7.13 POMALIDOMIDE
Capsule 3 mg,
Capsule 4 mg,
Pomalyst®, Celgene Pty Ltd

1 Purpose of Application

1.1 The minor resubmission sought to amend the current wording to the restriction of pomalidomide to include the treatment of patients who have experienced severe intolerance or toxicity to lenalidomide and/or bortezomib for relapsed/refractory multiple myeloma.

2 Requested listing

2.1 The submission requested the following changes (shown in *italics*) to the existing pomalidomide initial treatment restriction as below. The requested changes were based on the Secretariat's proposed changes to the restriction from the March 2017 PBAC meeting.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
POMALIDOMIDE				
pomalidomide 3 mg capsule, 21	1	0	$10,500 (Public) $10,547.15 (Private)	Pomalyst® Celgene Pty Ltd
pomalidomide 4 mg capsule, 21	1	0	$10,500 (Public) $10,547.15 (Private)	

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Multiple myeloma
PBS Indication:	Multiple myeloma
Treatment phase:	Initial treatment
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	The treatment must be in combination with dexamethasone, AND Patient must have undergone or be ineligible for a primary stem cell transplant, AND Patient must have experienced treatment failure with bortezomib, *unless contraindicated or not tolerated according to the Therapeutic Goods Administration (TGA) approved Product Information;* AND Patient must have experienced treatment failure with lenalidomide, *unless contraindicated or not tolerated according to the TGA approved Product Information;* AND Patient must not be receiving concomitant PBS-subsidised thalidomide, lenalidomide or bortezomib.
Prescriber Instructions	Bortezomib treatment failure is the absence of achieving at least a partial response or as progressive disease during treatment or within 6 months of discontinuing treatment with bortezomib. Lenalidomide treatment failure is progressive disease during treatment or within 6 months of discontinuing treatment with lenalidomide. *If treatment with either bortezomib or lenalidomide is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication.* *If intolerance to either bortezomib or lenalidomide treatment develops during the relevant period of use which is of a severity to necessitate withdrawal of the treatment, the application must provide details of the nature and severity of this intolerance.* Progressive disease defined as per existing restriction (no changes proposed)
Administrative Advice	As per existing restriction (no changes proposed)
Cautions	As per existing restriction (no changes proposed)

3 Background

3.1 Pomalidomide (in combination with dexamethasone) is TGA registered for the treatment of patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.

3.2 A major submission for pomalidomide seeking listing for treatment of patients with multiple myeloma who have previously received and failed, or are intolerant to treatment with lenalidomide or bortezomib was rejected by the PBAC at the July 2014 meeting on the basis that cost-effectiveness had not been demonstrated. The PBAC also considered that the words "or are intolerant to" should be removed from the proposed restriction, so that the restriction could read "for treatment of patients with multiple myeloma who have previously received and failed treatment with lenalidomide and bortezomib". Subsequently at its November 2014 meeting, the PBAC recommended the listing of pomalidomide for the treatment of patients who have received and failed prior treatment with both bortezomib and lenalidomide (with reference to "or are intolerant to" removed from the restriction).

3.3 At the March 2016 meeting, the PBAC rejected the request to change the definition of treatment failure of bortezomib and lenalidomide and amend the listing to include patients who have 'experienced severe intolerance or toxicity to bortezomib (or lenalidomide), unresponsive to clinically appropriate dose adjustment'. The PBAC considered that the issue was not whether pomalidomide is effective in these populations, but whether pomalidomide is cost-effective against the additional comparators that would apply in those circumstances (for example re-use of lenalidomide or bortezomib with adjusted scheduling). At this meeting, the PBAC also recommended changes to the restriction for lenalidomide to enable a treatment holiday, which it considered would address some of the issues raised in the submission. At the time of consideration of this recommendation was yet to be implemented.

3.4 At its March 2017 meeting, the PBAC rejected a submission requesting to amend the current restriction for pomalidomide to include the treatment of patients who have experienced severe intolerance or toxicity to lenalidomide and/or bortezomib for relapsed/refractory multiple myeloma on the basis of unknown cost-effectiveness of pomalidomide in this treatment setting.

