

7.19 RIBOCICLIB

Tablet, 200 mg, Kisqali[®], Novartis

1 Purpose of Application

- 1.1 The minor submission sought a Section 85, authority required listing for ribociclib in combination with a non-steroidal aromatase inhibitor (NSAI) for first-line endocrine based treatment of patients with non-premenopausal, hormone receptor positive (HR+) and human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer (ABC).
- 1.2 Major submissions for this listing were considered and rejected by the PBAC at its July and November 2017 meetings. The key differences from the November 2017 resubmission are:
 - A further price reduction was proposed, reducing the effective DPMQ for ribociclib 63 x 200 mg tablets from \$ [REDACTED] to \$ [REDACTED].
 - The reduced ribociclib price resulted in a cost/QALY gained of \$45,000-\$75,000 with a model time horizon of 7 years compared with a cost/QALY gained of \$75,000-\$105,000 with a model time horizon of 10 years in the November 2017 resubmission.
 - The reduced ribociclib price resulted in a net cost to the PBS/RPBS of more than \$100 million over the first 5 years of listing compared with more than \$100 million over 5 years.
 - A risk-share agreement involving a subsidisation cap of [REDACTED]. No annual subsidisation caps were proposed in the November 2017 resubmission.
 - If the forecasted use of ribociclib is as predicted (\$ [REDACTED] over 5 years), application of the proposed subsidisation cap (\$ [REDACTED] over 5 years) would result in a [REDACTED]% reduction in the DPMQ, giving an average effective DPMQ of \$ [REDACTED] for 63 x 200 mg tablets and a cost/QALY gained of \$15,000-\$45,000 with a model time horizon of 7 years.

2 Requested listing

- 2.1 The submission requested the following new listing. The requested listing is the same restriction that was proposed in the November 2017 resubmission [Public Summary Document (PSD), November 2017, page 2].

Public Summary Document – March 2018 PBAC Meeting

Name, Restriction, Manner of administration and form	Max. Qty (units)	No. of Rpts	Dispensed Qty	Price for Max.	Proprietary Name and Manufacturer
Ribociclib Tablet, 200mg	63			Published price: \$ [REDACTED] Effective price: \$ [REDACTED]	Kisqali Novartis Pharmaceuticals Australia Pty Ltd
	42	5		Published price: \$ [REDACTED] Effective price: \$ [REDACTED]	
	21			Published price: \$ [REDACTED] Effective price: \$ [REDACTED]	

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced
Condition:	Inoperable and metastatic breast cancer
PBS Indication:	Locally advanced inoperable and metastatic breast cancer
Treatment phase:	Initial treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be an initial endocrine-based therapy for this indication. AND The treatment must be in combination with a non-steroidal aromatase inhibitor (NSAI).
Clinical criteria:	The condition must be hormone receptor positive. AND The condition must be human epidermal growth factor receptor 2 (HER2) negative. AND The condition must be inoperable AND Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 1 or less. AND Patient must not have inflammatory breast cancer or uncontrolled brain metastases.
Population criteria:	Patient must not be premenopausal. Ovarian radiation or treatment with a luteinizing hormone-releasing hormone agonist (LHRHa) (goserelin acetate or leuprolide acetate) is not permitted for induction of ovarian suppression for patients receiving PBS ribociclib.

Public Summary Document – March 2018 PBAC Meeting

Prescriber Instructions	A patient who has progressive disease when treated with this drug is no longer eligible for PBS-subsidised treatment with this drug. Authority applications for treatment must be made in writing.
Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced
Condition:	Inoperable and metastatic breast cancer
PBS Indication:	Locally advanced inoperable and metastatic breast cancer
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be an initial endocrine-based therapy for this indication. AND The treatment must be in combination with a non-steroidal aromatase inhibitor (NSAI).
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition AND The condition must be hormone receptor positive. AND The condition must be human epidermal growth factor receptor 2 (HER2) negative. AND Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 1 or less. AND Patient must not have inflammatory breast cancer or uncontrolled brain metastases. AND Patient must not have progressive disease.
Population criteria:	Patient must not be premenopausal. Ovarian radiation or treatment with a luteinizing hormone-releasing hormone agonist (LHRHa) (goserelin acetate or leuprolide acetate) is not permitted for induction of ovarian suppression for patients receiving PBS ribociclib.
Prescriber Instructions	A patient who has progressive disease when treated with this drug is no longer eligible for PBS-subsidised treatment with this drug. Authority applications for continuing treatment may be made by telephone to Medicare Australia on 1800 700 720 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Public Summary Document – March 2018 PBAC Meeting

2.2 In the minor resubmission, consistent with the PBAC’s previous advice, the sponsor proposed that the grandfather restriction should reflect the initiation restriction; i.e. “patients who previously received non-PBS-subsidised treatment with this drug for this condition prior to [PBS listing date] would need to have met the criteria of the initiation restriction at the time of initiating ribociclib via the Novartis access program.” The grandfather restriction as provided by the sponsor is reproduced below. The sponsor noted in the pre-PBAC response that [REDACTED] grandfathered patients were included in the financial estimates. The PBAC considered that the approach to the proposed grandfather restriction was appropriate, with the exception that patients who are otherwise eligible under the grandfather criteria, should not have had to receive ribociclib through the Novartis access program. PBAC indicated that grandfathered patients should be the same as the PBS population and not a wider population. This means that grandfathered patients should be included in the subsidisation cap provided they would have met the PBS criteria at the time they commenced treatment with ribociclib. The same grandfathering criteria would apply to palbociclib if it was recommended for listing on the PBS.

Name, Restriction, Manner of administration and form	Max. Qty (units)	No. of Rpts	Dispensed Qty	Price for Max.	Proprietary Name and Manufacturer
Ribociclib Tablet, 200mg	63			Published price: \$ [REDACTED] Effective price: \$ [REDACTED]	Kisqali Novartis Pharmaceuticals Australia Pty Ltd
	42	5		Published price: \$ [REDACTED] Effective price: \$ [REDACTED]	
	21			Published price: \$ [REDACTED] Effective price: \$ [REDACTED]	

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	breast cancer
PBS Indication: <i>PBS Indication is the combination of the Episodicity, Severity and Condition.</i>	Locally advanced or metastatic breast cancer
Treatment phase:	Initial – grandfather restriction

Public Summary Document – March 2018 PBAC Meeting

Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input checked="" type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	<p>The treatment must have been the initial endocrine-based therapy for this indication at the time of initiating ribociclib via an approved Novartis access program AND The treatment must be in combination with a non-steroidal aromatase inhibitor (NSAI)</p>
Clinical criteria:	<p>The condition must be hormone receptor positive; AND The condition must be human epidermal growth factor receptor 2 (HER2) negative; AND The condition must be inoperable AND Patient must not have inflammatory breast cancer or uncontrolled brain metastases. AND Patients must have previously received non-PBS subsidised treatment with this drug for this condition prior to [PBS listing date] via an approved Novartis access program AND Patient must have met the following criteria at the time of initiating ribociclib via the Novartis access program:</p> <ul style="list-style-type: none"> • Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 1 or less.
Population criteria:	The patient must not be premenopausal
Prescriber Instructions	<p>A patient who has progressive disease when treated with this drug is no longer eligible for PBS-subsidised treatment with this drug</p> <p>Authority applications for initial treatment must be made in writing and continuing treatment must be made by telephone.</p> <p>A patient must not have received more than 28 days of treatment with a non-steroidal aromatase inhibitor for this condition prior to treatment with this drug.</p>
Administrative Advice	
Note	<p>No applications for increased maximum quantities will be authorised.</p> <p>No applications for increased repeats will be authorised.</p>

2.3 The requested restriction is considered to be complex.

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

3 Background

- 3.1 Ribociclib was TGA registered on 23 October 2017 for the following indication:

KISQALI [ribociclib] in combination with an aromatase inhibitor is indicated for the treatment of men and postmenopausal women with hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) advanced or metastatic breast cancer, as an initial endocrine-based therapy.
- 3.2 Ribociclib was initially considered by the PBAC for this indication at the July 2017 meeting and rejected on the basis of unfavourable and uncertain cost-effectiveness, and uncertainties regarding the magnitude of incremental benefit of ribociclib [PSD, July 2017, paragraph 7.1].
- 3.3 A major resubmission was considered by the PBAC at the November 2017 meeting and rejected on the basis of high and uncertain cost effectiveness, and uncertainties regarding the magnitude of incremental benefit of ribociclib. Additionally, the PBAC considered that the likely net cost of listing ribociclib on the PBS, though less than proposed in the July 2017 submission, represented a significant opportunity cost to the Commonwealth [PSD, November 2017, paragraph 7.1].
- 3.4 A summary of the outstanding matters of concern to the PBAC are provided in the table below.

