

**6.23 PALBOCICLIB,
Tablet 75 mg
Tablet 100 mg
Tablet 125 mg,
Ibrance[®],
Pfizer Australia Pty Ltd**

1 Purpose of Application

- 1.1 The Category 4 submission sought to list palbociclib 75 mg, 100 mg and 125 mg tablets under the same circumstances as the already listed palbociclib capsules.

2 Background

Registration status

- 2.1 Palbociclib 75 mg, 100 mg and 125 mg capsules were TGA registered on 3 May 2017. Palbociclib 75 mg, 100 mg and 125 mg tablets were TGA registered on 3 June 2020.
- 2.2 Palbociclib is approved by the TGA for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:
- an aromatase inhibitor as initial endocrine-based therapy
 - fulvestrant in patients who have received prior therapy.
- 2.3 Palbociclib capsules are currently listed on the PBS as an Authority Required listing for initial and continuing treatment of locally advanced or metastatic breast cancer.

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

3 Requested listing

- 3.1 The submission requested listing palbociclib tablets under the same circumstances as the PBS-listed palbociclib capsules.
- 3.2 The applicant gave notification that it intends to discontinue the capsule formulation shortly after the tablets are PBS-listed. The sponsor did not provide exact timing of the discontinuation.
- 3.3 The PBAC was asked to consider whether palbociclib 75 mg, 100 mg, 125 mg tablets and 75 mg, 100 mg, 125 mg capsules should be considered equivalent for the purposes of substitution. Any such advice would be relevant in the event that there is a period where both capsules and tablets are listed on the PBS.

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

4 Consideration of the evidence

Sponsor Hearing

- 4.1 There was no hearing for this item.

Consumer Comments

- 4.2 The PBAC noted and welcomed the input from Rare Cancers Australia. Rare Cancers Australia provided comments supporting the listing of 75 mg, 100 mg and 125 mg palbociclib tablets, describing the benefits of treatment including improving quality of life.

Clinical studies

- 4.3 This submission presented four biopharmaceutic studies in healthy volunteers to support development of the proposed tablets, assessing relative bioavailability (A5481042), bioequivalence and food effect (A5481081) and the effect of concomitant use of gastric acid reducing agents (A5481041 and A5481091) (TGA Delegate's overview). These studies are summarised in Table 1.

Table 1: Clinical Studies to Support the Development and Submission of the Tablet Formulation

Study number	Study overview
A5481041	Pilot Study to test the effect of concomitant administration of a PPI on the PK of 6 new experimental formulations of palbociclib (5 tablet formulations and 1 oral solution) when administered under fasting conditions
A5481042	Investigation to obtain data supporting the quality specifications for the proposed commercial tablet (investigation of BA between the proposed commercial tablet and 3 other aberrant tablet formulations).
A5481081	Investigation of BE/BA between the commercial capsules and the proposed commercial tablet (including effect of food on the proposed commercial tablet)
A5481091	A drug interaction study to test the effect of concomitant administration of a PPI on the PK of the proposed commercial tablet when administered under fasting conditions

Source: Table 3 of the submission, p5 of the submission.

- 4.4 The submission indicated that a ‘biowaiver’ was provided by the TGA to not conduct studies on the 75 mg and 100 mg strength tablets based on the following points:
- All strengths are manufactured by the same manufacturing process
 - A common blend is used for all strengths and the formulations are quantitatively proportional
 - At pH 1.2 and pH 4.5 all strengths have similar dissolution profiles (> 85% dissolution in 15 minutes). At pH 6.8, all strengths are similar (>f2 similarity).
- 4.5 The sponsor did not provide a bioequivalence statement from the TGA. The PBAC noted from the Pre-PBAC response that the TGA Evaluation Report concluded that the capsules and tablets were bioequivalent.

Clinical claim

- 4.6 The submission stated there is no anticipated change in the efficacy or safety of palbociclib treatment with use of the proposed tablet.
- 4.7 The submission claimed that patients are expected to benefit from the greater convenience provided by the proposed tablet formulation with the removal of the necessity for administration with food.
- 4.8 The submission mentioned that there are no products of animal origin or lactose in the commercial tablet formulation (the capsule is formulated with gelatin), thus providing increased options to patients who have tolerability issues and/or dietary preferences.
- 4.9 The submission stated that the possibility of medication administration errors between palbociclib capsules (PBS-listed formulation) and palbociclib tablets (proposed formulation) is considered to be low. This is because the tablets and capsules could be administered interchangeably since both formulations are bioequivalent when administered according to recommendations.

Pricing considerations

- 4.10 While not a matter for PBAC, the listing of a new bioequivalent form of palbociclib would trigger a 25% statutory price reduction (SPR) under s99ACB of the *National Health Act 1953 (the Act)*. The drug palbociclib will move into the F2 formulary and be subject to price disclosure. The sponsor has made a separate application to the Department requesting palbociclib tablets be considered a ‘new presentation’ of an existing brand of palbociclib and not trigger a statutory price reduction, under s99ACB(3A) of the Act.
- 4.11 The proposed daily dose of the palbociclib tablet is the same as the current approved capsule formulation. As such, the prices requested for the palbociclib tablet are consistent with the prices of the palbociclib capsule at Approved Ex-Manufacture Price (AEMP) (Table 2).