3.5 A summary of the March 2016, March 2017 and current November 2017 submission is presented below in Table 1.

Table 1: Summary of March 2016, March 2017 and November 2017 minor submissions

	March 2016 minor submission	March 2017 minor resubmission	November 2017 minor resubmission
Requested amendment to listing	Include patients who have experienced severe intolerance or toxicity to bortezomib and/or lenalidomide unresponsive to clinically appropriate dose. Remove requirement that patients must have demonstrated progressive disease within 6 months of discontinuing treatment with lenalidomide and bortezomib	Include patients who have 'experienced severe intolerance unresponsive to clinically appropriate dose adjustment scheduling and/or are contraindicated to bortezomib and lenalidomide.	Include patients who are contraindicated and/or not tolerant to bortezomib and lenalidomide according to the TGA approved PI. *Reference to clinically appropriate dose adjustment scheduling has been removed*
Requested DPMQ	No change from November 2014 submission	No change from November 2014 submission	Weighted average effective price of $[redacted] (includes [redacted]% rebate for the requested extended patient population only, estimated to be [redacted]% of total pomalidomide PBS population)
Clinical evidence	Presented subgroup analysis of trial MM-003 (Key trial of November 2014 submission) of following three patient groups: • Refractory subjects not progressed on or within 60 days of both lenalidomide and bortezomib based treatments (82.5%) • Relapsed refractory patients who achieved at least partial response and progressed within 6 months after stopping treatment with lenalidomide and/or bortezomib (2.6%) • Refractory/indolent patients who have developed intolerance/toxicity after a minimum of 2 cycles of bortezomib (14.9%)	No clinical data provided	No clinical data provided Presented subgroup analysis of trial MM-003 as per March 2016 submission.
Comparative safety	No safety data provided	No safety data provided **PBAC comment:** (paragraph 7.2) The PBAC	Naïve comparison of AEs in patients from MM-09/-10 trials (lenalidomide) vs the MM-003 trial.

	March 2016 minor submission	March 2017 minor resubmission	November 2017 minor resubmission
		considered there was a high risk that patients experiencing severe intolerance to lenalidomide would experience similar adverse effects on treatment with pomalidomide, given lenalidomide and pomalidomide have similar mechanisms of action.	
Comparator	No comparator nominated **PBAC comment:** (paragraph 5.2) The PBAC considered that the issue was not whether pomalidomide works in the broader group requested (that is those who have previously received lenalidomide or bortezomib), but whether pomalidomide in this setting is cost-effective against the additional comparators that would apply in those circumstances (for example re-use of lenalidomide or bortezomib with adjusted scheduling).	High dose dexamethasone (HDD) on the basis that the requested restriction has been revised to only include patients who are intolerant to bortezomib or lenalidomide with clinically appropriate dose adjustment. **PBAC comment:** (paragraph 5.1) The PBAC previously accepted that HDD was the appropriate main comparator in this context, while noting that other salvage therapies would also be replaced in practice (paragraph 7.3, July 2014 Public Summary Document (PSD)).	HDD
Economic analysis	No economic analysis provided	No economic analysis provided **PBAC comment:** (paragraph 7.3) The PBAC considered that the cost-effectiveness of pomalidomide in this treatment setting was unknown. Further, the PBAC recalled that at the November 2014 meeting when it recommended pomalidomide for treatment of patients who have received and failed prior treatment with both bortezomib and lenalidomide, it considered the ICER to be at the high end of what they would consider cost effective.	Presented analysis of cost-effectiveness in requested extended patient population Same model structure as November 2014 submission incorporating [redacted]% rebate for the proposed extended population and revised weighted total dose per pack of 80.7 (from 84.0). ICER: $45,000/QALY - $75,000/QALY gained (discounted)
Estimated PBS usage	No estimates of PBS usage	Additional [redacted] patients in	Additional [redacted] patients in

	March 2016 minor submission	March 2017 minor resubmission	November 2017 minor resubmission
	provided	year 1 increasing to [redacted] patients in year 5	year 1 increasing to [redacted] patients in year 5
Cost to PBS	No financial implications provided	less than $10 million in year 1 increasing to less than $10 million in year 5	less than $10 million in year 1 increasing to less than $10 million in year 5

Abbreviations: AEs=adverse events; DPMQ=dispensed price for maximum quantity; ICER=incremental cost-effectiveness ratio; PI=Product Information; QALY= quality adjusted life year; TGA=Therapeutic Goods Administration

Source: compiled from the July 2014 PSD, November 2014 PSD, March 2017 PSD and November 2017 minor submission.