Table 1: Summary of outstanding matters of concern

Matters of concern (November 2017 PBAC minutes)	How the resubmission addresses it
<p><u>Proposed restriction (paragraph 7.5).</u></p> <p>The PBAC noted that the proposed restriction was aligned better with the inclusion criteria of the MONALEESA-2 trial, compared with that considered in July 2017. However, if both listed on the PBS, the PBAC considered ribociclib and palbociclib should have similar restriction criteria given they belong to the same class of drug and are registered for similar indications.</p> <p>Further, the PBAC recalled that it had recommended a restricted benefit listing for goserelin 3.6 mg implant for anticipated premature ovarian failure for patients receiving treatment with an alkylating agent for a malignancy or an autoimmune disorder that has a high risk of causing premature ovarian failure. This listing may impact on some criteria proposed for the listing of ribociclib.</p> <p>(paragraph 7.6) The proposed Grandfather restriction was broader than the restriction proposed for initiating treatment. The PBAC considered that the requirement of, and criteria for, a grandfather restriction would need to be considered in a resubmission for ribociclib.</p>	<p>Not addressed.</p> <p>Sponsor proposed that the listing states patients must not have undergone ovarian radiation or treatment with a luteinizing hormone-releasing hormone agonist (LHRHa) (goserelin acetate or leuprolide acetate) for induction of ovarian suppression.</p> <p>Proposed grandfather restriction is now consistent with proposed restriction.</p>
<p><u>Clinical evidence (paragraph 7.8)</u></p> <p>PBAC's previous concerns regarding the clinical claim of superior efficacy being uncertain remained. The PBAC previously considered that the claim of superior efficacy based on PFS was likely to be reasonable; ribociclib resulted in a statistically significant improvement in PFS with a median increase of 9.3 months when investigator assessed. The difference in OS, although in favour of ribociclib, remained not statistically significant (p=0.059). Due to the immaturity of the OS data, the high degree of uncertainty in the magnitude of long-term benefit with ribociclib remained.</p>	<p>Not addressed.</p>
<p><u>Safety (paragraph 7.9)</u></p> <p>The PBAC noted the high rate of adverse events (AEs) associated with ribociclib, with the majority of ribociclib + letrozole patients in the MONALEESA-2 trial experiencing Grade ≥ 3 AEs (████%) and AEs leading to dose change or interruption (████%). The PBAC also noted the increased proportion of patients with prolongation of the QTc interval in the clinical trial which may be greater in the PBS population.</p>	<p>Not addressed.</p>
<p><u>Comparison with palbociclib (paragraph 7.10 and 7.11)</u></p> <p>The PBAC advised that the indirect comparison should be updated in any resubmission in the event that further follow-up data are available for either ribociclib or palbociclib. The PBAC advised that the equi-effective doses should be based on the most complete dosing data available for ribociclib and palbociclib.</p>	<p>Sponsor noted access to complete dosing data for palbociclib is not available.</p>

<p><u>Economic model (paragraph 7.12)</u> The PBAC considered that the gain in life years in the model was overly optimistic and highly uncertain. The PBAC recalled that it had previously considered that a time horizon no more than 5 years would be appropriate and that a shorter time horizon was appropriate given the immaturity of the existing OS data. The re-submission assumed that the treatment effect persists for the model duration. The PBAC considered that this assumption was overly optimistic. The PBAC noted a Weibull function was applied to extrapolate OS. Sensitivity analysis found that the application of any extrapolation function other than the Weibull function increased the ICER. The PBAC noted ESC's comments regarding the post-progression utility value largely being driven by a single end of treatment visit.</p>	<p>In the revised base case the time horizon is truncated to 7 years. The model projects an improvement of [redacted] undiscounted life years ([redacted] months) over ten years, which is reduced to [redacted] years ([redacted] months) when the time horizon is truncated to 7 years. Other issues were not addressed.</p>
<p><u>Financial estimates (paragraph 7.13)</u> The resubmission estimated the total net financial impact to the Australian Government of listing ribociclib was substantially more than \$100 million over the next 6 years. The PBAC considered that this is likely to be an underestimate given the issues raised in the evaluation and by the ESC.</p>	<p>Revised estimated 5 year net cost of more than \$100 million. Costs are reduced due to the lower effective DPMQ.</p>
<p><u>Risk share agreement</u> The associated revised financial forecasts should include a risk share agreement that appropriately limits the financial risk to the Commonwealth.</p>	<p>Risk share agreement is proposed with a proposed expenditure cap of \$ [redacted] over 5 years.</p>

Paragraph references refer to ribociclib ratified minutes, November 2017.

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

4 Comparator

- 4.1 The submission nominated the comparator as letrozole alone, as with the previous major submissions considered by the PBAC in July 2017 and November 2017. The PBAC previously considered that the main comparator should be a NSAI (i.e. letrozole or anastrozole) alone [PSD, July 2017, paragraph 7.8].
- 4.2 The previous major submissions nominated palbociclib as a secondary (near market) comparator. This is unchanged in the minor resubmission. The PBAC previously considered that this is an appropriate near market comparator [PSD, July 2017, item 7.8].

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

- 5.2 The PBAC noted that no consumer comments were received for this item.
- 5.3 The Medical Oncology Group of Australia (MOGA) expressed its strong support for the ribociclib submission, on the basis of improved PFS. The PBAC noted that MOGA

presented the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) for ribociclib as 3 compared to letrozole alone. MOGA noted that the score may increase to 4 when OS data matures (out of a maximum of 5, where 5 and 4 represent the grades with substantial improvement).¹

Clinical trials

- 5.4 The July 2017 submission and November 2017 resubmission were based on direct evidence from one head-to-head phase III randomised, double-blind trial comparing ribociclib + letrozole to letrozole alone in postmenopausal women with HR+, HER2-ABC (MONALEESA-2).
- 5.5 The November 2017 resubmission also presented an indirect comparison to palbociclib using the MONALEESA-2 trial (January 2017 data cut-off) and the PALOMA-2 trial (a phase III, randomised, double-blind trial of palbociclib + letrozole for first line treatment of ER+, HER2- ABC in postmenopausal women), using placebo + letrozole as the common comparator.
- 5.6 As a minor submission, no new clinical trials were presented in the re-submission. The sponsor stated that no new clinical data have become available that would further inform PBAC's decision.
- 5.7 Details of the trials presented in the November 2017 resubmission are provided in the table below.

