5.02 BELANTAMAB MAFODOTIN, Powder for injection 70 mg (50 mg per mL), Powder for injection 100 mg (50 mg per mL), Blenrep®, GLAXOSMITHKLINE AUSTRALIA PTY LTD

1 Purpose of submission

1.1 The Category 1 submission requested a Section 100 (Efficient Funding of Chemotherapy Program) Authority Required listing of belantamab mafodotin for use in combination with bortezomib and dexamethasone (BmBd) for initial and continuing treatment of relapsed and/or refractory multiple myeloma (RRMM) after one prior line of therapy.

1.2 Listing was requested on the basis of a cost-effectiveness analysis versus daratumumab in combination with bortezomib and dexamethasone (DBd).

Table 1: Key components of the clinical issue addressed in the submission

Component	Description
Population	Patients with relapsed or refractory multiple myeloma after one prior line of therapy (i.e., second line treatment).
Intervention	Belantamab in combination with bortezomib and dexamethasone (BmBd): - Belantamab mafodotin 2.5 mg/kg intravenously every 3 weeks until disease progression. - Bortezomib 1.3 mg/m^2 subcutaneously on Days 1, 4, 8 and 11 of each 21-day cycle for up to 8 cycles. - Dexamethasone 20 mg orally or intravenously on the day of and day after bortezomib treatment.
Comparator	Daratumumab in combination with bortezomib and dexamethasone (DBd): - Daratumumab 16 mg/kg intravenously once weekly in Cycles 1 to 3 (21-day cycles), every 3 weeks in Cycles 4 to 8 (21-day cycles), and every 4 weeks in Cycle 9+ (28-day cycles) until disease progression.[a] - Bortezomib 1.3 mg/m^2 subcutaneously on Days 1, 4, 8 and 11 of each 21-day cycle for up to 8 cycles. - Dexamethasone 20 mg orally or intravenously on the day of and day after bortezomib treatment.
Outcomes	Progression-free survival, overall survival, duration of response, MRD negativity, health-related quality of life, adverse events.
Clinical claim	In patients with relapsed or refractory multiple myeloma and one prior line of therapy, BmBd is superior in terms of efficacy, but inferior in terms of safety, compared to DBd.

Source: Table 1-1, p21 of the submission.
Abbreviations: BmBd, belantamab in combination with bortezomib and dexamethasone; DBd, daratumumab in combination with bortezomib and dexamethasone; MRD, minimal residual disease.
[a] Daratumumab is also available as a subcutaneous formulation. While the recommended treatment frequency is the same as the intravenous formulation, the recommended dose is 1,800 mg.

2 Background

Registration status

2.1 The submission was made under the TGA/PBAC Parallel Process. At the time of PBAC consideration, the TGA Delegate's Overview was available.

2.2 The proposed indication for belantamab mafodotin is for the treatment of adults with multiple myeloma:

- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy; and
- In combination with pomalidomide and dexamethasone in patients who have received at least one prior therapy including lenalidomide.

2.3 The first round TGA clinical evaluator considered that the benefit-risk balance for BmBd is favourable. The evaluator noted that the DREAMM-7 trial demonstrated improvements in progression-free survival and overall survival, but also that there was an increase in ocular impairment and no improvements in quality of life measures. The evaluator noted that the ocular adverse effects are significant and include 15.3% of participants treated with BmBd stopping reading due to eyesight issues and 17.8% stopping driving; but considered that this was counterbalanced by the improved survival. The evaluator stated that patients would need to be fully informed and accepting of the risks, including loss of the ability to read and/or drive.

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

3 Requested listing

MEDICINAL PRODUCT Form	Dispensed Price Max Amt	Max. Amount	№.of Rpts
BELANTAMAB MAFODOTIN	Public hospital $[redacted] published price $[redacted] effective price Private hospital $[redacted] published price $[redacted] effective price	300 mg	7
Available brands			
Blenrep (belantamab mafodotin 70 mg injection, 1 vial) Blenrep (belantamab mafodotin 100 mg injection, 1 vial)			
Category / Program: Section 100 – Efficient Funding of Chemotherapy			
Prescriber type: ☒Medical Practitioners			
Episodicity: Relapsed and/or refractory			
Condition: Multiple myeloma			
Indication: Relapsed and/or refractory multiple myeloma			
Treatment Phase: Initial treatment as second-line drug therapy for weeks 1 to 24			
Restriction type: ☒Authority Required (telephone/online PBS Authorities system)			
Clinical criteria:			
The condition must be confirmed by a histological diagnosis,			
AND			
Clinical criteria:			
The treatment must be in combination with bortezomib and dexamethasone,			
AND			
Clinical criteria:			
Patient must have progressive disease after only one prior therapy (i.e. use must be as second-line drug therapy; use as third-line drug therapy or beyond is not PBS-subsidised).			
Treatment Phase: Continuing treatment of second-line drug therapy from week 25 until disease progression			
Restriction type: ☒Authority Required (*STREAMLINED*)			
Clinical criteria:			
Patient must have previously received PBS-subsidised treatment with this drug for this condition,			
AND			
Clinical criteria:			
Patient must not have developed disease progression while receiving treatment with this drug for this condition.			
Treatment Phase: Grandfathered treatment - transitioning from non-PBS to PBS subsidised supply			
Restriction type: ☒Authority Required (STREAMLINED)			
Clinical criteria:			
Patient must have received non-PBS-subsidised treatment with this drug for this condition prior to *[insert listing date here]*,			
AND			
Clinical criteria:			
Patient must have met all initial treatment PBS-eligibility criteria applying to a non-grandfathered patient prior to having commenced treatment with this drug, which are: (i) the condition was confirmed by histological diagnosis, (ii) the treatment is/was being used as part of triple combination therapy with bortezomib and dexamethasone, and (iii) the condition progressed (see definition of progressive disease below) after one prior therapy, but not after more than two prior lines of therapies (i.e. this drug was commenced as second-line treatment),			
AND			

Clinical criteria:
Patient must not have developed disease progression while receiving treatment with this drug for this condition.
Prescribing instructions:
Progressive disease is defined as at least one of the following: (a) at least a 25% increase and an absolute increase of at least 5 g per L in serum M-protein (monoclonal protein); or (b) at least a 25% increase in 24-hour urinary light chain M-protein extraction, and an absolute increase of at least 200 mg per 24 hours; or (c) in oligo-secretory and non-secretory myeloma patients only, at least 50% increase in the difference between involved free light chain and uninvolved free light chain; or (d) at least a 25% relative increase and at least a 10% absolute increase in plasma cells in a bone marrow aspirate or on biopsy; or (e) an increase in the size or number of lytic bone lesions (not including compression fractures); or (f) at least a 25% increase in the size of an existing or the development of a new soft tissue plasmacytoma (determined by clinical examination or diagnostic imaging); or (g) development of hypercalcaemia (corrected serum calcium greater than 2.65 mmol per L not attributable to any other cause). Oligo-secretory and non-secretory patients are defined as having active disease with less than 10 g per L serum M protein. A line of therapy is defined as 1 or more cycles of a planned treatment program. This may consist of 1 or more planned cycles of single-agent therapy or combination therapy, as well as a sequence of treatments administered in a planned manner. A new line of therapy starts when a planned course of therapy is modified to include other treatment agents (alone or in combination) as a result of disease progression, relapse, or toxicity, with the exception to this being the need to attain a sufficient response for stem cell transplantation to proceed. A new line of therapy also starts when a planned period of observation off therapy is interrupted by a need for additional treatment for the disease.
Administrative advice:

3.1 The submission requested a special pricing arrangement, with an effective ex-manufacturer price (EMP) of $[redacted] per 70 mg vial and $[redacted] per 100 mg vial.

3.2 The submission proposed an Authority Required (Telephone/Online) Authority Required restriction for initial treatment, and an Authority Required (Streamlined) restriction for continuing treatment with belantamab mafodotin. The DUSC noted that this was inconsistent with the PBS listing for daratumumab, which includes an Authority Required (Telephone/Online) restriction for the initial and continuing treatment phases.

3.3 The proposed listing is narrower than the proposed TGA indication, which includes second or later line treatment. While the limitation to second line only treatment is consistent with the PBS restriction for DBd, the evaluation considered that it may not be reasonable to limit BmBd use to second line only, given that the DREAMM-7 trial included patients with one or more prior lines of therapy, and BmBd may be a useful treatment option for patients as a third or later line treatment, particularly prevalent patients currently receiving DBd in the second-line setting. Patients who receive BmBd in the second line setting will not be able to access PBS treatment with DBd. Additionally, the recommendation for DBd was made on the basis that daratumumab monotherapy would be made available on a compassionate basis to eligible multiple myeloma patients who have no other PBS-funded treatment options (paragraph 6.4,

daratumumab, Public Summary Document [PSD], July 2020 PBAC meeting). The Pre-Sub-Committee Response (PSCR) stated that the requested second line listing of BmBd ensured equitable access to superior therapies earlier in the treatment continuum. Given that BmBd demonstrated superiority over DBd, the PSCR stated that the approach avoids the inequitable scenario of displacement of BmBd to later lines. The ESC considered that restricting BmBd to the second line setting did not align with the clinical trial and did not align with how clinicians would like to use MM therapies. The Multiple Myeloma Stakeholder meeting (July 2025)[1] advised that treatment sequencing could be improved if determined by prior drug exposure rather than lines of therapy and that optimal care was an individualised approach. The ESC noted listing BmBd as a second line treatment would restrict patient access not only to BmBd, but to other therapies (i.e., daratumumab and other BCMA-directed therapies). The ESC considered that BmBd should be listed for the treatment of RRMM (consistent with the proposed TGA indication) to allow physician discretion as to when it is used. The pre-PBAC response maintained that a second-line listing was appropriate, stating that this was the setting where the (i) most patients would benefit with the greatest certainty of survival benefits and (ii) cost-effectiveness was the most certain. The pre-PBAC response stated that given the patient attrition with each line of therapy, it was imperative to prioritise access of BmBd for the majority of eligible patients before successive relapses diminish functional status.

3.4 It may be reasonable to include a caution or prescribing advice regarding the risk of ocular toxicity associated with belantamab mafodotin, the need for review by an eye care professional before each of the first 4 doses (and as clinically indicated thereafter), and the potential need for dose or administration frequency modifications to manage ocular toxicity. The PSCR stated that based on planned risk minimisation activities, information included in the belantamab mafodotin product information document, TGA monitoring and the extent of clinical expertise in Australia, additional advice or precautions regarding ocular events in the PBS restriction for belantamab mafodotin were not necessary. The ESC considered that it may be reasonable to include prescribing advice relating to ocular adverse events and the need for ocular assessments when treated with belantamab mafodotin.

3.5 The ESC noted that like elranatamab, which was recommended by the PBAC at the March 2025 meeting, and ciltacabtagene autoleucel (a CAR-T therapy), which was recommended by the MSAC at its April 2024 meeting, belantamab mafodotin is a B-cell maturation antigen (BCMA) directed therapy. The ESC considered that the initial

[1] Multiple Myeloma Stakeholder Meeting Outcome Statement. July 2025. Available at: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/pbac-stakeholder-meetings/Multiple-Myeloma-Meeting-Outcome-Statement.pdf

supply restriction should include the criterion "Patient must not have previously received treatment with another BCMA directed therapy for this condition".

3.6 The submission requested grandfathering provisions for patients treated with belantamab mafodotin under a patient access program that is anticipated to commence in [redacted]. The submission stated that eligibility for the program will be aligned with the proposed PBS restriction criteria for BmBd. The submission estimated that < 500 patients would be eligible for grandfathered treatment if belantamab mafodotin is recommended at the November 2025 PBAC meeting.

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

4 Population and disease

4.1 Multiple myeloma is a malignancy of B-cells characterised by clonal proliferation of plasma cells and abnormally high production of monoclonal immunoglobulin. Proliferation of plasma cells in the bone marrow is associated with impairment of haematopoiesis, while deposition of the monoclonal immunoglobulin protein in tissues leads to the development of organ dysfunction. A net increase in osteoclastic activity results in increased bone resorption and the development of lytic bone lesions.

4.2 Common symptoms associated with multiple myeloma include fatigue, weight loss, bone pain and bone fractures. Additionally, patients may develop symptoms related to hypercalcaemia and renal impairment and are at a higher risk of infections. An estimated 2,719 new cases of multiple myeloma were forecast in Australia in 2024 (1,637 males and 1,082 females; AIHW, 2024). The reported median (mean) age of patients diagnosed with multiple myeloma in Australia in 2020 was 72.4 (71.5) years.

4.3 Multiple myeloma is generally considered to be an incurable disease. While the survival rates for patients with multiple myeloma have improved with the availability of novel therapeutic agents, almost all patients experience disease progression. Treatment choice for patients with disease relapse or who are refractory to treatment is individualised, with consideration of prior therapy and associated toxicity, the duration of response to prior therapy, the rate of disease progression, and their current physical status.

4.4 Belantamab mafodotin is a humanised IgG1 kappa monoclonal antibody targeting B-cell maturation antigen (BCMA), which is conjugated to a cytotoxic agent (maleimidocaproyl monomethyl auristatin F; mcMMAF). BCMA is selectively expressed on malignant plasma cells.