4 Comparator

4.1 The submission nominated salvage therapy (high dose dexamethasone; HDD), or palliative care as the comparators (as per the July 2014 major submission).

4.2 The PBAC previously accepted that HDD was the appropriate main comparator in the context of the restriction only included patients who are intolerant to bortezomib or lenalidomide with clinically appropriate dose adjustment, while noting that other salvage therapies would also be replaced in practice (paragraph 7.3, July 2014 Public Summary Document, PSD).

4.3 The restriction requested in the current submission did not specifically preclude patients who are intolerant to bortezomib or lenalidomide with clinically appropriate dose adjustment and therefore notes that lenalidomide and/or bortezomib adjusted scheduling may be appropriate comparators in this context. However, the submission argued that patients are only deemed intolerant/contraindicated to therapy after clinically appropriate dose adjustment has been attempted and therefore this was unnecessary.

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.

Clinical trials

5.3 No new clinical trials were presented in the submission.

Comparative effectiveness

5.4 The submission claimed that the clinical evidence from the primary clinical trial MM-003 on which the pomalidomide PBS listing was based, demonstrates that the reason for discontinuation of treatment with bortezomib is unlikely to be a treatment effect modifier. The submission presented a subgroup analysis of trial MM-003 including the patient group comprised of patients who were

refractory/intolerant to bortezomib after a minimum of 2 cycles (N=45, 14.9%). The subgroup analysis was previously presented in the March 2016 submission. The submission claimed there was no significant difference in terms of progression free survival or overall survival for this patient subgroup compared with the broader trial population. The progression free survival and overall survival results for the subgroup and broader trial population are presented in Table 2 below.

Table 2: Results of PFS and OS from Trial MM-003

	Pomalidomide plus LDD (n = 302)	HDD (n=153)	Absolute difference	HR (95% CI)
September 2012 cut-off				
Median PFS (weeks) (95% CI)	15.7 (13.0, 20.1)	8.0 (7.0, 9.0)	7.7	0.45 (0.35, 0.59)
Median OS (weeks) (95% CI)	NE (48.1, NE)	34.0 (23.4, 39.9)	NE	0.53 (0.37, 0.74)
March 2013 cut-off				
Median PFS (weeks) (95% CI)	[redacted]	[redacted]	[redacted]	[redacted]
Median OS (weeks) (95% CI)	[redacted]	[redacted]	[redacted]	[redacted]
patients refractory/intolerant to bortezomib after a minimum 2 cycles (March 2013 cut-off)				
	n=45	**n=23**		
Median PFS (weeks) (95% CI)	[redacted]*	[redacted]	[redacted]	[redacted]
Median OS (weeks) (95% CI)	[redacted]	[redacted]	[redacted]	[redacted]

PFS = progression free survival; OS = overall survival; NE = not estimable; HR = hazard ratio; HDD = High dose dexamethasone; LDD = Low dose dexamethasone

*PFS time is stated to be consistent with overall ITT population, no value was provided.

Source: p6 of July 2014 PSD, Figure 1 & 2 p13 of the submission and p104 & 115 of CSR MM-003.

5.5 The submission claimed that there was no significant difference in terms of progression free survival or overall survival for patients who discontinued prior treatment with bortezomib due to intolerance or toxicity compared with the broader trial population (population 3(c) Figures 1 and 2). However, this analysis was based on small patient numbers (n=45) and while there was a statistically significant improvement in PFS for pomalidomide + LDD compared to HDD (HR [redacted], 95%CI: [redacted]), the difference in OS was not significant (HR [redacted], 95%CI [redacted]).

5.6 The submission claimed that because the average pomalidomide treatment duration for patients intolerant to lenalidomide on the sponsor's compassionate access program is comparable to that of the broader compassionate access program population, pomalidomide is an effective treatment option in the proposed patient group.