¹ Cherny NI, Sullivan R, Dafni U, et al: A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). *Ann Oncol* 26:1547-73, 2015

Table 2: Trials and associated reports presented in the submission

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Direct randomised trial vs placebo		
MONALEESA-2 NCT01958021 CLEEO11A2301 2013-003084-61	Title: A randomized double-blind, placebo-controlled study of LEE011 in combination with letrozole for the treatment of postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer who received no prior therapy for advanced disease.	
	Interim Clinical Study Report (CSR): Data cut off 29 Jan 2016, report date 27 July 2016.	27 July 2016
	Executive Summary for interim 90 Day Update: Data cut off 18 Aug 2016, report date 13 Sep 2016.	13 Sept 2016
	Second Overall Survival Interim Analysis: Data cut off 2 Jan 2017, report date 11 Feb 2017.	11 Feb 2017
	Publication: Hortobagyi, Stemmer et al. 2016. Ribociclib as First line Therapy for HR-Positive, Advanced Breast Cancer.	NEJM 2016; 375 (17): 38-48
Supplementary randomised trials for indirect comparison: palbociclib plus letrozole vs letrozole alone		
PALOMA-1 A5481003 [NCT00721409]	Finn, RS Crown, JP Lang, I et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study.	Lancet Oncol 2015; 16:25-35.
	Finn, RS Crown, JP, Ettl J et al. Efficacy and safety of palbociclib in combination with letrozole as first-line treatment of ER-positive, HER2-negative, advanced breast cancer: expanded analyses of subgroups from the randomised pivotal trial PALOMA-1/TRIO-18.	Breast Cancer Research (2016) 18:67.
	Bell, Crown et al. 2016. Impact of palbociclib plus letrozole on pain severity and pain interference with daily activities in patients with estrogen receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer as first line treatment	Current Medical Research and Opinion 2016; 32:5, 959-965.
PALOMA-2 NCT01740427 A5481008, 2012-004601-27	Finn, Martin et al. 2016. Palbociclib and Letrozole in Advanced Breast Cancer.	NEJM 2016; 375: 1925-1936.
	Finn, RS Martin, M Hope, S et al. PALOMA-2: Primary results from a phase III trial of palbociclib (P) with letrozole (L) compared with letrozole alone in postmenopausal women with ER+/HER2– advanced breast cancer (ABC). Rugo 2016. Impact of palbociclib plus letrozole on health related quality of life (HRQOL) compared with letrozole alone in treatment naïve postmenopausal patients with ER+ HER2-metastatic breast cancer (MBC): Results from PALOMA-2. An Oncol 27 (suppl_6): 225PD	J Clin Oncol 34, 2016 (suppl; abstract 507). An Oncol 27 (suppl_6): 225PD

Source: Table 2.1, p50 of the November 2017 re-submission

Comparative effectiveness

5.8 The trial results presented below remain unchanged from the previous major submissions considered in July and November 2017.

Table 3: Results of PFS and OS in MONALEESA-2

MONALEESA-2 interim analysis	Ribociclib + Letrozole, n with event/N (%)	Letrozole, n with event/N (%)	Ribociclib + Letrozole, median months (95% CI)	Letrozole, median months (95% CI)	Difference, median months	HR (95% CI) ^a
PFS						
Investigator Jan 2016	93/334 (27.8)	150/334 (44.9)	NR	NR	NR	0.556 (0.429, 0.720) p-value <0.0001
BICR Jan 2016	NR	NR	NR	NR	NR	0.592 (0.412, 0.852) p-value 0.002
Investigator Jun 2016	118/334 (35.3)	179/334 (53.9)	22.4 (20.8, not estimable)	15.3 (13.4, 16.7)	7.1	0.559 (0.443, 0.706) p-value <0.0001
Investigator Jan 2017	140/334 (41.9)	205/334 (61.4)	25.3 (23.0, 30.3)	16.0 (13.4, 18.2)	9.3	0.568 (0.457, 0.704) p-value <0.0001
OS						
Jan 2016	23/334 (6.9)	20/334 (6.0)	NR	NR	NR	1.128 (0.619, 2.055) p-value 0.653
Jun 2016	██████████	██████████	██	██	██	██
Jan 2017	50/334 (15.0)	66/334 (19.8)	NR	NR	NR	0.746 (0.517, 1.078) p-value 0.059

BICR: Blinded Independent Central Review; CI: confidence interval; NR: not reported, HR: Hazard Ratio; OS: overall survival; PFS: progression-free survival

^a hazard ratio < 1 indicates a reduction in hazard rate in favour of ribociclib + letrozole.

Source: November 2017 PBAC minutes, Table 5, p13.

5.9 At the January 2017 interim analysis, 15.0% of patients in the ribociclib + letrozole arm and 19.8% of patients in the letrozole alone arm had died. The difference in OS, although in favour of ribociclib (median increase not reached; 1.9/100 additional patients alive at 24 months), was not statistically significant (P=0.059) though there was a trend in favour of the ribociclib + letrozole arm, with a 25.4% risk reduction relative to placebo (HR 0.746; 95% CI: 0.517, 1.078). The PBAC noted that if there is no survival gain for patients treated with ribociclib, then gains in PFS would appear to be at the expense of reduced post-progression survival.

5.10 Details of the indirect comparison between ribociclib and palbociclib presented in the November 2017 resubmission are provided in the table below.

Table 4: Summary of results of the indirect comparison of PFS (ribociclib vs palbociclib)

Trial type or estimate	Trial ID	n with event/N (%)	Letrozole alone n with event/N (%)	HR (95%CI)
Ribociclib + letrozole vs letrozole alone	MONALEESA-2, Jan 2017 Investigator assessed PFS	██████████	██████████	██████████
Palbociclib + letrozole vs letrozole alone	PALOMA-2, Feb 2016 Investigator assessed PFS	194/444 (43.7)	137/222 (61.7)	██████████
	BICR assessed PFS	152/444 (34.2)	96/222 (42.3)	
Indirect estimate of effect adjusted for the common reference ^a				██████████
Indirect estimate of effect adjusted for the common reference (using BICR assessed PFS) ^a				██████████

CI = confidence interval; n = number of participants with event; N = total number of participants in group; HR = hazard ratio; PFS = progression free survival

^a hazard ratio < 1 indicates a reduction in hazard rate in favour of ribociclib + letrozole

Source: November 2017 PBAC minutes ribociclib, Table 7, p14.

Comparative harms

5.11 The table below presents the incidence of adverse events (AEs) for the direct comparison of ribociclib + letrozole to letrozole alone using the MONALEESA-2 trial data. This is unchanged from the November 2017 submission.

Table 5: Summary of key adverse events in MONALEESA-2 (June 2016 interim analysis)

Adverse events	Ribociclib + letrozole n with event/N (%)	Letrozole n with event/N (%)	RR (95% CI)
June 2016 interim analysis			
All AEs	██████████	██████████	██████████
Serious AEs	██████████	██████████	██████████
Grade ≥3 AE	██████████	██████████	██████████
Grade ≥3 AE requiring treatment	██████████	██████████	██████████
AEs leading to discontinuation	██████████	██████████	██████████
AEs requiring dose change/interruption	██████████	██████████	██████████
Deaths	██████████	██████████	██████████
On treatment deaths*	██████████	██████████	██████████
January 2017 interim analysis			
All AEs	331/334 (99.1)	322/330 (97.6)	1.02 (1.00, 1.04)
Grade 3 AE	283 (84.7)	120 (36.4)	2.33 (2.01, 2.71)
Grade 4 AE	56 (16.8)	6 (1.8)	9.22 (4.03, 21.11)

AE: Adverse event; n: patients with event; N: total patients; RR: Relative risk.

*Note: based on small patient numbers

Bold = statistically significant at 5% level

Source: November 2017 PBAC minutes ribociclib Table 9, p15.

5.12 In the indirect comparison of ribociclib + letrozole and palbociclib + letrozole in terms of Grade ≥ 3 AEs and discontinuation due to AE using the MONALEESA-2 and PALOMA-2 trials, ribociclib + letrozole was associated with a similar number of Grade ≥ 3 AEs, but a greater number of AEs leading to treatment discontinuation, compared with palbociclib + letrozole. Results of this analysis are shown in Tables 6 and 7.