4.5 The submission positioned BmBd as an alternative to second line treatment with DBd. Other PBS listed second line treatment options in the proposed algorithm include lenalidomide in combination with carfilzomib and dexamethasone (LCd), pomalidomide in combination with bortezomib and dexamethasone (PBd), selinexor in combination with bortezomib and dexamethasone (SBd), carfilzomib in combination with dexamethasone (Cd), pomalidomide in combination with dexamethasone (Pd), selinexor in combination with dexamethasone (Sd),

lenalidomide in combination with dexamethasone (Ld), and bortezomib in combination with dexamethasone (Bd).

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

5 Comparator

5.1 The submission nominated DBd as the main comparator. The main arguments provided in support of this nomination were:

- DBd represents the current Australian standard of care in the second line treatment setting.
- The PBAC previously considered that the PBS listing of DBd for use in the second line setting only would likely displace the other RRMM treatments to the third and later line settings (paragraph 7.4, ixazomib, PSD, March 2022 PBAC meeting). Therefore, DBd is the treatment most likely to be replaced if belantamab mafodotin is listed on the PBS in the second line treatment setting.

5.2 The evaluators considered that, for the PBS population proposed in the submission, DBd was an appropriate comparator. However, noting the PBS listing of DLd, the evaluators considered that DBd would not be an appropriate comparator for patients who have previously received DLd. The PSCR stated that the recommendation of DLd in the first line setting was anticipated to have a limited impact on the utilisation of DBd in the second line setting over the medium term. The ESC agreed, and considered that for the proposed PBS population, DBd was the appropriate comparator. However, as the ESC considered that BmBd should be listed for RRMM, rather than restricted to the second-line setting, the ESC considered that the most appropriate comparator would consist of a basket of treatments that included DBd.

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

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinician discussed the incidence of MM in the Australian setting and described the current treatment options and survival rates. The clinician described how BmBd would be used in clinical practice and highlighted the need for new and effective treatments in the second-line setting, particularly in patients who have previously been exposed to lenalidomide. The clinician discussed the results of the DREAMM-7 trial, highlighting the progression free and overall survival gains observed compared to DBd. Safety was also discussed with the clinician stating that BmBd has a low incidence of blood or haematological adverse and infection events. The ocular toxicity associated with belantamab mafodotin was acknowledged, and was described as predictable, manageable and usually reversible. The clinician stated that a baseline eye assessment by an ophthalmologist or optometrist is required before commencement of treatment, with review before

Cycles 2 to 4. Further review after Cycle 4 is only required if ocular issues arise. The PBAC considered that the hearing was informative and provided a clinical perspective.

Consumer inputs

6.2 The PBAC noted and welcomed the input from individuals (19), health care professionals (2) and organisations (4) via the Office of Health Technology Assessment Consultation Hub. The inputs from individuals described the diversity of responses to current treatments in the RRMM setting, as well as the high likelihood of relapse, and highlighted the need for additional lines of treatment to increase survival time. Individuals who have received BmBd described its advantages, including less frequent administration and reduced doses of bortezomib and dexamethasone compared to current treatment regimens, which improved quality of life.

6.3 The health professionals noted the number of treatment options available for multiple myeloma and the need for flexibility in when these medications are used. It was noted that the proposed restriction of BmBd to the second-line setting would force clinicians to choose between BmBd and DBd. The positive results of the DREAMM-7 trial were highlighted, and the health professionals also stated that very few patients stopped treatment because of ocular toxicity.

6.4 The PBAC noted the advice received from the Australasian Leukaemia and Lymphoma Group (ALLG) which supported the submission. The ALLG noted the positive results of the DREAMM-7 trial and stated that the choice of treatment should consider patient factors (age, fragility), disease factors (tempo of relapse, risk group stratification), prior treatment-related factors (responsiveness and side effects to prior treatments) and patient preferences.

6.5 Advice was also received from patient support organisations, Rare Cancers Australia, the Leukaemia Foundation and Myeloma Australia. These organisations strongly supported the PBS listing of belantamab mafodotin, highlighting the results of the DREAMM-7 trial. The groups highlighted the financial burden of accessing drugs that are not listed on the PBS and the equity issues this causes. Myeloma Australia stated that restricting BmBd to the second-line setting conflicted with the discussions at the Multiple Myeloma Stakeholder Group meeting in July 2025 and would limit patient access to beneficial treatments.

Clinical trials

6.6 The submission was based on one head-to-head randomised trial comparing BmBd to DBd in patients who had RRMM after at least one line of therapy (DREAMM-7).

6.7 The submission also identified a head-to-head randomised trial (DREAMM-8) comparing BmPd to pomalidomide in combination with bortezomib and dexamethasone (PBd) in lenalidomide-exposed patients who had RRMM after at least one line of therapy (N=302). The submission stated that listing of BmPd was not requested on the basis that the overall survival data for the DREAMM-8 trial are immature.

6.8 Details of the included trial presented in the submission are provided in Table 2.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
DREAMM-7 (NCT04246047)	A multicenter, open-label, randomised phase III study to evaluate the efficacy and safety of the combination of belantamab mafodotin, bortezomib, and dexamethasone (B-Vd) compared with the combination of daratumumab, bortezomib and dexamethasone (D-Vd) in participants with RRMM (DREAMM-7). Hungria V, Robak P, Hus M, *et al*. Belantamab mafodotin, bortezomib, and dexamethasone for multiple myeloma.	Clinical study report, February 2024, with June 2024 errata Clinical study report, January 2025 *NEJM* 2024; 391(5):393-407.

Source: Table 2-3, p54 of the submission; Attachment 2.1, 2.2 of Section 2 in the submission.
Note: Citations relating to conference abstracts omitted.

6.9 The key features of the DREAMM-7 trial are summarised in Table 3.

Table 3: Key features of the included evidence

Trial	N	Design/duration	Risk of bias	Patient population	Outcomes	Use in modelled evaluation
BmBd versus DBd						
DREAMM-7	494[a]	Phase 3, multicentre, open label, randomised controlled trial. Median follow-up of up to 39.4 months	Unclear	Adults with multiple myeloma who had received ≥1 line of therapy and had experienced disease progression during or after the most recent therapy	PFS, OS, DOR, MDR negativity rate, HRQoL, adverse events	PFS, OS, adverse events, EQ-5D-3L, use of subsequent treatments

Source: Section 2.3, Section 2.4, pp56-77 of the submission
Abbreviations: BmBd, belantamab mafodotin in combination with bortezomib and dexamethasone; DOR, duration of response; DBd, daratumumab in combination with bortezomib and dexamethasone; HRQoL, health-related quality of life; MDR, minimal residual disease negativity rate; OS, overall survival; PFS, progression-free survival.
[a] Two subjects in the ITT analysis of the DREAMM-7 trial were randomised, not treated, re-screened and re-randomised and are counted as 4 unique subjects in the analyses.

6.10 The DREAMM-7 trial is an ongoing trial with continuing follow-up of study participants until the accrual of 355 deaths or 5 years from the first visit of the last patient, whichever occurs first. Results in the submission are based on the first interim analysis (October 2023 data cut; median follow-up 28.2 months) and second interim analysis (October 2024 data cut; median follow-up 39.4 months).

6.11 The open-label trial design has the potential to introduce bias as knowledge of treatment assignment may affect disease management decisions and assessment of outcomes that are not centrally assessed. The risk of bias was minimised as disease response and disease progression were determined by a blinded independent review committee (IRC) as per the International Myeloma Working Group (IMWG) 2016 criteria.

6.12 Based on data from AIHW, patients in the PBS population accessing second line treatment are likely to be older than patients included in the DREAMM-7 trial (AIHW mean age at diagnosis of 71.5 years versus mean age of 64.0 years at baseline in the DREAMM-7 trial). Additionally, there were other differences affecting the applicability of the results, including the number of prior lines of therapy (one prior line of therapy for the proposed PBS population versus one or more prior lines in the trial), the performance status of patients (reflected by lower rates of ASCT in the proposed PBS population compared to the trial), a higher burden of comorbidities in the PBS

population, and potential differences in prior and subsequent multiple myeloma therapies. These factors may impact the effectiveness and safety of belantamab mafodotin in clinical practice.

6.13 The submission presented results of subgroup analyses for patients from the DREAMM-7 trial with exposure to lenalidomide in any prior line of therapy, which formed the basis of the modelled economic evaluation and financial estimates. The submission claimed that the lenalidomide-exposed subgroup was more applicable to the proposed PBS population than the ITT population, given increasing use of lenalidomide in the first line treatment setting in Australian clinical practice. However, the ESC noted that both the lenalidomide-exposed subgroup and the ITT population included large proportions of patients with more than one prior line of therapy (49% in the ITT population; 67% in the lenalidomide-exposed population[2]), which differs from the proposed PBS population which limits treatment to patients with only one prior line of therapy. While only 34% of the overall population of patients with 1 prior line of treatment reported previous use of lenalidomide, most patients received treatment with an immunomodulatory agent (lenalidomide: 34%; thalidomide 45%; pomalidomide: <1%)[2].

6.14 The submission claimed that the subgroup of lenalidomide-exposed patients with only 1 prior line of therapy is more closely aligned to the proposed circumstances of use for belantamab mafodotin. However, analyses based on this subgroup were limited by the small sample size (N=84), and the results may not be applicable to the proposed population, as the proposed restriction is not limited to patients with prior lenalidomide therapy. Detailed results for this subgroup were not presented in the submission.

6.15 The ESC agreed with the submission that the majority of first-line therapy in Australia includes lenalidomide but noted that the lenalidomide-exposed subgroup did not reflect the proposed second line population in terms of prior lines of therapy. The ESC considered that the use of the lenalidomide-exposed subgroup was poorly supported and, overall, the ITT population of the trial would provide the most robust data. The ESC considered that the lenalidomide-exposed subgroup would be useful as supporting evidence for the broader RRMM population.

---

[2] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

Comparative effectiveness

6.16 The primary outcome of the DREAMM-7 trial was progression-free survival, defined as the time from randomisation until the earliest date of confirmed disease progression (determined by the blinded IRC as per IMWG criteria), or death due to any cause.

6.17 Table 4, Figure 1 and Figure 2 below present the results of IRC-assessed progression-free survival in the ITT population and lenalidomide-exposed subgroup of the DREAMM-7 trial.

Table 4: Results for IRC-assessed progression-free survival in the DREAMM-7 trial (ITT population and lenalidomide-exposed subgroup)

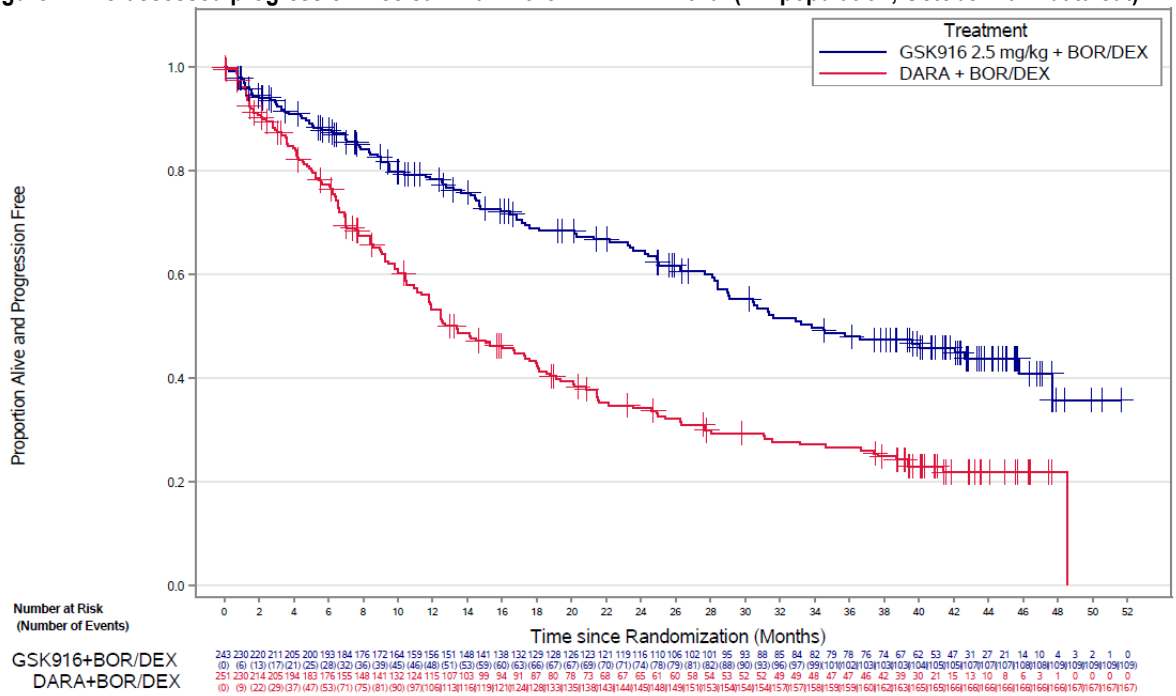
Outcome	ITT population		Lenalidomide-exposed subgroup[3]	
	BmBd (N=243)	DBd (N=251)	BmBd (N=127)	DBd (N=130)
IRC-assessed progression-free survival (October 2023 data cut)				
Median duration of follow-up, months (IQR)	29.2 (21.7, 32.5)	27.6 (12.3, 30.4)	Not reported	Not reported
Participants with event, n (%) - Disease progression, n (%) - Death, n (%)	91 (37) 67 (28) 24 (10)	158 (63) 139 (55) 19 (8)	44 (35) 39 (31) 5 (4)	88 (68) 79 (61) 9 (7)
Censored, n (%) - Follow-up ended, n (%) - Follow-up ongoing, n (%)	152 (62) 44 (18) 108 (44)	93 (37) 41 (16) 52 (21)	83 (65) 28 (22) 55 (43)	42 (32) 27 (21) 15 (12)
Median PFS, months (95% CI)	36.6 (28.4, NE)	13.4 (11.1, 17.5)	NE (23.5, NE)	10.4 (7.0, 12.7)
Hazard ratio (95% CI)	**0.41 (0.31, 0.53)**		0.29 (0.19, 0.42)	
IRC-assessed progression-free survival (October 2024 data cut)[3]				
Median duration of follow-up, months (IQR)	40.2 (21.7,43.6)	38.2 (12.3, 41.9)	39.9 (18.3, 43.6)	24.2 (8.4, 40.3)
Participants with event, n (%) - Disease progression, n (%) - Death, n (%)	109 (45) 81 (33) 28 (12)	167 (67) 147 (59) 20 (8)	55 (43) 49 (39) 6 (5)	88 (68) 79 (61) 9 (7)
Censored, n (%) - Follow-up ended, n (%) - Follow-up ongoing	124 (55) 54 (22) 80 (33)	84 (33) 45 (18) 39 (16)	72 (57) 34 (27) 38 (30)	42 (32) 30 (23) 12 (9)
Median PFS, months (95% CI)	33.8 (28.4, 45.8)	13.4 (11.1, 17.5)	34.5 (23.5, NE)	10.4 (7.0, 12.7)
Hazard ratio (95% CI)	0.46 (0.35, 0.59) [a]		0.34 (0.24, 0.48)	
Progression-free survival rate (95% CI) - 6 months - 12 months - 18 months - 24 months - 36 months	 0.88 (0.83, 0.91) 0.78 (0.72, 0.83) 0.69 (0.62, 0.75) 0.65 (0.58, 0.71) Not reported	 0.77 (0.71, 0.82) 0.53 (0.47, 0.60) 0.43 (0.36, 0.49) 0.34 (0.28, 0.41) Not reported	 0.90 (0.82, 0.94) 0.77 (0.68, 0.84) 0.67 (0.57, 0.75) 0.60 (0.49, 0.69) 0.48 (0.37,0.57)	 0.70 (0.61, 0.77) 0.43 (0.33, 0.52) 0.30 (0.22, 0.39) 0.23 (0.15, 0.31) 0.18 (0.11, 0.26)