Comparative harms

5.7 At its March 2017 meeting, the PBAC noted the submission did not provide any safety data on the use of pomalidomide in patients with severe intolerance to lenalidomide. The PBAC considered there was a high risk that patients experiencing severe intolerance to lenalidomide would experience similar adverse effects on

treatment with pomalidomide, given lenalidomide and pomalidomide have similar mechanisms of action (paragraph 7.2, March 2017 PSD).

5.8 To address the PBAC's concern, the submission presented a comparison of the most frequently (≥ 10.0%) reported treatment-emergent adverse events in the treatment arms of trial MM-003 and trials MM-009/010 (lenalidomide key trials on which the current lenalidomide listings for the treatment of multiple myeloma are based). The submission argued that because the dose-limiting toxicities observed in the pomalidomide + LDD treatment arm of trial MM-003 differed from those observed in the lenalidomide + high dose dexamethasone treatment arms of trials MM-009/010, there appears to be no class effect between pomalidomide and lenalidomide with regards to safety. The submission did not present any data specifically relating to adverse events in patients with severe intolerance to lenalidomide who have been treated with pomalidomide.

Special pricing arrangement

5.9 The special pricing arrangement (SPA) outlined in the current deed for pomalidomide consists of a rebate of [redacted]% for all expenditure.

5.10 The submission proposed a further [redacted]% rebate for the proportion of patients in the proposed extended population, to offset uncertainty around the cost-effectiveness of pomalidomide in the proposed population.

5.11 At its March 2016 meeting, the PBAC considered that to enable use in a broader group, a price reduction, in the order of [redacted]% would be required to address the concern about cost-effectiveness. The PBAC did not specify whether the price reduction should apply to the total population or the proposed extended population only.

5.12 The submission proposed a single weighted average effective price ($[redacted]) calculated using the number of PBS/RPBS items processed from January 2016 to December 2016 and based on the assumption that the proposed extended population constitutes [redacted]% of the total population. The submission calculated a revised rebate of [redacted]%.

Economic analysis

5.13 The submission presented an economic analysis using the same economic model structure presented in the July 2014 and November 2014 submissions to estimate the cost-effectiveness of pomalidomide in the extended population. The economic analysis incorporated the [redacted]% rebate for the proposed extended population and a revised weighted total dose per pack of 80.7 (from 84.0) based on the number of PBS & RPBS items processed from January 2016 to December 2016.

5.14 A summary of the overall incremental costs and outcomes, both discounted and undiscounted, along with the ICERs is presented in Table 3 below.

Table 3: Results of the economic analysis

	Discounted	Undiscounted
Total costs	$[redacted]	$[redacted]
LYs	1.00	1.07
QALYs	0.52	0.56
ICER		
Cost/LY	$[redacted]	$[redacted]
Cost/QALY	$[redacted]	$[redacted]

Abbreviations: LY=life year; QALY=quality adjusted life year; ICER= incremental cost-effectiveness ratio.
Source: Table 11, p19 of the submission.

The redacted table shows ICERs in the range of $15,000/LY - $45,000/LY and $45,000/QALY - $75,000/QALY.

5.15 The Department has verified that no additional revisions to the economic model have been incorporated apart from the inputs mentioned above (paragraph 5.9) to result in the ICER of $45,000/QALY - %75,000/QALY gained.

5.16 The submission noted that the ICER of $45,000/QALY - %75,000/QALY gained for the proposed extended population is below the range of $45,000/QALY - %75,000/QALY per QALY gained previously considered to be cost-effective by the PBAC for this treatment.

Estimated PBS usage & financial implications

5.1 The March 2017 submission estimated the utilisation for the proposed patient population based on the estimated number of patients left untreated under the current pomalidomide restriction who are intolerant to bortezomib and/or lenalidomide. The PBAC considered that the utilisation estimates were uncertain (paragraph 7.1 March 2017 PSD).

5.2 The current submission assumed an additional [redacted]% of patients each year would access treatment with pomalidomide under the expanded PBS listing. A summary of the utilisation estimates presented in the March 2017 submission and current submission are presented in Table 4 below. The resubmission did not provide an explanation for the difference in estimated patient numbers between the two submissions.