Table 2: Requested price for Ibrance (palbociclib) tablets.

	Palbociclib tablets AEMP	Palbociclib tablets Effective AEMP*	Palbociclib capsules AEMP	Palbociclib capsules Effective AEMP*
75 mg, 21	\$4,087.85	\$ [REDACTED]	\$4,087.85	\$ [REDACTED]
100 mg, 21	\$4,087.85	\$ [REDACTED]	\$4,087.85	\$ [REDACTED]
125 mg, 21	\$4,087.85	\$ [REDACTED]	\$4,087.85	\$ [REDACTED]

*Effective AEMP: Commercial in Confidence

- 4.12 Source: Table 2 of the submission of the submission.
For more detail on PBAC’s view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended listing palbociclib 75 mg, 100 mg and 125 mg tablets as General Schedule Authority Required benefits with the same circumstances of use as palbociclib capsules.
- 5.2 The PBAC considered the proposed price of palbociclib tablets, which was the same as the capsules, was appropriate. The PBAC considered that the palbociclib tablets and palbociclib capsules (for the equivalent strengths) were bioequivalent and equi-effective on a milligram for milligram basis.
- 5.3 The PBAC noted that the sponsor intends to discontinue the capsules and supply the tablets in place of the capsules. Therefore, PBS utilisation of palbociclib is not expected to change as a direct result of listing the tablets and PBS expenditure is not expected to change given no change in price.
- 5.4 The PBAC advised, under Section 101(4AACD) of the Act, that palbociclib (Ibrance®) tablets and the corresponding strengths of Palbociclib (Ibrance®) capsules should be considered equivalent for the purposes of substitution (i.e. ‘a’ flagged in the Schedule).
- 5.5 The PBAC advised that, because palbociclib tablets are not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity,

over palbociclib capsules, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.

- 5.6 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

- 6.1 Add three new medicinal product packs (75 mg, 21, 100 mg, 21, and 125 mg, 21 tablets) as shown below:
- 6.2 Add equivalence indicators (a-flag) only in the event that both forms are PBS-listed simultaneously, as shown below:
- 6.3 Add an equivalence NOTE (New AA1) only if condition 6.2 above is met; remove any such NOTE should only 1 form remain listed on the PBS.

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands	
PALBOCICLIB						
palbociclib 75 mg tablet, 21	New	1	21	5	^a lbrance	
palbociclib 100 mg tablet, 21	New	1	21	5	^a lbrance	
palbociclib 125 mg tablet, 21	New	1	21	5	^a lbrance	
palbociclib 75 mg capsule, 21	Supply Only	11699R	1	21	5	^a lbrance
palbociclib 100 mg capsule, 21		11700T	1	21	5	^a lbrance
palbociclib 125 mg capsule, 21		11698Q	1	21	5	^a lbrance
Restriction Summary: 10030 / Treatment of Concept: 10015 (as at 1 July 2021)						
Category / Program: GENERAL – General Schedule (Code GE)						
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners						
Restriction type: <input checked="" type="checkbox"/> Authority Required – immediate assessment via telephone / Online PBS Authorities system						
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: Special Pricing Arrangements apply.						
Administrative Advice: <i>Pharmaceutical benefits that have the form 'tablet' and pharmaceutical benefits that have the form 'capsule' of this drug are equivalent for the purposes of substitution where the strength is the same.</i>						
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.						
Indication: Locally advanced or metastatic breast cancer						
Treatment Phase: Initial treatment						
Clinical criteria:						
Patient must not have previously been treated with an aromatase inhibitor for advanced or metastatic breast cancer						

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	AND
	Clinical criteria:
	Patient must not have previously been treated with abemaciclib or ribociclib; or
	Patient must have developed an intolerance to abemaciclib or ribociclib of a severity necessitating permanent treatment withdrawal
	AND
	Clinical criteria:
	The condition must be hormone receptor positive
	AND
	Clinical criteria:
	The condition must be human epidermal growth factor receptor 2 (HER2) negative
	AND
	Clinical criteria:
	The condition must be inoperable
	AND
	Clinical criteria:
	Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or less
	AND
	Clinical criteria:
	The treatment must be in combination with anastrozole or letrozole
	AND
	Clinical criteria:
	The treatment must not be in combination with abemaciclib or ribociclib
	AND
	Population criteria:
	Patient must not be premenopausal
Restriction Summary: 10804 / ToC: 10735 (as at 1 July 2021)	
	Indication: Locally advanced or metastatic breast cancer
	Treatment Phase: Continuing treatment
	Clinical criteria:
	Patient must have previously received PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must not develop disease progression while receiving treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must have stable or responding disease according to the Response Evaluation Criteria In Solid Tumours (RECIST)
	AND
	Clinical criteria:
	The treatment must be in combination with anastrozole or letrozole
	AND
	Clinical criteria:
	The treatment must not be in combination with abemaciclib or ribociclib
	AND
	Population criteria:
	Patient must not be premenopausal
	Prescribing Instructions:
	A patient who has progressive disease when treated with this drug is no longer eligible for PBS-subsidised treatment with this drug.

These restrictions 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

The sponsor had no comment.