Source: Table 2-9, p66; Table 2-22, pp73-74; Table 2-43, p99; Table 2-48, p103 of the submission; Table 1.0025, pp353-354 and Table 2.0007, pp435-436 of the DREAMM-7 IA1 CSR; Table 2.1100206, pp1-2 of DREAMM-7 IA1 Supplementary data; Table 2.0007, pp1-2; Table 2.1100206, pp1-2 of DREAMM-7 IA2 supplementary data.

[3] *Note that the results presented in Table 4 for the lenalidomide-exposed subgroup are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These*

Abbreviations: BmBd, belantamab mafodotin in combination with bortezomib and dexamethasone; CI, confidence interval; DBd, daratumumab in combination with bortezomib and dexamethasone; IA1, interim analysis 2 (October 2023 data cut); IA2, interim analysis 2 (October 2024 data cut); IRC, independent review committee; NE, not estimable; PFS, progression-free survival.
Bolded results were statistically significant.
[a] Results are descriptive and were not formally re-tested at the October 2024 data cut, given statistical significance for PFS was achieved based on the October 2023 data cut.

Figure 1: IRC-assessed progression-free survival in the DREAMM-7 trial (ITT population, October 2024 data cut)[4]

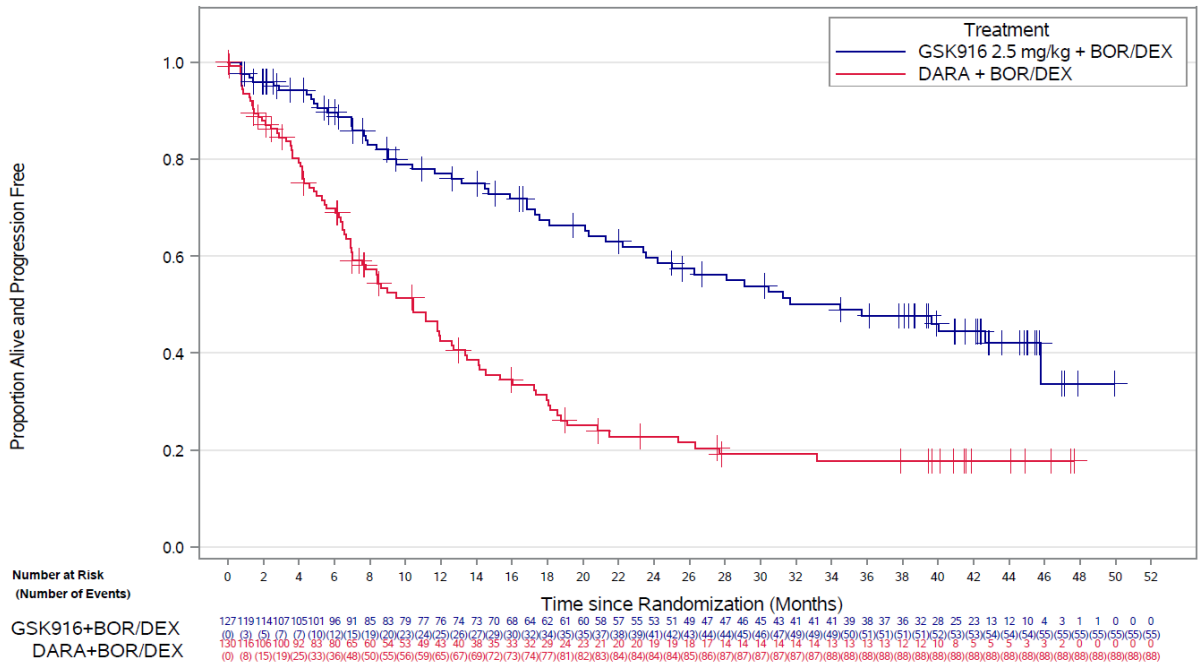


Source: Figure 2-6, p74 of the submission; Figure 2.0037, p1 of DREAMM-7 IA2 Supplementary data.
Abbreviations: BOR, bortezomib; DARA, daratumumab; DEX, dexamethasone; GSK916, belantamab mafodotin; IA2, interim analysis 2 (October 2024 data cut); IRC, independent review committee.

analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

[4] *Note that the results presented in Figure 1 is derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. PFS was not formally re-tested at IA2 given statistical significance was achieved at IA1 in DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

Figure 2: [redacted]RC-assessed progression-free survival in the DREAMM-7 trial (lenalidomide-exposed subgroup, October 2024 data cut)[5]



Source: Figure 2-16, p104 of the submission; Figure 2.1100106 of DREAMM-7 IA2 Supplementary data.
Abbreviations: BOR, bortezomib; DARA, daratumumab; DEX, dexamethasone; GSK916, belantamab mafodotin; IA2, interim analysis 2 (October 2024 data cut); IRC, independent review committee.

6.18 Based on the ITT analysis, treatment with BmBd was associated with a statistically significant improvement in progression-free survival compared to DBd (HR = 0.41; 95% CI: 0.31, 0.53) at the October 2023 data cut; with results based on the October 2024 data cut also favouring BmBd.

6.19 The lenalidomide-exposed subgroup was associated with a greater reduction in the risk of disease progression or death for BmBd versus DBd compared to the ITT population, based on the October 2024 data cut (HRs = 0.34 [95% CI: 0.24, 0.48] and 0.46 [95% CI: 0.35, 0.59], respectively).[6]

[5] *Note that the results presented in Figure 2 are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

[6] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

6.20 The trial included pre-specified subgroup analyses for progression-free survival. Based on the October 2024 data cut, most subgroups demonstrated a consistent trend in progression-free survival, favouring patients in the BmBd arm compared to the DBd arm (HR <1). While patients aged 75 years and older appeared to obtain a smaller benefit with BmBd compared to younger patients, the results should be interpreted with caution due to the small number of patients in the subgroup. No treatment effect interaction testing was performed.

6.21 Table 5, Figure 3 and Figure 4 below present the results of the key secondary outcome of overall survival in the ITT population and lenalidomide-exposed subgroup of the DREAMM-7 trial.

Table 5: Results for overall survival in the DREAMM-7 trial (ITT population and lenalidomide-exposed subgroup)

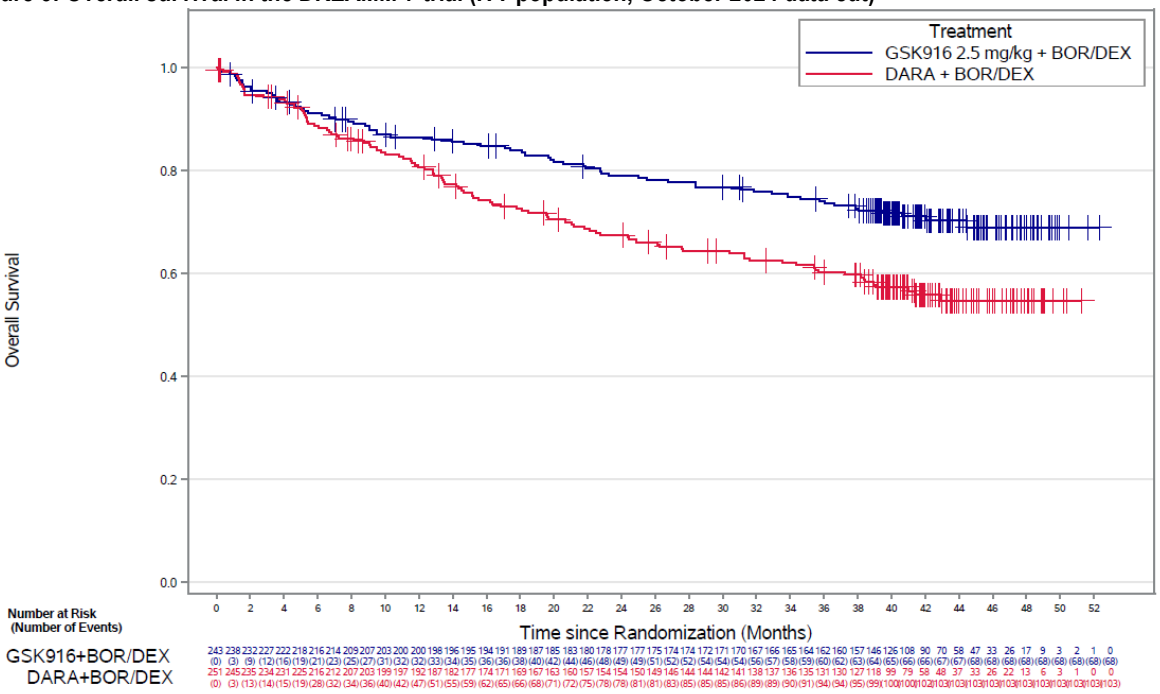
Outcome	ITT population		Lenalidomide-exposed subgroup[7]	
	BmBd (N=243)	DBd (N=251)	BmBd (N=127)	DBd (N=130)
Overall survival (October 2023 data cut)				
Median duration of follow-up, months (IQR)	29.2 (21.7, 32.5)	27.6 (12.3, 30.4)	Not reported	Not reported
Deaths, n (%)	54 (22)	87 (35)	31 (24)	60 (46)
Censored - Follow-up ended - Follow-up ongoing	189 (78) 20 (8) 169 (70)	164 (65) 28 (11) 136 (54)	96 (76) 9 (7) 87 (69)	70 (54) 18 (14) 52 (40)
Median OS, months (95% CI)	NE (NE, NE)	NE (NE, NE)	NE (NE, NE)	31.3 (21.1, NE)
Hazard ratio (95% CI)	0.57 (0.40, 0.80)[a]		0.43 (0.28, 0.67)	
Overall survival (October 2024 data cut)				
Median duration of follow-up, months (IQR)	40.2 (21.7,43.6)	38.2 (12.3, 41.9)	39.9 (18.3, 43.6)	24.2 (8.4, 40.3)
Deaths, n (%)	68 (28)	103 (41)	37 (29)	70 (54)
Censored, n (%) - Follow-up ended - Follow-up ongoing	175 (72) 26 (11) 149 (61)	148 (59) 33 (13) 115 (46)	*90* (71) 11 (9) 79 (62)	60 (46) 22 (17) 38 (29)
Median OS, months (95% CI)	NE (NE, NE)	NE (41.0, NE)	NE (NE, NE)	31.3 (21.1, 42.9)
Hazard ratio (95% CI)	**0.58 (0.43, 0.79)**		0.42 (0.28, 0.63)	
Overall survival rate (95% CI) - 6 months - 12 months - 18 months - 24 months - 36 months	 0.91 (0.87, 0.94) 0.87 (0.81, 0.90) 0.84 (0.79, 0.88) 0.79 (0.73, 0.84) 0.74 (0.68, 0.79)	 0.89 (0.84, 0.92) 0.81 (0.75, 0.85) 0.73 (0.67, 0.78) 0.67 (0.61, 0.73) 0.60 (0.54, 0.66)	 0.94 (0.88, 0.97) 0.87 (0.80, 0.92) 0.84 (0.76, 0.89) 0.78 (0.69, 0.84) 0.73 (0.64, 0.80)	 0.86 (0.79, 0.91) 0.74 (0.65, 0.81) 0.61 (0.52, 0.69) 0.58 (0.48, 0.66) 0.46 (0.36, 0.54)

Source: Table 2-9, p66; Table 2-23, p76; Table 2-50, p105 of the submission; Table 2.0024, pp461-462; Table 2.1100809, pp1-2 of the DREAMM-7 IA1 CSR; Table 2.0024, pp1-2, Table 2.1100809, pp1-2 of DREAMM-7 IA2 supplementary data.