5.3 The pre-PBAC Response (p3) clarified that the estimated patient numbers presented in the March 2017 submission were based on the difference between predicted and actual patient numbers accessing PBS subsidised pomalidomide, whereas the current predicted patient numbers were based on the number of patients accessing pomalidomide through the company's compassionate access program. In November 2017, the PBAC considered that this was likely an underestimate, as there are also compassionate access programs available for other medicines used in this treatment setting which means that there may be a larger pool of eligible patients than just those in the pomalidomide access program.

5.4 The sponsor also indicated that it would be willing to include this expenditure within the current risk sharing arrangement patient number cap for pomalidomide.

Table 4: Summary of utilisation estimates presented in the March 2017 and November 2017 submission

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Estimated additional patients treated						
March 2017						
November 2017[1]						
Total cost (PBS)						
March 2017						
November 2017						
Total cost (RPBS)						
March 2017						
November 2017						
Net cost to PBS						
March 2017						
November 2017						
Net cost to RPBS						
March 2017						
November 2017						
Net cost to PBS/RPBS						
March 2017						
November 2017						

[1]Estimated patient numbers based on 5% of patients accessing PBS subsidised pomalidomide between Jan 2017-Dec 2017 with assumption of 3% growth in each year

Source: Table 1 & 2 p2 March 2017 pre-PBAC response, Table 13 p21 of the submission.

5.5 The submission estimated an additional [redacted] patients under the proposed extended PBS listing in Year 1, increasing to [redacted] in Year 5. The submission estimated a net cost to the PBS/RPBS of less than $10 million in year 5 of listing with a total net cost to the PBS of less than $10 million over the first 5 years of listing.

5.6 The submission presented results of two sensitivity analyses of the financial estimates which increased the additional number of patient from [redacted]% to [redacted]% of the total PBS population and increased the estimated average number of cycles from [redacted] to [redacted]. When the estimated number additional patients was increased to [redacted]% of the total PBS population, the estimated total net cost to the PBS/RPBS increased to less than $10 million over the first 5 years of listing. When the estimated average number of cycles was increased to [redacted], the total net cost to the PBS/RPBS increased to less than $10 million over the first 5 years of listing.

5.7 The Department undertook a review of medicines to treat multiple myeloma including pomalidomide as requested by DUSC at its June 2017 meeting. An analysis of first initiators to pomalidomide within the first year of listing (August 2015 to July 2016) was performed to calculate the average number of prescriptions received within 12 months from the date of first initiation. The predicted versus actual use of pomalidomide is presented in Table 5 below.

Table 5: Predicted vs. actual utilisation of pomalidomide

	Year 1 (August 2015 – July 2016)	Year 2 (August 2016 – June 2017)[2]
Eligible PBS population[1]		
Predicted	[redacted]	[redacted]
Actual	1,378	1,607
Actual vs Predicted (n, %)	[redacted]	
Patients treated with pomalidomide		
Predicted	[redacted]	[redacted]
Actual	365	429
Actual vs Predicted (n, %)	[redacted]	
Total cost of pomalidomide[3]		
Predicted	[redacted]	[redacted]
Actual	$16,372,766	$22,596,805
Actual vs Predicted (n, %)	[redacted]	

Note: Figures are based on the date of supply.
[1]Patients who received treatment with bortezomib and lenalidomide (as per the restriction criteria for pomalidomide)
[2]Data presented for Year 2 is to date as complete data for a full year, to July 2017, was not available at time of analysis
[3]Costs are based on the pomalidomide published price excluding patient co-payments.
Source: p42 of September 2017 DUSC report on Analysis of medicines to treat multiple myeloma (available on PBS website).

5.8 The predicted versus actual analysis for pomalidomide found that the estimate for the eligible PBS population was reasonably consistent with the actual number of patients who have been previously treated with bortezomib and lenalidomide. The overall expenditure on pomalidomide was less than expected due to lower than anticipated uptake and a shorter time on therapy than expected. Based on the number of cycles patients received in trial MM-003 it was estimated that patients would receive an average of [redacted] cycles of pomalidomide per year. A mean of [redacted] prescriptions (each prescription representing a cycle) was actually received for this patient population over a 12 month period with the majority ([redacted]%) of patients receiving up to [redacted] prescriptions.