Table 6: Summary of results of the indirect comparison of Grade ≥ 3 adverse events (unadjusted, calculated from reported event counts) (ribociclib vs palbociclib)

Trial type or estimate	Trial ID	n with event/N (%)	Letrozole alone n with event/N (%)	OR (95%CI)
Ribociclib + letrozole vs letrozole alone	MONALEESA-2, Jun 2016	██████	██████	██████
Palbociclib + letrozole vs letrozole alone	PALOMA-2, Feb 2016	336/444 (0.76)	54/222 (0.24)	██████
Indirect estimate of effect adjusted for the common reference ^a				██████

CI = confidence interval; n = number of participants with event; N = total number of participants in group; HR = hazard ratio; PFS = progression free survival

^a hazard ratio < 1 indicates a reduction in hazard rate in favour of ribociclib + letrozole

Source: Table 2.36 of the November 2017 resubmission

Table 7: Summary of results of the indirect comparison of AEs leading to treatment discontinuation (unadjusted, calculated from reported event counts) (ribociclib vs palbociclib)

Trial type or estimate	Trial ID	n with event/N (%)	Letrozole alone n with event/N (%)	OR (95%CI)
Ribociclib + letrozole vs letrozole alone	MONALEESA-2, Jun 2016	██████	██████	██████
Palbociclib + letrozole vs letrozole alone	PALOMA-2, Feb 2016	43/444 (9.7%)	13/222 (5.9%)	██████
Indirect estimate of effect adjusted for the common reference ^a				██████

CI = confidence interval; n = number of participants with event; N = total number of participants in group; HR = hazard ratio; PFS = progression free survival

^a hazard ratio < 1 indicates a reduction in hazard rate in favour of ribociclib + letrozole

Source: Table 2.36 of the November 2017 re-submission

Clinical claim

5.13 The resubmission claimed that ribociclib + letrozole provides superior efficacy and inferior safety compared with letrozole alone. This is unchanged from the previous submission. At the July 2017 meeting, the PBAC considered that the claim of superior efficacy was likely to be reasonable for PFS, however the immaturity of the OS data resulted in a high degree of uncertainty in the assessment of its magnitude of long-term benefit [PSD, July 2017, item 7.9]. The PBAC noted without a gain in OS, the gain in PFS would be at the expense of reduced post-progression survival. The PBAC previously considered the claim of inferior safety to be reasonable [PSD, July 2017, item 7.11].

5.14 The resubmission claimed that ribociclib + letrozole provides similar effectiveness and safety to palbociclib + letrozole. Overall, the PBAC noted there is limited data to support the clinical claim for ribociclib compared with palbociclib but considered that the claim of non-inferior efficacy and safety appears reasonable.

Economic analysis – cost effectiveness versus letrozole alone

5.15 In the major submission considered by PBAC in November 2017, a cost-effectiveness and cost-utility analysis against letrozole alone was presented. The minor resubmission did not alter the model structure from November 2017 but sought to respecify the best estimate of the base case ICER by reducing the price of ribociclib from \$ [REDACTED] to \$ [REDACTED] (for 63 x 200 mg tablets) and reducing the model time horizon from 10 years to 7 years. Minor changes in the cost of other drugs in the model were also applied in the updated model. Key parameters changed in the minor resubmission model are shown in the table below.

Table 8: Summary of key parameter changes in the minor resubmission

Parameter	November 2017 resubmission	Minor resubmission
Ribociclib effective price (DPMQ): 63 x 200 mg tablets	\$ [REDACTED]	\$ [REDACTED]
Time horizon	10 years	7 years
Letrozole DPMQ	\$ [REDACTED]	\$ [REDACTED]
Everolimus DPMQ (weighted)	\$ [REDACTED]	\$ [REDACTED]
Exemestane DPMQ	\$ [REDACTED]	\$ [REDACTED]
Capecitabine DPMQ	\$ [REDACTED]	\$ [REDACTED]

Source: Minor submission March 2018, pg2.

5.16 Results of the economic evaluation in previous submissions and the minor resubmission are shown in Table 9.

Table 9: Results of the economic evaluation

	Ribociclib +letrozole	Letrozole	Increment
March 2018 resubmission – results of the economic evaluation			
Costs	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
LYs	[REDACTED]	[REDACTED]	[REDACTED]
QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/extra LY gained for a 7 year time horizon			\$ [REDACTED]
Incremental cost/extra QALY gained for a 7 year time horizon			\$ [REDACTED]
Incremental cost/QALY gained for a 10 year time horizon			\$ [REDACTED]
November 2017 resubmission - results of the economic evaluation as calculated during the evaluation			
Costs	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
LYs	[REDACTED]	[REDACTED]	[REDACTED]
QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/extra LY gained for a 10 year time horizon			\$ [REDACTED]
Incremental cost/extra QALY gained for a 10 year time horizon			\$ [REDACTED]
July 2017 submission - results of the economic evaluation			
Costs	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
LYs	[REDACTED]	[REDACTED]	[REDACTED]
QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/extra LY gained for a 10 year time horizon			\$ [REDACTED]
Incremental cost/extra QALY gained for a 10 year time horizon			\$ [REDACTED]

LY: Life years; QALYs: quality adjusted life years. Source: Table 1 of Ribociclib March 2018 minor resubmission and November 2017 PBAC ratified minutes, Table 13, p23.

^a Quoted as \$ [REDACTED] in table 1 of minor resubmission, ^b Quoted as \$ [REDACTED] in table 1 of minor resubmission - differences are the result of using a different approach for assigning response in the pre-progression state.

- 5.17 The reduced price for ribociclib (along with the other changes to the cost inputs although these had less than a \$100 impact on the ICER) decreased the ICER from \$45,000-\$75,000 to \$15,000-\$45,000 per QALY gained. Reducing the time horizon from 10 years to 7 years increased the ICER to \$45,000-\$75,000 per QALY gained.
- 5.18 If the forecasted use of ribociclib is as predicted (more than \$100 million over 5 years), application of the proposed subsidisation cap [REDACTED] over 5 years) would result in a [REDACTED]% reduction in the DPMQ, giving an average effective DPMQ of \$ [REDACTED] and a cost/QALY gained of \$15,000-\$45,000 with a model time horizon of 7 years. If the forecasted use is [REDACTED]% lower than predicted the average effective DPMQ is \$ [REDACTED] and the cost/QALY gained is \$45,000-\$75,000. If the forecasted use is [REDACTED]% higher than predicted the average effective DPMQ is \$ [REDACTED] and the cost/QALY gained is \$15,000-\$45,000. The minor resubmission presented additional multivariate sensitivity analyses assessing different time horizons and extrapolation functions for overall survival.

- 5.19 The PBAC noted a number of issues with the model presented in the November 2017 resubmission that are unchanged in the March 2018 minor resubmission:
- The use of a time horizon beyond 5 years;
 - The model assumption that treatment effect persists for the model duration;
 - Uncertainty of the size of the extrapolated benefit due to limited OS data; and
 - The post-progression utility value largely being driven by a single end of treatment visit.
- 5.20 The PBAC previously considered that the gain in life years in the economic model was overly optimistic and highly uncertain given there is only 26.4 months (median) of follow-up in the MONALEESA-2 trial (January 2017), the median difference in OS in the trial is currently unknown, and the difference was not statistically significant ($P=0.059$) (PSD, November 2017, item 7.12). The minor submission noted that the model projects an improvement of [REDACTED] undiscounted life years ([REDACTED] months) over ten years, which is reduced to [REDACTED] years ([REDACTED] months) when the time horizon is truncated to 7 years.
- 5.21 The PBAC noted the challenges of making comparisons across the ribociclib and palbociclib submissions given that the two submissions adopted different modelling approaches. The PBAC reiterated that the available comparative evidence suggested that the two drugs are likely to be similarly clinically effective. Accordingly, the PBAC considered that any difference in incremental quality adjusted life years gained between the models contradicted the clinical evidence and was an artefact of the different modelling approaches.
- 5.22 The PBAC considered, based on the available clinical data, that the modelled gain in life years for ribociclib remained overly optimistic and uncertain even with the time horizon truncated to 7 years, and this resulted in the ICER being highly uncertain and underestimated. The PBAC considered the primary driver of the model should be the benefits associated with delaying progression rather than increasing survival, and that based on the gain in progression free survival as observed in the clinical trials and modelled, that the cost effectiveness of ribociclib could be brought into an acceptable range with a reduced effective price.