[7] *Note that the results presented in Table 5 for the lenalidomide-exposed subgroup are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

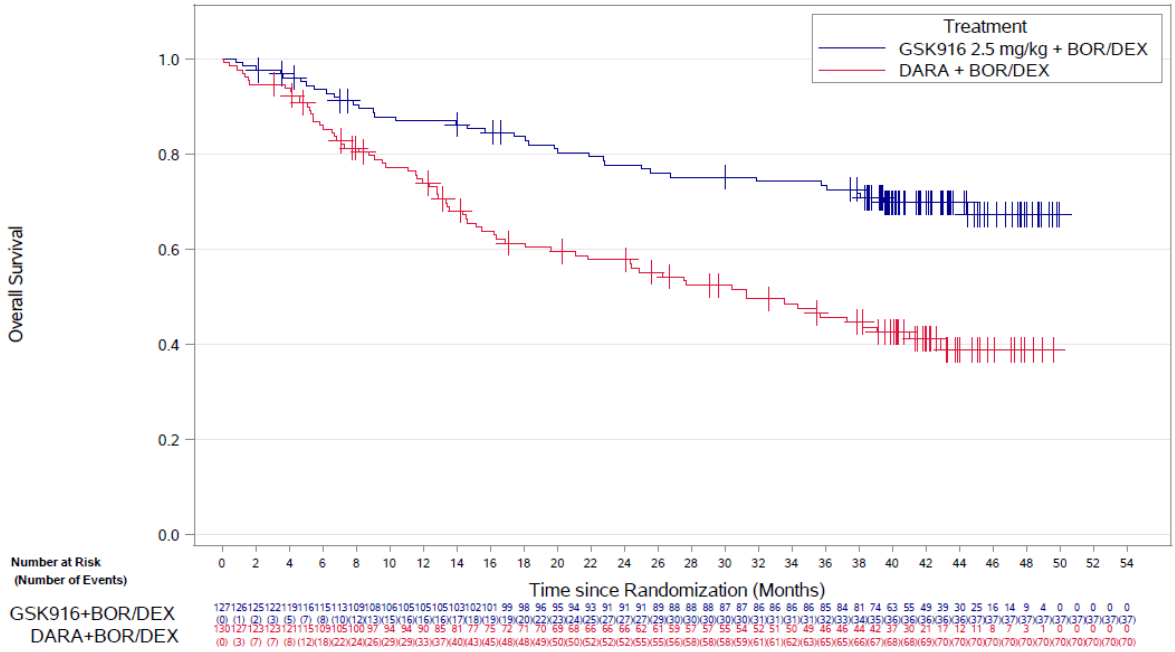
Abbreviations: BmBd, belantamab mafodotin in combination with bortezomib and dexamethasone; CI, confidence interval; CSR, clinical study report; DBd, daratumumab in combination with bortezomib and dexamethasone; IA1, interim analysis 1 (October 2023 data cut); IA2, interim analysis 2 (October 2024 data cut); IQR, interquartile range; NE, not estimable; OS, overall survival.
Bolded results were statistically significant.
[a] OS was formally tested at the October 2023 data cut as per the Multiple Testing Strategy; however, did not meet statistical significance at this time despite showing a strong and meaningful clinical benefit (nominal p-value of 0.00049). Statistical significance was subsequently reached at IA2.

Figure 3: Overall survival in the DREAMM-7 trial (ITT population, October 2024 data cut)



Source: Figure 2-8, p76 of the submission; Figure 2.0038, p1 DREAMM-7 IA2 supplementary data.
Abbreviations: BOR, bortezomib; DARA, daratumumab; DEX, dexamethasone; GSK916, belantamab mafodotin; IA2, interim analysis 2 (October 2024 data cut).

Figure 4: Overall survival in the DREAMM-7 trial (lenalidomide-exposed subgroup, October 2024 data cut)[8]



Source: Figure 2-17, p106 of the submission; Figure 2.1100206, p1 of DREAMM-7 IA2 Supplementary data.
Abbreviations: BOR, Bortezomib; DARA, Daratumumab; DEX, Dexamethasone; GSK916, Belantamab mafodotin; IA2, interim analysis 2 (October 2024 data cut); OS, overall survival.

6.22 Based on the ITT analysis, treatment with BmBd was associated with a statistically significant improvement in overall survival compared to DBd at the October 2024 data cut (HR = 0.58; 95% CI: 0.43, 0.79).

6.23 The lenalidomide-exposed subgroup was associated with a greater reduction in the risk of death for BmBd versus DBd compared to the ITT analysis, based on the October 2024 data cut (HRs = 0.42 [95% CI: 0.28, 0.63][9] and 0.58 [95% CI: 0.43, 0.79], respectively).

6.24 Pre-specified subgroup analyses of overall survival based on the October 2024 data cut showed most subgroups demonstrated a consistent trend in overall survival,

[8] *Note that the results presented in Figure 4 are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

[9] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

favouring patients in the BmBd arm compared to the DBd arm (HR<1). However, there were subgroups where the hazard ratio was ≥1 including patients aged 75 years and older, patients who had relapsed at least 18 months after their most recent therapy, and those with extramedullary disease at baseline. No treatment effect interaction testing was performed. A numerically greater benefit in overall survival was observed for patients who had received more than one prior line of therapy compared to those with only one prior line of therapy; as well as those with prior lenalidomide exposure at baseline compared to those without prior lenalidomide.

6.25 The submission presented results from other key secondary outcomes of the DREAMM-7 trial, showing longer duration of response, and higher MRD negativity (based on a sensitivity of 10^{-5}) for the BmBd arm compared to the DBd arm at both data cuts.

6.26 The sponsor provided health utility values from the DREAMM-7 trial based on the EQ-5D-3L, indexed using the Australian value set (Viney 2011). Based on the October 2023 data cut, trial participants had a mean utility of 0.77 at baseline, and mean utility scores remained broadly similar between the BmBd and DBd arms across study visits, with a gradual increase in utilities from Week 31. Utilities at the end-of-treatment visit showed a slight decrease relative to baseline across the 2 treatment arms.[10]

6.27 The submission presented patient-reported outcomes based on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-30 (EORTC QLQ-C30) based on October 2023 data cut. EORTC QLQ-C30 global health status scores remained broadly similar between the BmBd and DBd arms across study visits, with participants in both treatment arms showing a small mean deterioration in Global Health Status between Week 4 and Week 40, before stabilising. A similar pattern was observed for the physical functioning, role functioning and fatigue domains of the EORTC QOL-C30.

6.28 Patient-reported outcomes related to visual function, measured by the Ocular Surface Disease Index (OSDI) were presented in the DREAMM-7 study report (October 2023 data cut). In the BmBd arm, deterioration of vision-related functioning scores became notable starting at Week 7; however, a small percentage of participants (20%) reported meaningful deterioration in vision-related functioning as early as Week 4. Levels of deterioration in vision-related functioning appeared to peak between Weeks 10 and 13 (74% and 70% of participants with meaningful deterioration) then slightly

[10] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

decrease and remain stable. Deteriorated scores from baseline persisted through to Week 130. A similar pattern was observed for OSDI total score by study visit.[11]

Comparative harms

6.29 Table 6 presents the safety outcomes in DREAMM-7 trial based on October 2024 data cut. Adverse event data were based on patient incidence only, which does not capture the occurrence of multiple events of the same type in individual patients.

Table 6: Summary of adverse events in the DREAMM-7 trial (safety population; October 2024 data cut)

	BmBd (N=242)	DBd (N=246)
Median duration of follow-up, months (95% CI)	40.2 (21.7, 43.6)	38.2 (12.3, 41.9)
Any adverse event, n (%) - Treatment related	242 (100) 242 (100)	246 (100) 234 (95)
Serious adverse event, n (%) - Treatment related	129 (53) 50 (21)	94 (38) 32 (13)
Grade 3/4 adverse event, n (%) - Treatment related	230 (95) 222 (92)	191 (78) 166 (67)
Fatal serious adverse event - Treatment related	26 (11) 7 (3)	20 (8) 2 (<1%)
AEs leading to treatment discontinuation, n (%) - Treatment related	77 (32) 67 (28)	47 (19) 36 (15)
AEs leading to dose reduction, n (%)	181 (75)	146 (59)
AEs leading to dose interruption/delay, n (%)	229 (95)	186 (76)

Source: Table 2-27, p82; Table 2-28, p83; Table 2-29, p84 of the submission; Table 3.0003, pp1-31; Table 3.1016, pp1-2; Table 3.0108100, pp1-2; Table 3.0046, pp1-2; Table 3.0049, pp1-4; Table 3.0048, p1; Table 3.0050, pp1-10 of the DREAMM-7 IA2 Supplementary data.
Abbreviations: AE, adverse event; BmBd, belantamab mafodotin in combination with bortezomib and dexamethasone; CI, confidence interval; DBd, daratumumab in combination with bortezomib and dexamethasone; IA2, interim analysis 2 (October 2024 data cut).

6.30 All patients in both treatment arms had at least one treatment-related adverse event. Patients in the BmBd arm more frequently experienced adverse events compared to those in the DBd arm. Adverse events reported in at least 20% of patients in either treatment arm and in at least 10% more patients in the BmBd arm than in the DBd arm were thrombocytopenia, blurred vision, dry eye, photophobia, eye irritation, foreign body sensation in eyes, eye pain, cataract and pneumonia.

6.31 More patients in the BmBd arm experienced a grade ≥3 adverse event compared to those in the DBd arm. The most commonly reported grade ≥3 adverse events in the BmBd arm were thrombocytopenia (56%), blurred vision (24%), and decreased platelet count (18%); and in the DBd arm were thrombocytopenia (35%), decreased platelet count (11%) and anaemia (10%).

[11] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

6.32 Fatal serious adverse events occurred in 26 (11%) patients in the BmBd arm and 20 (8%) patients in the DBd arm. Among these, 9 deaths (7 in the BmBd arm and 2 in the DBd arm) were considered treatment-related, with the major causes being pneumonia, COVID-19, COVID-19 pneumonia and sepsis.

6.33 Patients in the BmBd arm more frequently experienced treatment discontinuation (32% versus 19%), dose reduction (75% versus 59%), and treatment interruption (95% versus 76%) compared to the DBd arm. Thrombocytopenia and blurred vision were the main adverse events leading to dose reduction, interruption or delay in the BmBd arm.

6.34 Table 7 summarises the ocular adverse events of special interest with an incidence of at least 10% in the DREAMM-7 trial, based on the October 2024 data cut.

Table 7: Summary of adverse events (CTCAE grade) of special interest in the DREAMM-7 trial (safety population; October 2024 data cut)

Ocular AE category, n (%)	BmBd (N=242)		DBd (N=246)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any ocular adverse event	194 (80)	85 (35)	76 (31)	8 (3)
Vision blurred	165 (68)	58 (24)	27 (11)	3 (1)
Dry eye	129 (53)	17 (7)	19 (8)	0 (0)
Photophobia	120 (50)	7 (3)	6 (2)	0 (0)
Foreign body sensation in eye	111 (46)	9 (4)	12 (5)	0 (0)
Eye irritation	110 (45)	12 (5)	14 (6)	0 (0)
Eye pain	81 (33)	2 (<1)	9 (4)	1 (<1)
Visual impairment	26 (11)	12 (5)	4 (2)	*1 (<1)*
Lacrimation increased	24 (10)	2 (<1)	8 (3)	0 (0)

Source: Table 2-35, p85 of the submission, Table 3.0034 pp1-5 DREAMM-7 IA2 Supplementary data.
Abbreviations: AE, adverse event; BmBd, belantamab mafodotin in combination with bortezomib and dexamethasone; CTCAE, Common Terminology Criteria for Adverse Events; DBd, daratumumab in combination with bortezomib and dexamethasone; IA2, interim analysis 2 (October 2024 data cut).

6.35 More patients in the BmBd arm experienced ocular adverse events of special interest in the BmBd arm compared with the DBd arm (80% versus 31%). The most commonly reported ocular adverse events of special interest in the BmBd arm were blurred vision, dry eye, photophobia, foreign body sensation in the eye and eye irritation.

6.36 The DREAMM-7 study report (October 2023 data cut) also reported that, of the participants who were able to read with little or no difficulty at baseline, more participants in the BmBd arm than in the DBd arm stopped reading due to eyesight issues at some point on treatment (27% versus 2%). Of the participants who were able to drive with little or no difficulty at baseline, more participants in the BmBd arm than in the DBd arm stopped driving due to eyesight issues at some point on treatment (40% versus 3%).

6.37 The submission also presented ocular adverse events based on the Keratopathy and Visual Acuity (KVA) scale. The KVA has two components: the first grades corneal findings from the ocular exam (e.g., presence of microcysts, corneal haze, etc.) and the second grades the change in vision based on best corrected visual acuity (BCVA); with the overall KVA grade determined by the more severe grade of the 2 components.

