was lower than estimated in the previous submission (\$60 million to < \$70 million over 6 years), despite higher script numbers in the first three years (and similar script numbers in Years 4 to 6) due to the lower proposed AEMP. The pre-PBAC response estimated a net cost to the PBS/RPBS of \$0 to < \$10 million in Year 1, increasing to \$10 million to < \$20 million in Year 6, a total of \$40 million to < \$50 million over 6 years.

Financial Management – Risk Sharing Arrangements

- 4.20 In March 2022, the PBAC considered “that given the overall uncertainty with the economic model a risk sharing arrangement (RSA) would be required to manage the risk of use outside the narrow restriction in a less responsive patient group, given clinical judgement will be required to identify stable patients” (paragraph 7.17, vericiguat PSD, March 2022 PBAC Meeting).
- 4.21 The resubmission proposed an RSA based on the expenditure estimates in Table 34 with a 1% rebate for expenditure beyond these estimates. The resubmission argued that the risk of use in a broader patient population is low as the initial restriction: is Telephone/online PBS Authority; requires the supervision of a cardiologist; and includes criteria for identifying stabilised patients following a recent decompensation event. It can be inferred that the key risks of use beyond the caps relate to uncertain and likely overestimated patient numbers as well as uncertain cost-effectiveness at the proposed price for patients with more severe disease.

For more detail on PBAC’s view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended listing of vericiguat as an Authority Required (telephone/online PBS Authorities system) for the initial restriction and an Authority Required (Streamlined) for the continuing restriction, for the treatment of symptomatic (NYHA class II, III or IV) chronic heart failure in patients with a reduced ejection fraction (left ventricular ejection fraction less than 45%) and who are stabilised after a recent decompensation heart failure event requiring hospitalisation and/or intravenous diuretic therapy.
- 5.2 The PBAC was satisfied that vericiguat, with concomitant use of standard of care therapies, provides for some patients, a significant improvement in efficacy over standard of care in high-risk patients in a late-line of therapy.
- 5.3 The PBAC considered that the resubmission had addressed the substantive outstanding issues identified at the March 2022 PBAC meeting via its restriction amendments, respecified economic model and revised financial estimates, which also incorporated the reduced price proposed in the resubmission. The PBAC’s

recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of vericiguat would be acceptable at the price proposed in the resubmission and using the ITT population in the VICTORIA trial. The PBAC considered the uptake rate in the estimated PBS usage remained optimistic, however the PBAC acknowledged the uncertainty in estimating the uptake and considered a Risk Sharing Arrangement (RSA) was appropriate to address any residual uncertainty regarding estimated patient numbers.

- 5.4 The PBAC noted the restriction was amended in line with its previous advice from March 2022 (see paragraph 3.3). The PBAC reaffirmed that prescribing by a cardiologist or under the supervision of a cardiologist was appropriate.
- 5.5 The PBAC recalled it had considered that the claim of superior comparative effectiveness was reasonable although the magnitude of the treatment effect was modest in high-risk patients in a late-line of therapy in the ITT population.
- 5.6 The PBAC recalled it had considered that the claim of comparable safety was likely reasonable but noted that vericiguat was associated with a slight increase in drug-related adverse events compared with placebo (14.6% versus 11.7%, respectively). Overall, the PBAC remained of the view that vericiguat appeared to be reasonably well tolerated.
- 5.7 The PBAC noted that the economic model had been revised in line with its previous advice, as shown in Table 1. The PBAC accepted the revised ICER of \$35,000 to < \$45,000/QALY using the ITT population from the VICTORIA trial and including a 30% price reduction.
- 5.8 As noted above in Table 2 and paragraph 5.3, the financial estimates remained optimistic and uncertain, however the PBAC accepted the revisions as proposed in the resubmission along with the proposed RSA to address the residual uncertainty.
- 5.9 The PBAC advised that vericiguat is suitable for prescribing by nurse practitioners in the continuation phase only.
- 5.10 The PBAC recommended that the Early Supply Rule should not apply.
- 5.11 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for vericiguat:
 - a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy over standard of care. This is because, based on the available evidence in the submission, the magnitude of benefit was not considered substantial and was primarily driven by differences in the rate of hospitalisation for heart failure in high-risk patients in a late-line of therapy;
 - b) The treatment is not expected to address a high and urgent unmet clinical need as it

is positioned in a later-line after multiple effective therapies used as standard of care for these patients.