Economic analysis – cost minimisation versus palbociclib

- 5.23 The November 2017 resubmission presented a cost-minimisation analysis comparing ribociclib + letrozole and palbociclib + letrozole. The estimation of equi-effective doses was based on relative dose intensity (RDI) and regimen intensity of 21 days in each 28-day cycle. The November 2017 resubmission calculated the equi-effective doses to be ribociclib [REDACTED] mg ([REDACTED] mg x [REDACTED] % RDI [mean from MONALEESA-2 trial] x 21/28 days) and palbociclib [REDACTED] mg ([REDACTED] mg x [REDACTED] % RDI [median from

PALOMA-2 trial] x 21/28 days). The pre-PBAC response for the November 2017 resubmission stated the median RDI from the published interim analysis (█%) was used for palbociclib as a mean value was not publically available.

5.24 No additional costs or offsets were included in the cost-minimisation analysis.

Drug cost/patient/year: \$ █

Drug cost/patient/course: \$ █

5.25 The drug cost per patient per year was based on a cost of \$ █ for 63 tablets x 200mg, \$ █ for 42 tablets x 200mg and \$ █ for 21 tablets x 200mg, assuming a full year of treatment (12 months, 13.04 scripts) and inclusive of dose adjustments (based on doses received in the MONALEESA-2 trial). This is reduced from a drug cost/patient/year of \$ █ in the November 2017 resubmission. The cost of letrozole is not included in these estimates.

5.26 The drug cost per patient per course was based on the drug cost per patient per year multiplied by the median PFS from MONALEESA-2 (25.3 months).

5.27 In the economic model the drug cost/patient/course was estimated to be \$ █. This is reduced from that estimated using the November 2017 economic model where the total cost of ribociclib per patient was \$ █.

Estimated PBS usage & financial implications

5.28 The minor submission provided updated estimates of the financial impact to the Australian Government of listing ribociclib on the PBS. These estimates have been updated with the reduced DPMQ for ribociclib and minor price changes for other PBS drugs.

5.29 The minor submission estimated a net cost to the PBS of \$60-\$100 million in Year 5 of listing, with a total net cost to the PBS of more than \$100 million over the first 5 years of listing. This is reduced from more than \$100 million in the November 2017 submission.

5.30 At the November 2017 meeting, the PBAC considered the financial estimates were likely to be underestimated. Issues noted with the estimates included uncertain uptake, which was likely underestimated in initial years and overestimated in outer years, possible differences in dose intensity in practice versus the trials and potential use beyond progression. The estimates are likely to be further underestimated due to, as noted in the prePBAC response, excluding patients with ECOG ≥2 and patients with ovarian radiation or treatment with LHRHa for induction of ovarian suppression.

5.31 The financial estimates presented in the minor submissions apply the full number of scripts per year to the estimated number of treated patients. This overestimates the number of prescriptions as not all patients will be fully compliant to treatment. The

Public Summary Document – March 2018 PBAC Meeting

July 2017 submission for ribociclib estimated that there would be 10.5 scripts for this drug per year based on the mean relative dose intensity (█████%) observed in interim results from the MONALESSA-2 trial. DUSC (July 2017) considered that the adherence to ribociclib in practice may be lower than observed in the trial.

Table 10: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
	2018	2019	2020	2021	2022	2023
Estimated extent of use						
Eligible and suitable patients	█████	█████	█████	█████	█████	█████
Treatment uptake assumption	█████%	█████%	█████%	█████%	█████%	█████%
Number of patients treated	█████	█████	█████	█████	█████	█████
Number of scripts dispensed (PBS/RPBS) ^a						
Ribociclib 21 tab packs	█████	█████	█████	█████	█████	█████
Ribociclib 42 tab packs	█████	█████	█████	█████	█████	█████
Ribociclib 63 tab packs	█████	█████	█████	█████	█████	█████
Total	█████	█████	█████	█████	█████	█████
Estimated financial implications of ribociclib - March 2018 Minor						
Cost to PBS/RPBS	\$█████	\$█████	\$█████	\$█████	\$█████	\$█████
Copayments	-\$█████	-\$█████	-\$█████	-\$█████	-\$█████	-\$█████
Cost to PBS/RPBS less copayments	\$█████	\$█████	\$█████	\$█████	\$█████	\$█████
Estimated financial implications for tamoxifen, letrozole, anastrozole, and exemestane						
Cost to PBS/RPBS	\$█████	-\$█████	-\$█████	-\$█████	-\$█████	-\$█████
Copayments	\$█████	\$█████	\$█████	\$█████	\$█████	\$█████
Cost to PBS/RPBS less copayments	\$█████	\$█████	\$█████	\$█████	-\$█████	-\$█████
Estimated financial implications of ribociclib – November 2017 resubmission						
Cost to PBS/RPBS	\$█████	\$█████	\$█████	\$█████	\$█████	\$█████
Copayments	-\$█████	-\$█████	-\$█████	-\$█████	-\$█████	-\$█████
Cost to PBS/RPBS less copayments	\$█████	\$█████	\$█████	\$█████	\$█████	\$█████
Estimated financial implications for tamoxifen, letrozole, anastrozole, and exemestane						
Cost to PBS/RPBS	\$█████	-\$█████	-\$█████	-\$█████	-\$█████	-\$█████
Copayments	\$█████	\$█████	\$█████	\$█████	\$█████	\$█████
Cost to PBS/RPBS less copayments	\$█████	\$█████	\$█████	-\$█████	-\$█████	-\$█████

^a Calculated as the number of treated patients multiplied by the number of prescriptions per year, 13.04. Patients are assumed to be fully compliant.

Source: Table 4.7 and 4.8 p153-4, 4.12 p157 of the November 2017 re-submission and Section 4 Workbook.xlsx, Sheet 4c. Displaced –

EFF, Section 4 Workbook – Minor FINAL.xlsx, Sheet 4c. Displaced – EFF.

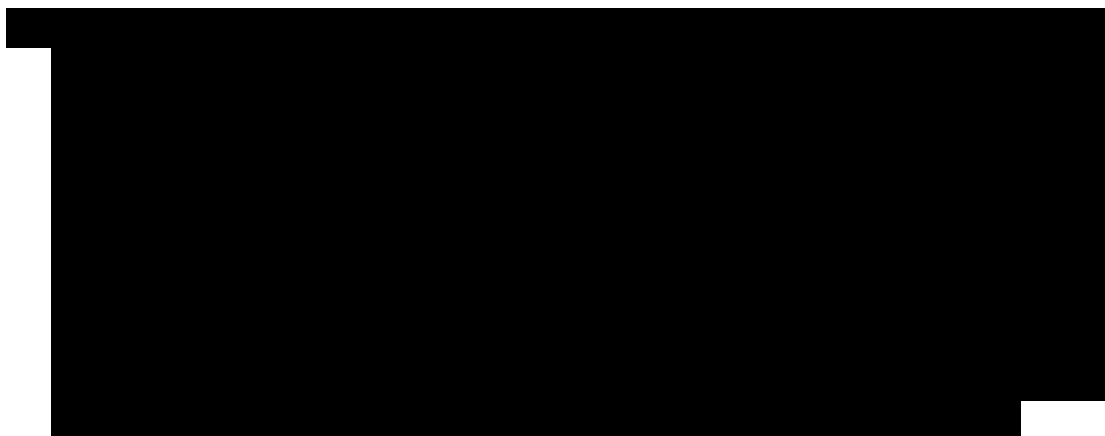
The redacted table shows that at year 6, the estimated number of patients was less than 10,000 per year and the net cost to the PBS would be more than \$100 million per year.