6.38 At the October 2024 data cut, 83% of patients in the BmBd arm experienced treatment-related corneal adverse events based on KVA scale grading. Based on the 81% of patients with grade ≥2 KVA scale events, the median time to onset of the first occurrence was 58.0 days, the median duration of the first occurrence was 106.0 days, and 58% of patients had 3 or more events. Results indicated that 154 (64%) patients in the BmBd arm had unresolved corneal events at the end of treatment, with 94 (61%) of these patients having symptoms unresolved at the end of follow-up/time of the data cut. The longer-term impacts of belantamab mafodotin on the cornea and vision are unclear.

6.39 The PSCR and pre-PBAC response stated that the ocular adverse events were predictable, manageable and reversible with dose modifications (including delays, interruptions or reductions) and follow-up. The PSCR also stated that of 899 KVA-graded events across 5,315 exams in DREAMM-7, 87% had resolved by the data cut-off, with consistent resolutions times (median ~85–117 days) and no evidence of cumulative worsening, see Table 8. Additionally, Grade ≥ 2 events resolved to Grade ≤ 1 in 80-95% of cases across multiple recurrences, and dose modifications effectively managed toxicity, indicating that the ocular effects were unlikely to be progressive and can be effectively mitigated in clinical practice.

Table 8: DREAMM-7 KVA Grade ≥ 2 recurrences (IA2)

Occurrence KVA Grade ≥2	% patients with Grade ≥2 KVA finding [a]	% occurrences resolved to Grade ≤1 (N=242)	Time to resolution to Grade ≤1 (days)[b], median (IQR) (N=242)
1st	88%	80%	117 (64, 294)
2nd	60%	92%	96 (45, 148)
3rd	48%	93%	102 (64, 134)
4th	38%	95%	85 (47, 109)
5th	33%	89%	97 (64, 117)
All occurrences (5,315 exams, 899 occurrences)		87% Resolved	85 (47, 127)

Source: Table 2, p3 of the PSCR
Abbreviations: IQR, interquartile range; KVA, Keratopathy and Visual Acuity
[a] Based on all treated patients
[b] Based on patients with Grade ≥ 2 KVA event

6.40 The ESC considered that the KVA-graded results presented in the PSCR should be interpreted with caution as they reflected resolution to Grade ≤ 1 rather than complete resolution (based on the KVA scale, Grade 1 events are defined as mild superficial keratopathy on corneal examination and/or a decline from baseline of 1 line in visual acuity based on the Snellen chart). The median time to resolution to Grade ≤1 was relatively long, particularly for the first occurrence (117 days), with a reported interquartile range of 64 to 294 days. Additionally, the ESC noted that the longer-term impacts of belantamab mafodotin on the cornea and vision remain unclear.

6.41 The PSCR and pre-PBAC response also stated that pooled analysis from the DREAMM-7 and DREAMM-8 trials found that fewer than 10% stopped driving due to eyesight issues and fewer than 6% stopped reading, and nearly all patients subsequently returned to baseline function (97% for reading, 92% for driving).

Benefits/harms

6.42 On the basis of direct evidence presented in the submission, after a median duration of follow-up of 39.4 months (October 2024 data cut), for every 100 patients treated with BmBd compared to DBd:

- Approximately 31 additional patients would remain progression-free after 24 months.
- Approximately 12 additional patients would remain alive after 24 months.
- Approximately 15 more patients would experience serious adverse events that are life-threatening or required hospitalisation.
- Approximately 49 more patients would experience ocular adverse events, such as blurred vision, photophobia, and dry eye.
- In patients with little or no difficulty reading or driving, approximately 25 more patients would stop reading and approximately 37 more patients would stop driving due to eyesight issues at some point while on treatment.

Clinical claim

6.43 The submission described belantamab mafodotin in combination with bortezomib and dexamethasone as superior in terms of efficacy and inferior in terms of safety compared to daratumumab in combination with bortezomib and dexamethasone for treatment of RRMM after one prior line of therapy.

6.44 The ESC considered that although the therapeutic conclusion was adequately supported, for the proposed PBS population, the applicability of the results from the DREAMM-7 overall population and lenalidomide-exposed subgroup was uncertain, due to the large proportion of patients with more than one prior line of therapy (49% in the overall population and 67% in the lenalidomide-exposed subgroup).[12]

6.45 Additionally, the ESC considered that the proposed place in therapy as a second line only treatment was not appropriate. The ESC considered that restricting BmBd to the second line setting did not align with the clinical trial, did not align with how clinicians would like to use MM treatments (as discussed in the Multiple Myeloma Stakeholder meeting (July 2025)) and would restrict patient access not only to BmBd, but to other therapies. Therefore, the ESC considered that BmBd should be listed for the treatment of RRMM to allow physician discretion as to when it is used. The ESC considered that

[12] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

the appropriate comparator for BmBd in the RRMM setting would consist of a basket of treatments that included DBd.

6.46 The ESC also noted that treatment with BmBd was associated with high rates of ocular toxicity. Although the PSCR stated that ocular events were manageable and reversible, the ESC considered that the longer-term impacts of belantamab mafodotin on the cornea and vision remained unclear.

6.47 The PBAC considered that the claim of superior comparative effectiveness was reasonable.

6.48 The PBAC considered that the claim of inferior comparative safety was reasonable.

Economic analysis

6.49 The submission presented a modelled economic evaluation comparing BmBd with DBd for the treatment of patients with multiple myeloma after one prior line of therapy. The economic evaluation was based on the results of the DREAMM-7 trial (lenalidomide-exposed subgroup), with additional modelled data. The economic evaluation was presented as a stepped cost-effectiveness/cost-utility analysis. Noting the issues with the place in therapy, the PBAC considered that the model presented in the submission was largely uninformative.

Table 9: Summary of model structure, key inputs and rationale

Component	Summary
Treatments	Belantamab in combination with bortezomib and dexamethasone (BmBd) versus daratumumab in combination with bortezomib and dexamethasone (DBd)
Time horizon	20 years in the model base case versus a median follow-up of 39.4 months in the DREAMM-7 ITT population and 37.5 months in the lenalidomide-exposed subgroup[13]. The pre-PBAC response presented a re-specified base case in which convergence was applied from Year 15 to 20.
Outcomes	Life years; quality-adjusted life years.
Methods used to generate results	Partitioned survival analysis.
Health states	Progression-free (on- and off-treatment); progressed disease; dead.
Cycle length	1 week.
Allocation to health states	The proportions of patients who were progression-free (on- and off-treatment), progressed and dead were informed by modelled overall survival (OS), progression-free survival (PFS) and time to treatment discontinuation (TTD) curves.

[13] *Note that the results presented in Table 9 for the lenalidomide-exposed subgroup are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

Component	Summary
	In the base case, Kaplan-Meier estimates for OS, PFS and TTD were derived from the DREAMM-7 trial subgroup with prior lenalidomide exposure and were used directly in the model up to the median duration of follow-up for each arm, then extrapolated to 20 years using standard parametric functions. The re-specified base case presented in the pre-PBAC response was based on the ITT population. Australian life tables were used to ensure that the risk of death in any model cycle was no lower than general population mortality. Adjustments were also incorporated in the model to ensure that TTD did not exceed PFS, and PFS did not exceed general population mortality or OS in any model cycle.
Health related quality of life	Health state utilities were derived from DREAMM-7 EQ-5D-3L utility data analysed using a mixed-effects linear regression model including coefficients for progression status and treatment status, indexed using the Australian value set (Viney 2011). Progression-free on treatment: 0.7793[14] (lenalidomide-exposed subgroup); 0.7831[14] (ITT) Progression-free off treatment: 0.7751[14] (lenalidomide-exposed subgroup); 0.7837[14] (ITT) Progressed disease: 0.7431[14] (lenalidomide-exposed subgroup); 0.7568[14] (ITT) The QALY loss associated with adverse events in each arm was based on the incidence of grade ≥3 adverse events occurring in ≥5% of patients and grade ≥2 KVA scale ocular adverse events in the DREAMM-7 trial, and disutilities and durations of adverse events derived from various published sources and assumptions
Costs	BmBd treatment: Belantamab mafodotin costs were derived from an analysis of weekly utilisation data for belantamab mafodotin in the DREAMM-7 trial (lenalidomide-exposed subgroup). Bortezomib and dexamethasone costs were derived based on recommended doses with adjustment for treatment adherence reported in the DREAMM-7 trial. Treatment persistence for belantamab mafodotin, bortezomib and dexamethasone was based on modelled time to treatment discontinuation for the BmBd arm of the DREAMM-7 trial (lenalidomide-exposed subgroup). DBd treatment: Daratumumab, bortezomib and dexamethasone costs were derived based on recommended doses with adjustment for treatment adherence reported in the DREAMM-7 trial. Treatment persistence for daratumumab, bortezomib and dexamethasone were based on modelled time to treatment discontinuation for the DBd arm of the DREAMM-7 trial (lenalidomide-exposed subgroup). Daratumumab was assumed to be administered intravenously. The cost of administration for parenteral treatments was based on MBS Item 13950 (administration of one or more antineoplastic agents). Grade ≥3 non-ocular adverse events with an incidence of ≥5% in the DREAMM-7 trial (ITT population) were mapped to AR-DRGs. Costs were derived using 2022/23 National Hospital Cost Data Collection admitted acute cost weights for AR-DRG Version 11.0 and the 2025/26 National Efficient Price of $7,258. Costs associated with Grade ≥2 KVA events were based on MBS Item 10918 (optometrical services) and were included for patients with 2 or more occurrences (57%), with application from Cycle 5 until treatment discontinuation.

[14] *Note that the results presented for Australia-specific utility values are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

Component	Summary
	Costs associated with subsequent therapies were based on published PBS prices, with the assumed distribution of therapies based on an analysis of the DREAMM-7 trial (lenalidomide-exposed subgroup). Subsequent therapy costs were included for 60.8% of patients in the BmBd arm and 59.3% of patients in the DBd arm, based on an analysis of data from the DREAMM-7 trial. Terminal care costs were based on terminal care costs among patients with cancer reported by Goldsbury et al. (2018).

Source: Section 3, pp123-170 of the submission.
Abbreviations: 3L, 3-level; BmBd, belantamab in combination with bortezomib and dexamethasone; DBd, daratumumab in combination with bortezomib and dexamethasone; ITT, intention to treat; KVA, Keratopathy Visual Acuity; MBS, Medicare Benefits Schedule; OS, overall survival; PFS, progression-free survival; QALY, quality-adjusted life years; TTD, time to treatment discontinuation.

6.50 A partitioned survival approach was used to distribute patients between model health states. The progression-free health state was partitioned into on- and off-treatment, based on time to treatment discontinuation curves. The model structure limited the ability to appropriately incorporate the costs and consequences associated with the use of subsequent anti-cancer treatments in the progressed disease health state, which may be associated with periods of disease remission, and subsequent progression. The PSCR acknowledged limitations associated with the partitioned survival approach in modelling subsequent therapy utilisation but stated that the specific combination regimens used as subsequent therapy in the economic model reflected those most used in Australian practice. The ESC noted that the number and types of subsequent therapies are likely to differ between the modelled population (based on data for the lenalidomide-exposed subgroup) and the proposed PBS population.

6.51 The economic model was based on a 20-year time horizon. The submission argued that this was reasonable given the mean age of patients in the model (64.8 years) and the average life expectancy of Australians at birth (83.2 years). The submission also noted that the PBAC previously considered a 15-year time horizon (with linear convergence between the overall survival curves applied between 10 and 15 years) appropriate for DBd versus bortezomib and dexamethasone (Bd) in second line multiple myeloma (paragraphs 6.6 and 6.7, daratumumab, PSD, July 2020 PBAC meeting). The submission argued that, given the overall survival gain for BmBd versus DBd demonstrated in the DREAMM-7 trial, a longer time horizon of 20 years was considered appropriate to adequately reflect key differences in costs and outcomes between treatment arms. The PSCR further stated that the 20-year time horizon was reasonable given the mean age of entry of patients in the model (64.8 years) was representative of the Australian RRMM population and that age-standardised mortality for MM patients under 70 is expected to be the same as the general