5.9 At its March 2017 meeting, the PBAC noted that utilisation for Year 1 of the deed was only 51.24% of Cap 1 ($10 - $20 million). The PBAC considered that these data may indicate that the mean treatment duration of pomalidomide is shorter than expected and may suggest that pomalidomide was less effective in practice than modelled as part of the original submission (paragraph 7.4 March 2017 PSD).

6 PBAC Outcome

6.1 The PBAC recommended extending the restriction for pomalidomide to include the treatment of patients contraindicated to, or who have experienced severe intolerance to lenalidomide and/or bortezomib for relapsed/refractory multiple myeloma. The PBAC made its recommendation on the basis that treatment could be considered cost-effective in this population with the proposed additional [redacted]% rebate for this patient population.

6.2 The PBAC recalled that it had previously accepted that pomalidomide treatment in

this patient population could be effective.

6.3 The PBAC noted that the submission did not present any data specifically relating to adverse events in patients with severe intolerance to lenalidomide who have been treated with pomalidomide. The PBAC recalled it previously considered there was a high risk that patients experiencing severe intolerance to lenalidomide would experience similar adverse effects on treatment with pomalidomide, given lenalidomide and pomalidomide have similar mechanisms of action. While the PBAC noted that the submission did not fully address its concerns, it considered that the appropriateness of treatment with pomalidomide could be left to the judgement of the clinician. The PBAC considered that the proposed [redacted]% rebate on the effective price for the extended population would render pomalidomide acceptably cost-effective in this setting noting that the resulting ICER of $45,000/QALY - $75,000/QALY is within the range previously considered to be cost-effective by the PBAC for this treatment.

6.4 The PBAC noted the discrepancy in the estimated number of additional patients between the March 2017 and current submission and considered this was indicative of the uncertainty in the size of the extended patient population. The PBAC also noted that there were a number of other medicines in this treatment setting for which compassionate access programs may also be available, which would be currently taking up some of the eligible patient pool. The PBAC therefore considered the utilisation estimates based on the assumption of an additional [redacted]% of patients accessing treatment with pomalidomide each year to be underestimated and that an estimate of [redacted]% of the current population using pomalidomide on the PBS was more reasonable. The PBAC therefore considered that the proposed [redacted]% rebate should apply to [redacted]%, rather than the proposed [redacted]%, of the current pomalidomide patient population to offset this uncertainty.

Outcome:

Recommended

7 Recommended listing

7.1 Extend existing listing as follows (the changes to the existing listing are shown in italics):

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
POMALIDOMIDE			
pomalidomide 3 mg capsule, 21	1	0	Pomalyst® Celgene Pty Ltd
pomalidomide 4 mg capsule, 21	1	0	

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Multiple myeloma
PBS Indication:	Multiple myeloma
Treatment phase:	Initial treatment
Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☐Authority Required - Telephone ☐Authority Required – Emergency ☐Authority Required - Electronic ☐Streamlined
Clinical criteria:	The treatment must be in combination with dexamethasone, AND Patient must have undergone or be ineligible for a primary stem cell transplant, AND Patient must have experienced treatment failure with bortezomib*, unless contraindicated or not tolerated according to the Therapeutic Goods Administration (TGA) approved Product Information;* AND Patient must have experienced treatment failure with lenalidomide*, unless contraindicated or not tolerated according to the TGA approved Product Information;* AND Patient must not be receiving concomitant PBS-subsidised thalidomide, lenalidomide or bortezomib.
Prescriber Instructions	Bortezomib treatment failure is the absence of achieving at least a partial response or as progressive disease during treatment or within 6 months of discontinuing treatment with bortezomib. Lenalidomide treatment failure is progressive disease during treatment or within 6 months of discontinuing treatment with lenalidomide. *If treatment with either bortezomib or lenalidomide is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication.* *If intolerance to either bortezomib or lenalidomide treatment develops during the relevant period of use which is of a severity to necessitate withdrawal of the treatment, the application must provide details of the nature and severity of this intolerance.* Progressive disease defined as per existing restriction (no changes proposed)

Administrative Advice	As per existing restriction (no changes proposed)
Cautions	As per existing restriction (no changes proposed)

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

The sponsor had no comment.