- c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

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

Outcome:

Recommended

6 Recommended listing

6.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
VERICIGUAT					
vericiguat 2.5 mg tablet, 28	NEW	1	28	5	Verquvo®
vericiguat 5 mg tablet, 28	NEW	1	28	5	
vericiguat 10 mg tablet, 28	NEW	1	28	5	
Restriction Summary [new] / Treatment of Concept: [new]					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)					
Severity: Chronic					
Condition: Heart failure					
Indication: Chronic heart failure					
Treatment Phase: Initial treatment					
Treatment criteria					
Must be treated by a cardiologist OR					
Must be treated by a medical practitioner who has been directed to prescribe this medicine by a cardiologist					
AND					
Clinical criteria:					
Patient must be symptomatic with NYHA classes II, III or IV					
AND					
Clinical criteria:					
Patient must have a documented left ventricular ejection fraction (LVEF) of less than 45%					
AND					
Clinical criteria:					

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The condition must be stabilised following a decompensation event that required either (i) hospitalisation in the past 6 months (ii) intravenous diuretic therapy in the past three months
AND
Clinical criteria:
Patient must not have clinical signs of fluid overload
AND
Clinical criteria:
Patient must not have received intravenous treatment for fluid overload in the previous 24 hours
AND
Clinical criteria:
Patient must not have a systolic blood pressure less than 100 mmHg
AND
Clinical criteria:
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include a beta-blocker, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated
AND
Clinical criteria:
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an ACE inhibitor, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin II antagonist, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin receptor with neprilysin inhibitor combination therapy unless contraindicated according to the TGA-approved Product Information or cannot be tolerated,
Administrative Advice: Special Pricing Arrangements apply
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
Administrative Advice: The date of the decompensation event and date of initiation of treatment with this drug must be documented in the patient's medical records when PBS-subsidised treatment is initiated.
Treatment Phase: Continuing treatment
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners
Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [new code]
Clinical criteria:
Patient must have previously received PBS-subsidised treatment with this drug for this condition
AND
Clinical criteria:
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include a beta-blocker, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated
AND
Clinical criteria:
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an ACE inhibitor, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or

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The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin II antagonist, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin receptor with neprilysin inhibitor combination therapy unless contraindicated according to the TGA-approved Product Information or cannot be tolerated,
Administrative Advice: Special Pricing Arrangements apply
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
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.
Treatment Phase: Grandfather treatment
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)
Treatment criteria
Must be treated by a cardiologist OR
Must be treated by a medical practitioner who has been directed to prescribe this medicine by a cardiologist
AND
Clinical criteria:
Patient must have received non-PBS-subsidised treatment with this drug for this this condition prior to [insert listing date]
AND
Clinical criteria:
Patient must have been symptomatic with NYHA classes II, III or IV prior to initiating non-PBS subsidised treatment with this drug for this condition
AND
Clinical criteria:
Patient must have had a documented left ventricular ejection fraction (LVEF) of less than 45% prior to initiating non-PBS subsidised treatment with this drug for this condition
AND
Clinical criteria:
At the time of initiating non-PBS subsidised treatment with this drug, the condition must have been stabilised following a decompensation event that required either (i) hospitalisation in the 6 months prior to initiating non-PBS subsidised drug for this PBS indication (ii) intravenous diuretic therapy in the three months prior to initiating non-PBS subsidised drug for this PBS indication
AND
Clinical criteria:
Patient must not have had clinical signs of fluid overload at the time of initiating non-PBS subsidised treatment with this drug for this condition
AND
Clinical criteria:
Patient must not have received intravenous treatment in the 24 hours prior to initiating non-PBS subsidised treatment with this drug for this condition
AND
Clinical criteria:
Patient must not have a systolic blood pressure less than 100 mmHg

AND
Clinical criteria:
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include a beta-blocker, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated
AND
Clinical criteria:
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an ACE inhibitor, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin II antagonist, unless contraindicated according to the TGA-approved Product Information or cannot be tolerated; or
The treatment must be an add-on therapy to optimal standard chronic heart failure treatment, which must include an angiotensin receptor with neprilysin inhibitor combination therapy unless contraindicated according to the TGA-approved Product Information or cannot be tolerated,
Administrative Advice: Special Pricing Arrangements apply
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: The date of the decompensation event and date of initiation of treatment with this drug must be documented in the patient's medical records when PBS-subsidised treatment is initiated.
Administrative Advice: A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the continuing treatment criteria.
Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.

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

7 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.

8 Sponsor's Comment

Bayer welcomes the PBAC's recommendation to include vericiguat (Verquvo) on the PBS for use in addition to standard of care therapy for the treatment of symptomatic chronic heart failure in adult patients with reduced ejection fraction less than 45% (HFrEF) who are stabilised after a recent heart failure decompensation event requiring hospital admission and/or

intravenous diuretic therapy. We continue to work with the Department to have vericiguat made available on the PBS at the earliest opportunity for eligible patients.