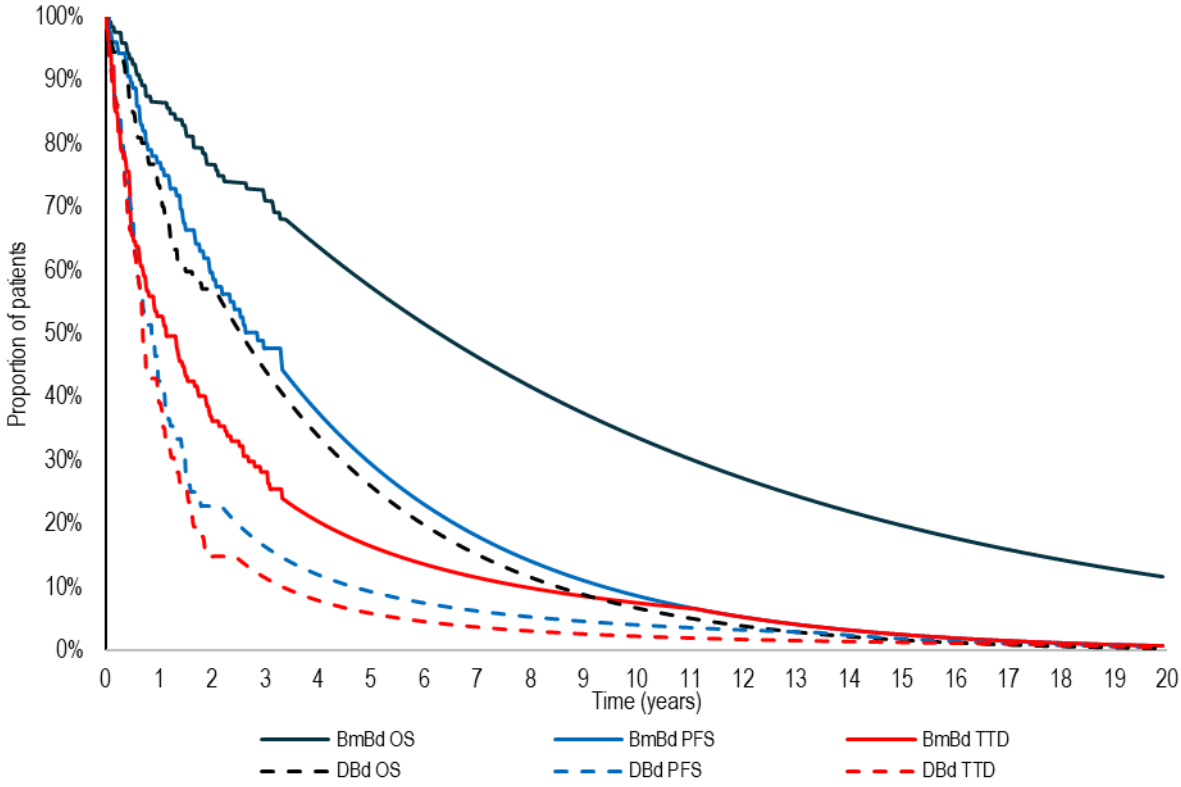
population by 2028 (Luo, 2024[15]). The ESC, noting that there was a substantial amount of uncertainty associated with the extrapolation of the results from 37.5 months in the DREAMM-7 trial (lenalidomide-exposed subgroup) to 20 years (see Figure 5), considered that a time horizon of 15 years would be more appropriate. The pre-PBAC response presented a revised based case which applied convergence of the overall survival curves from Year 15 to 20.

6.52 In the base case of the submission, the proportions of patients in each health state were derived from extrapolated time to treatment discontinuation, progression-free survival and overall survival curves for the BmBd and DBd arms of the DREAMM-7 lenalidomide-exposed trial subgroup. However, noting the issues discussed in paragraph 6.13, the ESC considered that the ITT population would provide the most robust data. The re-specified base case presented in the pre-PBAC response used the ITT population to inform the model.

6.53 Figure 5 presents the extrapolated overall survival, progression-free survival and time to treatment discontinuation curves used in the base case of the modelled economic evaluation (lenalidomide-exposed subgroup).

[15] Luo Q. Multiple myeloma incidence, mortality, and prevalence estimates and projections, Australia, 1982-2043: a statistical modelling study. Med J Australia. 2024;221(2):103-110.

Figure 5: Overall survival, progression-free survival and time to treatment discontinuation curves used in the base case of the modelled economic evaluation (based on the DREAMM-7 lenalidomide-exposed subgroup)[16]



Source: 'Blenrep (belantamab mafodotin) CUA_July 2025' model spreadsheet provided with the submission.
Abbreviations: BmBd, belantamab mafodotin in combination with bortezomib and dexamethasone; DBd, daratumumab in combination with bortezomib and dexamethasone; OS, overall survival; PFS, progression-free survival; TTD, time to treatment discontinuation.

6.54 In the base case of the model, overall survival for the BmBd and DBd arms were extrapolated using exponential functions, which represented the most pessimistic extrapolations among the tested parametric functions.

6.55 DBd was PBS listed for second line treatment of multiple myeloma based on evidence from the CASTOR trial, a randomised, open-label, phase 3 study comparing to Bd in patients with RRMM and at least 1 prior line of therapy. Based on visual inspection of the CASTOR trial Kaplan-Meier plots, the proportion of patients remaining alive at 5 years was approximately 45% for the ITT population and approximately 60% in the second line subgroup. This compares with modelled overall survival for the DBd arm of 42% at 5 years based on the DREAMM-7 ITT population and 26% at 5 years based on the DREAMM-7 lenalidomide-exposed subgroup. This suggests that, while

[16] *Note that the Kaplan Meier plots and fitted curves depicted in Figure 5 are presented specifically for the purposes of informing the PBAC consideration. Their interpretation and application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

modelled estimates for the DBd arm based on the DREAMM-7 ITT population were similar to estimates from the CASTOR trial ITT population, the use of the DREAMM-7 lenalidomide-exposed subgroup underestimated survival in the DBd arm of the proposed second line population. The PSCR stated that the outcomes from the CASTOR trial have not eventuated in practice, with survival observations from the Australian and New Zealand Myeloma and Related Diseases Registry (MRDR)[17] similar to those reported in the lenalidomide-exposed subgroup of DREAMM-7. The ESC noted trial patients were generally fitter than those in the real world setting and that the efficacy of BmBd in clinical practice has not yet been observed.

6.56 Figure 5 shows a survival benefit for BmBd compared to DBd that persists over the 20 year time horizon of the model. The proportions of patients remaining alive in the BmBd arm at 15 and 20 years were 19.9% and 11.7%, respectively, compared to 1.8% and 0.5% in the DBd arm.

6.57 There was a relatively large difference between the progression-free survival and time to next treatment curves, suggesting that a large proportion of patients discontinued treatment despite not having experienced disease progression. The difference between the time to treatment discontinuation and progression-free survival curves was more pronounced in the BmBd arm compared to the DBd arm. Based on the October 2024 data cut for the ITT population, the primary reasons for treatment discontinuation in the BmBd arm were progressive disease (30%), adverse event (21%) and physician decision (13%); and in the DBd arm were progressive disease (64%), adverse event (9%), and withdrawal by subject (4%).

6.58 The ESC noted that the economic model did not appear to adequately capture the costs and quality of life impacts associated with severe ocular toxicity events. While disutilities were applied to model adverse events including dry eyes and eye irritation, these were assumed to be transient in nature with an overall disutility per event of <0.05. The ESC considered this substantially underestimated the quality of life impact of more severe ocular toxicity, which may persist over a longer period of time.

6.59 Belantamab mafodotin costs were based on an analysis of weekly utilisation data for the lenalidomide-exposed subgroup of the DREAMM-7 trial. The method used to estimate the utilisation of belantamab mafodotin was complex. Due to the potential for dose interruptions, dose reductions and changes in administration frequency, the use of weekly utilisation data from the trial to capture costs associated with belantamab mafodotin treatment may be reasonable. However, the number of 100 mg and 70 mg vials required for each dose was derived separately, with separate

[17] ANZ MRDR (2024). Australian and New Zealand Myeloma and Related Diseases Registry (ANZ MRDR) 2024 Annual Report.

PBS markups applied to the estimated number of required 100 mg and 70 mg doses. This resulted in overestimation of PBS markups given that 100 mg and 70 mg vials for each dose would be dispensed together.

6.60 There were differences in the methods used to estimate the utilisation for belantamab mafodotin (analysis of weekly utilisation data for the lenalidomide-exposed subgroup of the DREAMM-7 trial) and the other included initial treatments (daratumumab, bortezomib and dexamethasone; derived based on reported mean relative dose intensities). The ESC noted that it was unclear whether the use of different methods resulted in consistent costing of therapies between treatment arms.

6.61 The submission assumed that daratumumab would be administered intravenously on the basis that intravenous use of daratumumab was used in the DREAMM-7 trial. The eviQ guidelines note that the DBd regimen using subcutaneous, rather than intravenous daratumumab, is now the preferred regimen.

6.62 Table 10 summarises the key drivers of the economic model.

Table 10: Key drivers of the model

Description	Method/Value	Impact
Comparative effectiveness	The submission did not adequately justify the use of the lenalidomide-exposed subgroup in the base case. While approximately 52% of patients in each treatment arm of the DREAMM-7 trial reported prior lenalidomide use, most patients in the ITT population (81% in the BmBd and 86% in the DBd arm) reported prior exposure to an immunomodulatory agent (lenalidomide, thalidomide or pomalidomide). The lenalidomide-exposed subgroup included patients with one or more prior lines of therapy, which differs from the proposed PBS population with regard to the number of lines of prior therapy.	High, favours BmBd
Extrapolation	Extrapolation of the trial data (based on a median follow-up of 37.5 months in the lenalidomide-exposed subgroup)[18] to 20 years was associated with a substantial amount of uncertainty. The exponential function used to extrapolate overall survival for the DBd arm appeared to underestimate survival among patients treated with DBd.	High, favours BmBd
Subsequent treatments	There are likely to be differences in the number and types of subsequent treatments used among patients included in the DREAMM-7 trial and patients in the proposed PBS population. Due to the partitioned survival structure of the model, alternative assumptions for subsequent therapy use (e.g., lines of therapy, distribution of therapies, duration of therapies) affected costs only (and not outcomes).	Moderate, favours BmBd
BmBd treatment utilisation	Dose reductions occurred in 70% of patients who received belantamab mafodotin in the lenalidomide-exposed subgroup of the DREAMM-7 trial, and dose delays occurred in 54% of patients.[18] It is unclear whether the utilisation of belantamab mafodotin in the clinical trial will reflect dosing in the proposed PBS population, given differences in the number of lines of prior therapy, and potential differences in age, performance status and comorbidities. Lower doses will reduce the cost of treatment but may also reduce the effectiveness of treatment.	Unclear impact

Source: Constructed during the evaluation with reference to Section 3, pp123-170 of the submission.
Abbreviations: BmBd, belantamab in combination with bortezomib and dexamethasone; DBd, daratumumab in combination with bortezomib and dexamethasone; ITT, intention to treat.

6.63 Table 11 presents the results of the economic evaluation for the DREAMM-7 lenalidomide-exposed subgroup (submission base case) and the DREAMM-7 ITT population based on published prices for daratumumab and subsequent therapies. The results of the re-specified base case presented in the pre-PBAC response which used the ITT population from DREAMM-7 to inform the model and applied convergence from Year 15 to 20 is also presented below.

[18] *Note that the results presented in Table 10 for the lenalidomide-exposed subgroup are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

Table 11: Results of the economic evaluation

Step and component	BmBd	DBd	Increment
DREAMM-7 lenalidomide-exposed subgroup			
Costs	$[redacted]	$285,389	$[redacted]
Life years	6.0063	3.0922	2.9142
QALYs	4.5263	2.3459	2.1803
Incremental cost per life year gained			$[redacted][1]
Incremental cost per QALY gained			$[redacted][1]
DREAMM-7 ITT population			
Costs	$[redacted]	$325,137	$[redacted]
Life years	6.1801	4.3711	1.8090
QALYs	4.7194	3.3610	1.3584
Incremental cost per life year gained			$[redacted][2]
Incremental cost per QALY gained			$[redacted][3]
Pre-PBAC response re-specified base case (ITT population and convergence applied from Year 15 to 20)			
Costs	$[redacted]	$325,137	$[redacted]
Life years	6.09	4.37	1.71
QALYs	4.65	3.36	1.29
Incremental cost per life year gained			$[redacted][4]
Incremental cost per QALY gained			$[redacted][3]

Source: Table 3-42, p166 of the submission; and 'Blenrep (belantamab mafodotin) CUA_July 2025' model spreadsheet provided with the submission and the pre-PBAC response.

Abbreviations: BmBd, belantamab mafodotin in combination with bortezomib and dexamethasone; DBd, daratumumab in combination with bortezomib and dexamethasone; ITT, intention-to-treat; QALY, quality adjusted life year.

The redacted values correspond to the following ranges:

[1] *55,000 to < $75,000*

[2] *$75,000 to < $95,000*

[3] *$115,000 to < $135,000*

[4] *$95,000 to < $115,000*

6.64 Based on the economic model, treatment with BmBd compared to DBd was associated with an incremental cost per QALY gained of $55,000 to < $75,000 based on the DREAMM-7 lenalidomide-exposed subgroup and an incremental cost per QALY gained of $115,000 to < $135,000 based on the DREAMM-7 ITT population. The revised base case presented in the pre-PBAC response resulted in an ICER of $115,000 to < $135,000 per QALY.

6.65 In the model base case, based on the DREAMM-7 lenalidomide-exposed subgroup, 84% of incremental QALYs and 55% of incremental costs were accrued in the extrapolated period beyond the median duration of follow-up of 37.5 months (3.1 years).

6.66 For every patient treated with BmBd versus DBd and followed for up to 20 years, the economic model based on the DREAMM-7 lenalidomide-exposed subgroup (without discounting) estimated that there would be:

- An additional 4.4 years of life lived.
- An additional 2.1 years spent progression-free.
- Additional second line therapy costs of $[redacted].
- Additional disease management costs of $17,747 and additional adverse event costs of $3,074.

- Reduced subsequent therapy costs of $424 and reduced terminal care costs of $6,044.

6.67 The results of key univariate sensitivity analyses for the lenalidomide-exposed population are summarised in Table 12.