Financial management – risk sharing arrangements

5.32 In the minor resubmission the sponsor offered to enter into a risk sharing agreement (RSA) under which the net cost to the Australian Government of listing ribociclib would not exceed \$ [REDACTED] over five years. The PBAC agreed, as acknowledged by the sponsor, that if both ribociclib and palbociclib are listed on the PBS for the same population, any financial caps will be shared between the two drugs.

5.33 The minor resubmission stated the following conditions on the proposed risk sharing agreement:





- 5.34 The PBAC advised the listing should include patients with an ECOG performance status of 0 to 2 and that the proposed cap [REDACTED]
- 5.35 The PBAC noted that the sponsor provided alternative proposals for risk sharing arrangements in the Pre-PBAC response including [REDACTED]. The PBAC considered that these approaches were less preferable than agreed total annual caps.

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

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of ribociclib in combination with a non-steroidal aromatase inhibitor (NSAI) (anastrozole or letrozole) as initial endocrine-based therapy in patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced inoperable or metastatic breast cancer. The PBAC was satisfied that for some patients, ribociclib provides additional progression free survival compared with an NSAI alone, though its effect on overall survival is unknown. The PBAC considered that the modelled cost-effectiveness was highly uncertain, but the Committee considered that the cost effectiveness of ribociclib could be brought into an acceptable range with a reduced effective price. The PBAC considered the uncertainty with the means of improving the cost-effectiveness could occur via a reduction in price in conjunction with financial caps.
- 6.2 The PBAC advised that the listing for ribociclib should:
- include patients with an ECOG performance status of 0 to 2 as the small proportion of patients with ECOG performance status of 2 should not be excluded from treatment with ribociclib;
 - not exclude patients with inflammatory breast cancer or uncontrolled brain metastases, rather, that clinicians are able to decide whether these patients are

suitable for treatment with ribociclib;

- not exclude patients with ovarian radiation or treatment with luteinizing hormone-releasing hormone agonist (LHRHa) (goserelin acetate or leuprolide acetate) for the induction of ovarian suppression. The PBAC noted that pre-menopausal women are excluded from treatment in the proposed restriction and considered that it is unnecessary to exclude patients with ovarian radiation or treatment with luteinizing hormone-releasing hormone agonist (LHRHa) (goserelin acetate or leuprolide acetate) for the induction of ovarian suppression; and
- exclude patients who develop disease progression whilst on treatment with ribociclib.

- 6.3 The PBAC noted that in the pre-PBAC response the sponsor proposed that patients with disease progression following first line chemotherapy should be eligible for PBS subsidised ribociclib. The PBAC disagreed with this proposal and indicated that this proposal was not appropriate as evidence for use in this population has not been considered.
- 6.4 The PBAC advised wording of the treatment criteria for the initial restriction should specify that patients must have had no prior systemic endocrine-based therapy for this indication. The PBAC also recommended a cautionary statement be included in the restriction advising that QT monitoring is required for patients treated with ribociclib.
- 6.5 The PBAC advised that both initial and continuing restrictions should be authority required (telephone).
- 6.6 The PBAC considered that the approach to the grandfather restriction was appropriate, although patients should not be required to have accessed ribociclib only through the sponsor's access program in order to be eligible for grandfathering. The PBAC also recommended that only patients who met the PBS initiation criteria at the time they initiated treatment with ribociclib should be grandfathered to the PBS. That is that grandfathered patients should be the same as the PBS population and not a wider population.
- 6.7 The PBAC recommended that if the currently near market product palbociclib and ribociclib are both listed on the PBS, the listing of ribociclib should be amended to state that ribociclib and palbociclib are not to be used in combination, and that patients should only be treated with either ribociclib or palbociclib, unless the patient develops an intolerance of a severity necessitating permanent treatment withdrawal. These amendments are outlined in the flow-on changes to listing in Section 7.
- 6.8 The PBAC acknowledged the previously expressed significant public interest in the listing of ribociclib and noted that the Medical Oncology Group of Australia (MOGA)

expressed its strong support for the ribociclib submission, on the basis of PFS benefit.

- 6.9 The PBAC considered that the nominated main comparator, a NSAI (i.e. letrozole or anastrozole) alone, remained appropriate. The PBAC considered that palbociclib was an appropriate near market comparator, and noted palbociclib was also considered by the Committee for a similar indication at its March 2018 meeting.
- 6.10 The PBAC noted the minor resubmission was based on the same head-to-head phase III, randomised, double-blind trial comparing ribociclib + letrozole to letrozole alone in postmenopausal women with HR+, HER2- ABC (MONALEESA-2) as presented in the original submission. The PBAC previously considered that the claim of superior efficacy based on PFS was likely to be reasonable; ribociclib resulted in a statistically significant improvement in PFS with a median increase of 9.3 months when investigator assessed. The difference in OS, although in favour of ribociclib, was not statistically significant ($p=0.059$) and the PBAC recalled that due to the immaturity of the OS data, there is a high degree of uncertainty in the magnitude of long-term benefit with ribociclib. Based on the available data, the PBAC considered that if there was no overall survival gain then the gains in progression free survival for patients treated with ribociclib are likely to be at the expense of reduced post-progression survival. The PBAC considered that the claim of superior comparative effectiveness over an NSAI alone was adequately supported on the basis of the improvement in progression free survival. However, the overall the magnitude of long term clinical benefit from the addition of palbociclib is highly uncertain.
- 6.11 The PBAC recalled that it had previously considered the claim of inferior safety compared with a NSAI alone to be reasonable. The inferior safety profile could impact on the quality of life in the progression free state.
- 6.12 The PBAC recalled from the November 2017 resubmission, based on the indirect comparison with palbociclib, though there is limited data it is reasonable to conclude that the two agents are non-inferior in clinical effectiveness and safety.
- 6.13 The PBAC considered that the ribociclib economic model generated implausible estimates of gains in life years, even with the time horizon truncated to 7 years, and this resulted in the ICER being highly uncertain and underestimated. The PBAC considered the primary driver of the model should be the benefits associated with delaying progression, such as improved quality of life and reduced medical resource use, rather than increasing survival, and that based on the gain in progression free survival as observed in the clinical trials and modelled, that the cost effectiveness of ribociclib could be brought into an acceptable range (██████████ per QALY gained) with a reduced effective price. The PBAC considered the uncertainty with the cost-effectiveness could be adequately addressed through a reduction in price in conjunction with financial caps, noting that the proposed caps are likely to be reached. The PBAC further noted that the financial caps should be distributed

proportionally to uptake rates and so there will be a lower Cap in year 1 than in later years.

- 6.14 The PBAC considered the doses used in the trials, including RDI adjustments, should be used as a basis for the equi-effective doses for ribociclib and palbociclib. On this basis the equi-effective doses would be ribociclib [REDACTED] mg ([REDACTED] mg x mean RDI of [REDACTED]%) and palbociclib [REDACTED] per day for 21 days of a 28 day cycle.
- 6.15 The PBAC noted that the minor resubmission estimated the total net financial impact to the Australian Government of listing ribociclib was more than \$100 million over 5 years. The PBAC considered that the estimated costs are uncertain but that financial risk will be mitigated by the proposed risk sharing arrangement. The PBAC considered that the uptake rates in the initial years are likely to be underestimated given the public interest in ribociclib, however uptake rates may be overestimated in outer years of the forward estimates. The PBAC also noted that the number of prescriptions per patient may be overestimated because the submission assumes all treated patients will receive 13.04 prescriptions per year and does not account for discontinuations. In addition as some patients will commence therapy partway through the year the number of scripts per patient in Year 1 may be overestimated.
- 6.16 The PBAC noted the risk sharing arrangements proposed by the sponsor in the minor resubmission and the pre-PBAC response. The PBAC considered [REDACTED] should be set and the total net cost to the Australian Government for ribociclib for the first five years after listing should not exceed \$[REDACTED]. The PBAC agreed, as acknowledged by the sponsor, that if both ribociclib and palbociclib are listed on the PBS for the same population, any financial caps will be shared between the two drugs.
- 6.17 The PBAC noted that final overall survival results from the MONALEESA-2 trial are expected to be available in 2020 and advised that if listed, the sponsor should provide these results to the PBAC.
- 6.18 The PBAC advised that ribociclib should be treated as interchangeable on an individual patient basis with palbociclib.
- 6.19 The PBAC advised that ribociclib is not suitable for prescribing by nurse practitioners.
- 6.20 The PBAC noted that this submission is not eligible for an Independent Review as it is a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Add new items:

Name, Restriction, Manner of administration and form	Max. Qty (units)	No. of Rpts	Proprietary Name and Manufacturer
Ribociclib Tablet, 200mg	63	5	Kisqali Novartis Pharmaceuticals Australia Pty Ltd
Category / Program	GENERAL – General Schedule (Code GE)		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
Episodicity:			
Severity:	Locally advanced or metastatic		
Condition:	Breast cancer		
PBS Indication:	Locally advanced or metastatic breast cancer		
Treatment phase:	Initial treatment		
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined		
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole.		
Clinical criteria:	Patient must not have previously been treated with an aromatase inhibitor AND The condition must be hormone receptor positive. AND The condition must be human epidermal growth factor receptor 2 (HER2) negative. AND The condition must be inoperable AND Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or less.		
Population criteria:	Patient must not be premenopausal.		
Caution	QT monitoring is required for patients treated with this drug.		
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.		
Category / Program	GENERAL – General Schedule (Code GE)		

Public Summary Document – March 2018 PBAC Meeting

Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	Breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole.
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition AND Patient must not develop disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease
Population criteria:	Patient must not be premenopausal.
Prescriber Instructions	A patient who has progressive disease when treated with this drug for this condition is no longer eligible for PBS-subsidised treatment with this drug.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Initial – grandfather restriction
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined

Public Summary Document – March 2018 PBAC Meeting

Treatment criteria:	The treatment must be in combination with anastrozole or letrozole.
Clinical criteria:	<p>Patient must have previously received non-PBS-subsidised treatment with this drug for this condition prior to [listing date] AND Patient must not have previously been treated with an aromatase inhibitor prior to initiating treatment with this drug for this condition AND The condition must be hormone receptor positive; AND The condition must be human epidermal growth factor receptor 2 (HER2) negative; AND The condition must be inoperable AND Patient must have had a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 0 to 2 prior to initiating treatment with this drug for this condition AND Patient must not have developed disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease</p>
Population criteria:	The patient must not be premenopausal
Prescriber Instructions	A patient may qualify for PBS-subsidised treatment under this restriction once only.
Administrative Advice	<p>No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.</p>
Caution	QT monitoring is required for patients treated with this drug.

Name, Restriction, Manner of administration and form	Max. Qty (units)	No. of Rpts	Proprietary Name and Manufacturer
Ribociclib Tablet, 200mg	42	5	Kisqali Novartis Pharmaceuticals Australia Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	Breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Initial treatment

Public Summary Document – March 2018 PBAC Meeting

Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole.
Clinical criteria:	Patient must not have previously been treated with an aromatase inhibitor AND The condition must be hormone receptor positive. AND The condition must be human epidermal growth factor receptor 2 (HER2) negative. AND The condition must be inoperable AND Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or less. AND Patient must require dosage reduction requiring a pack of 42 tablets.
Population criteria:	Patient must not be premenopausal.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	Breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole.

Public Summary Document – March 2018 PBAC Meeting

Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition AND Patient must not develop disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease AND Patient must require dosage reduction requiring a pack of 42 tablets.
Population criteria:	Patient must not be premenopausal.
Prescriber Instructions	A patient who has progressive disease when treated with this drug for this condition is no longer eligible for PBS-subsidised treatment with this drug.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Initial – grandfather restriction
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole.

Public Summary Document – March 2018 PBAC Meeting

Clinical criteria:	<p>Patient must have previously received non-PBS-subsidised treatment with this drug for this condition prior to [listing date] AND Patient must not have previously been treated with an aromatase inhibitor prior to initiating treatment with this drug for this condition AND The condition must be hormone receptor positive; AND The condition must be human epidermal growth factor receptor 2 (HER2) negative; AND The condition must be inoperable AND Patient must have had a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 0 to 2 prior to initiating treatment with this drug for this condition AND Patient must not have developed disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease AND Patient must require dosage reduction requiring a pack of 42 tablets.</p>
Population criteria:	The patient must not be premenopausal
Prescriber Instructions	A patient may qualify for PBS-subsidised treatment under this restriction once only.
Administrative Advice	<p>No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.</p>
Caution	QT monitoring is required for patients treated with this drug.

Name, Restriction, Manner of administration and form	Max. Qty (units)	№.of Rpts	Proprietary Name and Manufacturer
Ribociclib Tablet, 200mg	21	5	Kisqali Novartis Pharmaceuticals Australia Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	Breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Initial treatment

Public Summary Document – March 2018 PBAC Meeting

Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole.
Clinical criteria:	Patient must not have previously been treated with an aromatase inhibitor AND The condition must be hormone receptor positive. AND The condition must be human epidermal growth factor receptor 2 (HER2) negative. AND The condition must be inoperable AND Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or less. AND Patient must require dosage reduction requiring a pack of 21 tablets.
Population criteria:	Patient must not be premenopausal.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	Breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole.

Public Summary Document – March 2018 PBAC Meeting

Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition AND Patient must not develop disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease AND Patient must require dosage reduction requiring a pack of 21 tablets.
Population criteria:	Patient must not be premenopausal.
Prescriber Instructions	A patient who has progressive disease when treated with this drug for this condition is no longer eligible for PBS-subsidised treatment with this drug.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Initial – grandfather restriction
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole.

Public Summary Document – March 2018 PBAC Meeting

Clinical criteria:	<p>Patient must have previously received non-PBS-subsidised treatment with this drug for this condition prior to [listing date] AND Patient must not have previously been treated with an aromatase inhibitor prior to initiating treatment with this drug for this condition AND The condition must be hormone receptor positive; AND The condition must be human epidermal growth factor receptor 2 (HER2) negative; AND The condition must be inoperable AND Patient must have had a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 0 to 2 prior to initiating treatment with this drug for this condition AND Patient must not have developed disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease AND Patient must require dosage reduction requiring a pack of 21 tablets.</p>
Population criteria:	The patient must not be premenopausal
Prescriber Instructions	A patient may qualify for PBS-subsidised treatment under this restriction once only.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.
Caution	QT monitoring is required for patients treated with this drug.