Table 12: Results of sensitivity analyses for the lenalidomide-exposed subgroup of the DREAMM-7 trial

Analyses	Incremental cost	Incremental QALY	ICER	% change
Base case	**$** [redacted]	**2.180**	**$** [redacted][1]	**-**
Time horizon (base case: 20 years)				
15 years	$ [redacted]	1.950	$ [redacted][2]	[redacted]%
Discount rate (base case: 5% for costs and outcomes)				
0%	$ [redacted]	3.322	$ [redacted][1]	-[redacted]%
3.5%	$ [redacted]	2.454	$ [redacted][1]	-[redacted]%
BmBd overall survival extrapolation (base case: exponential function)				
Weibull	$ [redacted]	2.497	$ [redacted][1]	-[redacted]%
DBd overall survival extrapolation (base case: exponential function)				
Weibull	$ [redacted]	2.046	$ [redacted][2]	[redacted]%
Generalised gamma	$ [redacted]	1.803	$ [redacted][2]	[redacted]%
BmBd time to treatment discontinuation extrapolation (base case: lognormal function)				
Loglogistic	$ [redacted]	2.180	$ [redacted][2]	[redacted]%
Generalised gamma	$ [redacted]	2.180	$ [redacted][2]	[redacted]%
Weibull	$ [redacted]	2.180	$ [redacted][1]	-[redacted]%
DBd time to treatment discontinuation extrapolation (base case: loglogistic function)				
Exponential	$ [redacted]	2.180	$ [redacted][2]	[redacted]%
Weibull	$ [redacted]	2.180	$ [redacted][2]	[redacted]%
Generalised gamma	$ [redacted]	2.180	$ [redacted][2]	[redacted]%
Utilities (base case: lenalidomide-exposed subgroup – progression-free on treatment: 0.7793; progression-free off treatment: 0.7751; post-progression: 0.7431)[19]				
ITT population (progression-free on treatment: 0.7831; progression-free off treatment: 0.7837; post-progression: 0.7568)	$ [redacted]	2.208	$ [redacted][1]	-[redacted]%
Post-progression 0.70	$ [redacted]	2.129	$ [redacted][2]	[redacted]%
Daratumumab dose intensity (base case: 97%)				
92%	$ [redacted]	2.180	$ [redacted][2]	[redacted]%
87%	$ [redacted]	2.180	$ [redacted][2]	[redacted]%
Weekly health state costs (base case: BmBd on treatment $[redacted], DBd on treatment $74.83; pre-progression off treatment and progressed disease: $74.83)				
Doubled	$ [redacted]	2.180	$ [redacted][2]	[redacted]%
Terminal care cost (base case: $53,945)				
Removed	$ [redacted]	2.180	$ [redacted][2]	[redacted]%

Source: Table 3-44, p169 of the submission; additional sensitivity analyses conducted during the evaluation using the Section 3 economic model Excel workbook.

Abbreviations: BmBd, belantamab in combination with bortezomib and dexamethasone; DBd, daratumumab in combination with bortezomib and dexamethasone; ICER, incremental cost-effectiveness ratio; ITT, intention to treat; QALY, quality-adjusted life year.

The redacted values correspond to the following ranges:

[1] *$55,000 to < $75,000*

[2] *$75,000 to < $95,000*

[19] *Note that the results presented for Australia-specific utility values are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their*

6.68 The modelled results were most sensitive to the time horizon, the discount rate, the choice of parametric extrapolations for overall survival for the BmBd and DBd arms, the choice of parametric extrapolations for time to treatment discontinuation for the BmBd and DBd arms, and the dose intensity for daratumumab.

Drug cost/patient/course

6.69 Table 13 presents a comparison of drug costs per patient for BmBd and DBd included in the economic model and financial estimates.

application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

Table 13: Drug cost per patient for BmBd and DBd

	Clinical evidence	Economic model	Financial estimates
BmBd			
BELANTAMAB MAFODOTIN			
Cost per script	-	Not estimable [a]	100 mg: $[redacted] [b] 70 mg: $[redacted] [b]
Treatment regimen	2.5 mg/kg IV every 3 weeks until disease progression.		
Adherence	57.1% [c,l]	Y1: 100% [e] Y2: 52.8% [e] Y3: 36.2% [e] Y4: 28.2% [e] Y5: 20.4% [e] Y6: 16.5% [e]	100 mg vials [f] Y1 (init.): 49.5%; Y1 (cont.): 11.8%; Y2: 13.0%; Y3: 7.2%; Y4: 5.2%; Y5: 4.1%; Y6: 3.3%. 70 mg vials [f] Y1 (init): 57.6%; Y1 (cont): 16.4%; Y2: 19.8%; Y3: 11.9%; Y4: 8.6%; Y5: 6.8%; Y6: 5.5%.
Persistence	13.2 cycles [d,l]		
Cost/patient/course	-	$[redacted] [g]	$[redacted] (over 6 years)
BORTEZOMIB			
Cost/patient/course	-	$3,902	$3,082
DEXAMETHASONE			
Cost/patient/course	-	$139	$140
DBd			
DARATUMUMAB			
Cost per script	-	$7,776.99 [h]	$7,776.99 [i]
Treatment regimen	16 mg/kg IV once a week for 3 × 21-day cycles (9 weeks), once every 3 weeks for 5 × 21-day cycles (15 weeks), and once 4 weeks thereafter (until disease progression).		
Adherence	Cycles 1-3: 87.1% [c] Cycles 4-8: 95.6% [c] Cycle 9+: 97.0% [c]	97.2% [j]	97.0% [j]
Persistence	15.5 cycles [d]	Cycles 1-3: 8.42 weeks [k] Cycles 4-8: 11.72 weeks [k] Cycle 9+: 59.50 weeks [k]	Cycles 1-3: 8.42 weeks [k] Cycles 4-8: 11.72 weeks [k] Cycle 9+: 59.50 weeks [k]
Cost/patient/course	-	$214,781	$205,201
BORTEZOMIB			
Cost/patient/course	-	$3,887	$3,025
DEXAMETHASONE			
Cost/patient/course	-	$139	$137

Source: Table 3.1101406, Table 3.1101506, Table 3.1101606, Table 3.1101706 of the October 2024 clinical study report supplementary data; Section 3 economic model Excel workbook; Section 4 financial implications Excel workbook.

Abbreviations: BmBd, belantamab mafodotin in combination with bortezomib and dexamethasone; cont., continuing treatment; DBd, daratumumab in combination with bortezomib and dexamethasone; init., initial treatment; IV, intravenous; PO, per oral; SC, subcutaneous; Y, Year.

[a] The cost of belantamab mafodotin was derived based on an analysis of weekly vial utilisation in the DREAMM-7 trial and varied from week to week.

[b] Based on the proposed effective AEMP of $[redacted] per 100 mg vial and $[redacted] per 70 mg vial. The average required number of 100 mg and 70 mg vials were derived separately, with markups applied on a proportional basis. The submission assumed that an average of 1.25 × 100 mg vials and 1.19 × 70 mg vials were required for a 2.5 mg/kg dose.

[c] Mean relative dose intensity for the lenalidomide-exposed subgroup in the DREAMM-7 trial at the October 2024 data cut.

[d] Mean number of treatment cycles at the time of the October 2024 data cut.

[e] The proportion of patients remaining on treatment at the start each year in the economic model.

[f] Assumed dose intensity per dosing period versus a full dose of 2.5 mg/kg derived from weekly dosing data for the lenalidomide-exposed subgroup of the DREAMM-7 trial, including adjustment for the proportion of patients remaining on treatment.

[g] The cost per patient for belantamab mafodotin over the initial 6 years in the economic model was $[redacted].

[h] Based on a dispensed price of $7,776.99 per script, assuming a requirement of 1,300 mg (derived assuming a dose of 16 mg/kg, a mean weight of 77.8 kg, including treatment adherence of 97.2%, with rounding of the resulting dose of 1,209 mg to the nearest vial), assuming 100% use of the intravenous formulation, and a 39%/61% weighted public/private hospital split.

[i] Based on a dispensed price of $7,776.99 per script, assuming a requirement of 1,300 mg (derived assuming a dose of 16 mg/kg, a mean weight of 77.8 kg, with rounding of the resulting dose of 1,245 mg to the nearest vial), assuming 100% use of the intravenous formulation, and a 39%/61% weighted public/private hospital split.
[j] In the economic model, treatment adherence was applied as part of the dose calculation; whereas in the financial estimates, treatment adherence was applied to the estimated number of scripts.
[k] Persistence based on the modelled time to treatment discontinuation for the DBd arm, assuming a maximum of 8 cycles for bortezomib and dexamethasone, and ongoing treatment for daratumumab.
[l] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

Estimated PBS usage & financial implications

6.70 This submission was considered by DUSC.

6.71 The submission used a mixed epidemiological/market share approach to estimate the utilisation and financial implications of listing belantamab mafodotin for the treatment of patients with relapsed or refractory multiple myeloma after one prior line of therapy.

6.72 Table 14 presents the key inputs relied on in the financial estimates.

Table 14: Key data sources and parameter values applied in the utilisation and financial estimates

Data	Value	Source	Comments
Eligible population			
Prevalent first line MM patients in 2020-2024	2020: [redacted]1 2021: [redacted]1 2022: [redacted]1 2023: [redacted]2 2024: [redacted]2	Patients receiving first line MM treatment from a 10% PBS sample data.	There was limited information provided regarding the methodology used to identify first line prevalent patients. It was unclear whether the analysis captured all first line MM patients.
Prevalent first line MM patients in 2025 and Year 1 of listing	2025: [redacted]2 2026: [redacted]2	Derived by applying the average annual growth rate in prevalent patients from 2020 to 2024 (7.16%) to the estimated number of prevalent patients in 2024. The 2026 number was assumed to equal the 2025 number.	While the approach to estimate the growth rate appeared reasonable, it was unclear whether the 10% PBS sample data analysis accurately captured all first line MM patients in 2020-2024. No patients experiencing death or disease progression were removed from the prevalent pool in 2025, resulting in an overestimation of the prevalent population in Year 1 of listing (which carried over into subsequent years). However, a proportion of patients experiencing disease progression in 2025 would represent grandfathered patients.
Number of transplant eligible incident MM patients in 2022-2024	2022: [redacted]1 2023: [redacted]1 2024: [redacted]1	Based on a 10% PBS sample, determined by post-ASCT PBS item codes, PBS item codes specific to transplant eligibility/ineligibility, and patient age (patients not categorised on the basis of PBS item codes were assumed to be transplant eligible if aged ≤70 years).	There was a lack of information provided regarding the methodology used to identify first line incident patients. The item codes used to determine transplant eligibility were not provided and it was unclear how accurately the included criteria identified incident transplant eligible/ineligible patients.
Transplant ineligible incident MM patients in 2022-2024	2022: [redacted]1 2023: [redacted]1 2024: [redacted]1		
First line treatment utilisation among transplant ineligible prevalent patients	LBd: 68% Ld: 32%	Based on MRDR data included in the March 2023 daratumumab resubmission.	In the context of the daratumumab submission, the PBAC considered that weighting of the data from the MRDR would be appropriate (paragraph 7.6, daratumumab, PSD, March 2023 PBAC meeting).

Data	Value	Source	Comments
Annual disease progression and death rates on first line LBd and Ld treatment	LBd progression: 20.4%; Ld progression: 28.7%; LBd death: 7.4% Ld death: 12.1%	Estimated from median PFS and OS reported for the LBd and Ld arms of the SWOG S0777 trial (Durie et al., 2020). Converted to an annual rate.	The assumed linear rate of disease progression over time may not reflect the natural history of the disease. The median OS for the LBd arm was not reached at the time trial publication. Therefore, the rate was derived from the proportion of patients remaining alive at 5 years. Additionally, the applicability of the data to the PBS population was unclear. The DUSC considered that the annual death rates were over-estimated. The DUSC Analysis of medicines to treat multiple myeloma 2017 report had a 2-year death rate of 11% which was before triple therapy was recommended.
Incident first line patient growth rate for 2025 to 2031	2024-25: 2.2% 2025-26: 3.6% 2026-27: 3.7% 2027-28: 3.4% 2028-29: 2.9% 2029-30: 2.9% 2030-31: 2.7%	Derived from annual projected cases of incident MM reported by the AIHW.	The DUSC considered that it was not necessary to use an incident approach here. A prevalent approach would capture incident use, thus the prevalent growth already factors in incident growth.
Treatment utilisation			
BmBd uptake rate (prevalent and incident patients)	Year 1: [redacted]% Year 2: [redacted]% Years 3-6: [redacted]%	Assumption based on expert opinion.	While the DREAMM-7 trial demonstrated improvements in PFS and OS for BmBd versus DBd, treatment with BmBd was associated with high rates of ocular adverse events which may reduce the uptake of belantamab mafodotin. The listing of DLd as a first line treatment and potential listing of elranatamab in a later line may also impact the uptake of BmBd in the second line setting. The DUSC considered that the uptake rate would be dependent on access to co-ordinated care with ophthalmologists/ optometrists to manage ocular adverse events.
Grandfathered patients	[redacted]^3 patients	An additional [redacted]^3 patients were included in Year 1.	-
Belantamab mafodotin vials required for a 2.5 mg/kg dose*	100 mg: 1.25 70 mg: 1.19	Assumed a normal distribution of body weight around the mean weight reported for the lenalidomide-exposed subgroup of the DREAMM-7 trial (77.8 kg)*.	-
Belantamab mafodotin vials required for a 1.9 mg/kg dose*	100 mg: 0.74 70 mg: 1.28		
Belantamab mafodotin 100 mg dose intensity	Y1 init: 49.5% Y1 cont: 11.8% Y2 cont: 13.0% Y3 cont: 7.2% Y4 cont: 5.2% Y5 cont: 4.1% Y6 cont: 3.3%	Estimated for each dosing period (initial treatment: 24 weeks in Year 1, continuing treatment: 28 weeks in Year 1, continuing treatment 52 weeks in Years 2 to 6).	The dose intensity for the 28-week continuing treatment period in Year 1 was inappropriately derived by dividing the number of vials used over the 28-week period by the number of vials required for a full 52 weeks of with 2.5 mg/kg. However, this issue appeared to be balanced by the assumption of a 52-week treatment period in the duration of treatment groups worksheet.
Belantamab mafodotin 70 mg dose intensity	Y1 init: 57.6% Y1 cont: 16.4% Y2 cont: 19.8%		