7.2 Flow-on changes to listing. The listing of ribociclib should be amended as follows should the currently near market product palbociclib be listed on the PBS prior to ribociclib. The changes are highlighted in italics and strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty (units)	No. of Rpts	Proprietary Name and Manufacturer
Ribociclib Tablet, 200mg	63	5	Kisqali Novartis Pharmaceuticals Australia Pty Ltd
Category / Program	GENERAL – General Schedule (Code GE)		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
Episodicity:			
Severity:	Locally advanced or metastatic		
Condition:	Breast cancer		
PBS Indication:	Locally advanced or metastatic breast cancer		

Public Summary Document – March 2018 PBAC Meeting

Treatment phase:	Initial treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole. AND <i>The treatment must not be in combination with palbociclib</i>
Clinical criteria:	Patient must not have previously been treated with an aromatase inhibitor AND <i>Patient must not have previously been treated with palbociclib</i> OR <i>Patient must have developed an intolerance to palbociclib of a severity necessitating permanent treatment withdrawal</i> AND The condition must be hormone receptor positive. AND The condition must be human epidermal growth factor receptor 2 (HER2) negative. AND The condition must be inoperable AND Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or less.
Population criteria:	Patient must not be premenopausal.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	Breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Continuing treatment

Public Summary Document – March 2018 PBAC Meeting

Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole. <i>AND</i> <i>The treatment must not be in combination with palbociclib</i>
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition <i>AND</i> Patient must not develop disease progression whilst being treated with this drug for this condition. <i>AND</i> Patient must have stable or responding disease
Population criteria:	Patient must not be premenopausal.
Prescriber Instructions	A patient who has progressive disease when treated with this drug for this condition is no longer eligible for PBS-subsidised treatment with this drug.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Initial – grandfather restriction
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole. <i>AND</i> <i>The treatment must not be in combination with palbociclib</i>

Public Summary Document – March 2018 PBAC Meeting

Clinical criteria:	<p>Patient must have previously received non-PBS-subsidised treatment with this drug for this condition prior to [listing date] AND Patient must not have previously been treated with an aromatase inhibitor prior to initiating treatment with this drug for this condition AND <i>Patient must not have previously been treated with palbociclib</i> OR <i>Patient must have developed an intolerance to palbociclib of a severity necessitating permanent treatment withdrawal</i> AND The condition must be hormone receptor positive; AND The condition must be human epidermal growth factor receptor 2 (HER2) negative; AND The condition must be inoperable AND Patient must have had a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 0 to 2 prior to initiating treatment with this drug for this condition AND Patient must not have developed disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease</p>
Population criteria:	The patient must not be premenopausal
Prescriber Instructions	A patient may qualify for PBS-subsidised treatment under this restriction once only.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.
Caution	QT monitoring is required for patients treated with this drug.

Name, Restriction, Manner of administration and form	Max. Qty (units)	No. of Rpts	Proprietary Name and Manufacturer
Ribociclib Tablet, 200mg	42	5	Kisqali Novartis Pharmaceuticals Australia Pty Ltd
Category / Program	GENERAL – General Schedule (Code GE)		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
Episodicity:			
Severity:	Locally advanced or metastatic		
Condition:	Breast cancer		
PBS Indication:	Locally advanced or metastatic breast cancer		
Treatment phase:	Initial treatment		

Public Summary Document – March 2018 PBAC Meeting

Restriction Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	<p>The treatment must be in combination with anastrozole or letrozole. <i>AND</i> <i>The treatment must not be in combination with palbociclib</i></p>
Clinical criteria:	<p>Patient must not have previously been treated with an aromatase inhibitor <i>AND</i> <i>Patient must not have previously been treated with palbociclib</i> <i>OR</i> <i>Patient must have developed an intolerance to palbociclib of a severity necessitating permanent treatment withdrawal</i> <i>AND</i> The condition must be hormone receptor positive. <i>AND</i> The condition must be human epidermal growth factor receptor 2 (HER2) negative. <i>AND</i> The condition must be inoperable <i>AND</i> Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or less. <i>AND</i> Patient must require dosage reduction requiring a pack of 42 tablets.</p>
Population criteria:	Patient must not be premenopausal.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	Breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Continuing treatment

Public Summary Document – March 2018 PBAC Meeting

Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole. <i>AND</i> <i>The treatment must not be in combination with palbociclib</i>
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition <i>AND</i> Patient must not develop disease progression whilst being treated with this drug for this condition. <i>AND</i> Patient must have stable or responding disease <i>AND</i> Patient must require dosage reduction requiring a pack of 42 tablets.
Population criteria:	Patient must not be premenopausal.
Prescriber Instructions	A patient who has progressive disease when treated with this drug for this condition is no longer eligible for PBS-subsidised treatment with this drug.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Initial – grandfather restriction
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole. <i>AND</i> <i>The treatment must not be in combination with palbociclib</i>

Public Summary Document – March 2018 PBAC Meeting

Clinical criteria:	<p>Patient must have previously received non-PBS-subsidised treatment with this drug for this condition prior to [listing date] AND Patient must not have previously been treated with an aromatase inhibitor prior to initiating treatment with this drug for this condition AND <i>Patient must not have previously been treated with palbociclib</i> OR <i>Patient must have developed an intolerance to palbociclib of a severity necessitating permanent treatment withdrawal</i> AND The condition must be hormone receptor positive; AND The condition must be human epidermal growth factor receptor 2 (HER2) negative; AND The condition must be inoperable AND Patient must have had a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 0 to 2 prior to initiating treatment with this drug for this condition AND Patient must not have developed disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease AND Patient must require dosage reduction requiring a pack of 42 tablets.</p>
Population criteria:	The patient must not be premenopausal
Prescriber Instructions	A patient may qualify for PBS-subsidised treatment under this restriction once only.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.
Caution	QT monitoring is required for patients treated with this drug.

Name, Restriction, Manner of administration and form	Max. Qty (units)	No. of Rpts	Proprietary Name and Manufacturer
--	------------------	-------------	-----------------------------------

Ribociclib Tablet, 200mg	21	5	Kisqali Novartis Pharmaceuticals Australia Pty Ltd
-----------------------------	----	---	--

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	Breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Initial treatment

Public Summary Document – March 2018 PBAC Meeting

Restriction Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	<p>The treatment must be in combination with anastrozole or letrozole. <i>AND</i> <i>The treatment must not be in combination with palbociclib</i></p>
Clinical criteria:	<p>Patient must not have previously been treated with an aromatase inhibitor <i>AND</i> <i>Patient must not have previously been treated with palbociclib</i> <i>OR</i> <i>Patient must have developed an intolerance to palbociclib of a severity necessitating permanent treatment withdrawal</i> <i>AND</i> The condition must be hormone receptor positive. <i>AND</i> The condition must be human epidermal growth factor receptor 2 (HER2) negative. <i>AND</i> The condition must be inoperable <i>AND</i> Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or less. <i>AND</i> Patient must require dosage reduction requiring a pack of 21 tablets.</p>
Population criteria:	Patient must not be premenopausal.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	<p>No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.</p>

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	Breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Continuing treatment

Public Summary Document – March 2018 PBAC Meeting

Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole. AND <i>The treatment must not be in combination with palbociclib</i>
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition AND Patient must not develop disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease AND Patient must require dosage reduction requiring a pack of 21 tablets.
Population criteria:	Patient must not be premenopausal.
Prescriber Instructions	A patient who has progressive disease when treated with this drug for this condition is no longer eligible for PBS-subsidised treatment with this drug.
Caution	QT monitoring is required for patients treated with this drug.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	
Severity:	Locally advanced or metastatic
Condition:	breast cancer
PBS Indication:	Locally advanced or metastatic breast cancer
Treatment phase:	Initial – grandfather restriction
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	The treatment must be in combination with anastrozole or letrozole. AND <i>The treatment must not be in combination with palbociclib</i>

Clinical criteria:	<p>Patient must have previously received non-PBS-subsidised treatment with this drug for this condition prior to [listing date] AND Patient must not have previously been treated with an aromatase inhibitor prior to initiating treatment with this drug for this condition AND <i>Patient must not have previously been treated with palbociclib</i> OR <i>Patient must have developed an intolerance to palbociclib of a severity necessitating permanent treatment withdrawal</i> AND The condition must be hormone receptor positive; AND The condition must be human epidermal growth factor receptor 2 (HER2) negative; AND The condition must be inoperable AND Patient must have had a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of 0 to 2 prior to initiating treatment with this drug for this condition AND Patient must not have developed disease progression whilst being treated with this drug for this condition. AND Patient must have stable or responding disease AND Patient must require dosage reduction requiring a pack of 21 tablets.</p>
Population criteria:	The patient must not be premenopausal
Prescriber Instructions	A patient may qualify for PBS-subsidised treatment under this restriction once only.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.
Caution	QT monitoring is required for patients treated with this drug.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

9 Sponsor's Comment

Novartis is pleased with the PBAC recommendation. This is an important outcome for patients with advanced or metastatic breast cancer.