Data	Value	Source	Comments
	Y3 cont: 11.9% Y4 cont: 8.6% Y5 cont: 6.8% Y6 cont: 5.5%		
Daratumumab treatment adherence (DBd)	97%	Based on the mean relative dose intensity for daratumumab reported in the DREAMM-7 trial.	The dose intensity for daratumumab was based on the mean relative dose intensity reported for Cycle 9+. It would have been preferable to use separate dose intensities for the respective treatment periods.
Daratumumab treatment persistence	Cycles 1-3: 8.42 weeks Cycles 4-8: 11.72 weeks Cycle 9+: 59.50 weeks	Based on an analysis of time to treatment discontinuation for DBd in the economic model, which indicated a mean time on treatment of 79.64 weeks.	The submission inappropriately attributed 72.14 weeks of daratumumab treatment to the initial year of treatment, rather than 52 weeks in the initial treatment year and 27.64 weeks of treatment in the second year. This resulted in a larger daratumumab cost offset in Year 1 than would be realised in clinical practice (culminating in a net saving to the PBS/RPBS in Year 1 of listing).
Costs			
Belantamab cost per script (100 mg vial component)	$[redacted]	Based on the proposed effective EMP of $[redacted] per 100 mg vial and $[redacted] per 70 mg vial, a 51.25%/48.75% split of the applicable PBS markups between the 100 mg and 70 mg vials, and a weighted 38.81%/61.19% public/private hospital split.	The method used to derive the utilisation and financial estimates for belantamab mafodotin was complex, and it is unclear whether the separate derivation of 100 mg and 70 mg vial costs with pricing applied on a proportional basis was reasonable.
Belantamab cost per script (70 mg vial component)	$[redacted]		
Daratumumab cost per script	$7,776.99	Based on a published dispensed price of $7,776.99 per script, assuming a requirement of 1,300 mg, 100% use of the IV, and a 39%/61% weighted public/private hospital split.	The subcutaneous formulation of daratumumab is likely to be used more frequently in clinical practice and is based on a flat dose of 1,800 mg. The submission presented the results of a sensitivity analysis in which the cost of daratumumab was based on 100% utilisation of the subcutaneous daratumumab formulation. A cost associated with daratumumab premedication with dexamethasone was included in the economic model.
Eye care professional visits	$28.58	MBS Item 10918, based on 75% of the Schedule fee. Four services for each patient initiating BmBd were assumed	Costs associated with monitoring and management of eye toxicity are likely to be substantially higher in clinical practice given the frequency of eye related adverse events among patients in the DREAMM-7 trial. Additionally, the submission only included costs associated with optometrist consultations. In clinical practice, some patients may be managed by an ophthalmologist, or by an optometrist and an ophthalmologist. The MBS cost should be based on 80% of the Schedule fee.
Administration cost (BmBd and DBd)	$92.29	MBS Item 13950, based on 75% of the Schedule fee.	Bortezomib administrations were not included. The MBS cost should be based on 80% of the Schedule fee. For BmBd, the submission based the number of administrations on the number of 70 mg vials, which was higher than the estimated number of 100 mg vials required.

Source: Table 4.1.1, pp146-153 of the Commentary.

Abbreviations: AEMP, approved ex-manufacturer price; AIHW, Australian Institute of Health and Welfare; ASCT, autologous stem cell transplant; BmBd, belantamab in combination with bortezomib and dexamethasone; cont, continuing; DBd, daratumumab in combination with bortezomib and dexamethasone; init, initial; ITT, intention to treat; LBd, lenalidomide in combination with bortezomib and dexamethasone; Ld, lenalidomide in combination with dexamethasone; MBS, Medicare Benefits Schedule; MM = multiple myeloma; MRDR, Myeloma and Related Diseases Registry; OS = overall survival; PFS = progression free survival.

The redacted values correspond to the following ranges:

[1] 500 to < 5,000

[2] 5,000 to < 10,000

[3] < 500

** Note that the results presented for the lenalidomide-exposed subgroup are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for DREAMM-7. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

6.73 Table 15 presents the estimated utilisation and financial implications of listing belantamab mafodotin on the PBS/RPBS.

Table 15: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Total patients initiating BmBd	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Number of scripts dispensed for BmBd						
Dispensed belantamab mafodotin 100 mg vials	[redacted][2]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Dispensed belantamab mafodotin 70 mg vials	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]
Bortezomib scripts	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Dexamethasone scripts	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated financial implications of BmBd						
Cost to PBS/RPBS less copayments	$[redacted][5]	$[redacted][6]	$[redacted][7]	$[redacted][7]	$[redacted][7]	$[redacted][8]
Estimated financial implications for DBd						
Cost to PBS/RPBS less copayments	$[redacted][5]	$[redacted][6]	$[redacted][6]	$[redacted][6]	$[redacted][6]	$[redacted][6]
Net financial implications						
Net cost to PBS/RPBS [a]	-$[redacted][9]	$[redacted][10]	$[redacted][11]	$[redacted][12]	$[redacted][5]	$[redacted][5]
Net cost to MBS [b]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]
Net cost to PBS/RPBS/MBS	**-$**[redacted][9]	**$**[redacted][10]	**$**[redacted][11]	**$**[redacted][12]	**$**[redacted][5]	**$**[redacted][5]

Source: Section 4 financial implications Excel workbook.

Abbreviations: BmBd, belantamab in combination with bortezomib and dexamethasone; DBd, daratumumab in combination with bortezomib and dexamethasone; MBS, Medicare Benefits Schedule; PBS, Pharmaceutical Benefits Scheme; RPBS, Repatriation Pharmaceutical Benefits Scheme.

[a] The submission inappropriately attributed 72.14 weeks of daratumumab treatment to the initial year of treatment year, rather than 52 weeks in the initial treatment year and 27.64 weeks of treatment in the second year. This resulted in a larger daratumumab cost offset in Year 1 than would be realised in clinical practice (culminating in a net saving to the PBS/RPBS in Year 1 of listing).

[b] Includes additional eye examinations associated with belantamab mafodotin (MBS Item 10918); changes in administration costs associated with belantamab mafodotin, daratumumab and bortezomib (MBS Item 13950); and changes in the utilisation of blood grouping associated with initiation of daratumumab (MBS Item 65090).

The redacted values correspond to the following ranges:

[1] *500 to < 5,000*
[2] *5,000 to < 10,000*
[3] *10,000 to < 20,000*
[4] *20,000 to < 30,000*
[5] *$100 million to < $200 million*
[6] *$200 million to < $300 million*
[7] *$300 million to < $400 million*
[8] *$400 million to < $500 million*
[9] *net cost saving*
[10] *$20 million to < $30 million*
[11] *$60 million to < $70 million*
[12] *$90 million to < $100 million*

6.74 The submission estimated a net saving to the PBS/RPBS/MBS of $20 million to < $30 million in Year 1 (this was due to an error in the duration of treatment attributed to daratumumab in Year 1), and a net cost of $20 million to < $30 million in Year 2, increasing to a net cost of $100 million to < $200 million in Year 6. The estimated net cost over the initial 6 years of listing was $400 million to < $500 million.

6.75 The estimated net cost to the PBS/RPBS was considered uncertain by the DUSC due to the following reasons:

- There was limited information provided regarding the methodology used to identify the prevalent patients receiving first line therapy, based on an analysis of 10% PBS sample data, and it was unclear whether the analysis identified all first line multiple myeloma patients. Additionally, it is unclear whether the 10% Medicare sample analysis appropriately identified transplant eligible/ineligible patients. The PSCR provided additional details on the methodology for the analysis of 10% PBS sample data. The DUSC considered that rather than a combined epidemiological/market share approach, a standard market share approach, accounting for increased survival, would have provided more accurate estimates of the initial population as the submission assumed that BmBd will replace DBd.
- The approach used to derive the utilisation and financial estimates for belantamab mafodotin was complex, and it remained unclear whether the separate derivation of 100 mg and 70 mg vial costs with markups applied on a proportional basis was reasonable.
- The assumed uptake rates were considered uncertain. While the DREAMM-7 trial demonstrated improvements in progression-free survival and overall survival for BmBd versus DBd, treatment with BmBd was associated with high rates of ocular adverse events, including blurred vision. The high rates of ocular adverse events may reduce the uptake of belantamab mafodotin given the potential impacts on activities of daily living and driving, particularly among older patients. The DUSC considered that the assumptions around prescriber and patient willingness to use BmBd due to toxicities was unclear.
- No patients experiencing death or disease progression were removed from the prevalent pool in 2025, resulting in an overestimation of the prevalent population in Year 1 of listing (which carried over into subsequent years). A proportion of patients experiencing disease progression in 2025 would represent grandfathered patients. The PSCR noted that as the prevalent population in 2025 was projected from earlier years (2020-2024, PBS 10% sample), this cohort already accounts for disease progression and death. The 2025 value was then projected using progression/death rates to discern the number of progressing patients.
- Costs associated with monitoring and management of eye toxicity are likely to be substantially higher in clinical practice given the frequency of eye related adverse events among patients in the DREAMM-7 trial. Additionally, there are likely to be additional costs to the PBS associated with eye drops. The draft product information for belantamab mafodotin recommends that patients should administer preservative-free artificial tears at least 4 times a day beginning on the first day of infusion and continuing until completion of treatment, as this may reduce ocular symptoms. The PSCR stated that the ocular events observed in DREAMM-7 were predictable, manageable, and reversible with appropriate dose modifications (including delays, interruptions, or reductions) and follow-up, with ocular effects unlikely to be progressive and can be effectively mitigated in clinical

practice. The DUSC considered the care required to monitor and treat the ocular toxicities will be complex and require the optimal coordination between haematologists, ophthalmologists/ optometrists, and general practitioners to identify and manage any toxic side effects and that this will need to form part of any quality use of medicine activities.

6.76 The pre-PBAC response presented revised financial estimates which corrected the duration of daratumumab in Year 1 and applied a lower death rate, lower uptake rates in Years 1 to 3 and treatment costs based on the ITT population. This resulted in a net cost to the PBS/RPBS over the first 6 years of listing of $40 million to < $50 million.

Quality Use of Medicines

6.77 The submission listed the following activities to support the quality use of medicines:

- Medical education for health care professionals, including peer to peer medical education, nurse education, a myeloma clinical education workshop, and formation of a team providing education for eye care professionals.
- Support materials for health care professionals, including an ophthalmic examination guide and findings materials, an eye-related side effects guide for health care professionals, and local guidelines on dosing and management of ocular adverse events for haematologists and eye care professionals.
- Support materials for patients, including a patient wallet card and an eye-related side effects guide.
- Support of patient organisations, including consultation with Myeloma Australia, sponsorship of patient advocacy groups for educational activities, and delivery of a patient education workshop.
- General quality use of medicines activities, including sponsorship of key clinical groups/societies, and inclusion of a black triangle on the belantamab mafodotin product information and consumer medicines information.
- Consumer market research to understand multiple myeloma.
- Disease awareness communications, including via myeloma peak bodies.

6.78 Treatment with belantamab mafodotin is associated with high rates of ocular adverse events, with potential impacts on reading, driving and other activities of daily living. Patients receiving treatment will require access to eye care professionals for monitoring and management of ocular side effects. The PSCR stated that patients receiving BmBd treatment would be predominantly managed by optometrists but noted that serious ocular events (such as corneal ulcers) may require ophthalmologist consultation. The DUSC considered that the management of the ocular toxicity will be complex and involve the coordinated effort of a multidisciplinary care team in both the hospital and community settings, and that patients may have difficulty accessing ophthalmologist/optometrist at the recommended appointment frequencies. The ESC noted that the proportion of patients who will be managed by optometrists versus ophthalmologists was unclear. Costs associated with ophthalmologist attendances are likely to be higher than those associated with optometrist attendances.

Financial Management – Risk Sharing Arrangements

6.79 The submission noted that a risk-sharing arrangement based on agreed budget impact estimates would be required for the PBS listing of belantamab mafodotin. The submission stated that utilisation beyond the expenditure cap would be associated with an alternative rebate level that is yet to be determined.

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

7 PBAC Outcome

7.1 The PBAC did not recommend belantamab mafodotin, in combination with bortezomib and dexamethasone (BmBd), for the treatment of relapsed and/or refractory multiple myeloma (RRMM) after one prior line of therapy. The PBAC considered that a broader listing for use in the wider RRMM setting, rather than just the second-line setting would be more appropriate. The PBAC noted that the trial evidence suggested that BmBd was associated with benefits in terms of progression free survival and overall survival compared to the comparator in the second line setting, daratumumab in combination with bortezomib and dexamethasone (DBd), but were concerned about the adverse events associated with BmBd. The PBAC considered that the dose modifications required to address the high rates of ocular toxicity and the recent listing of daratumumab, in combination with lenalidomide and dexamethasone (DLd), in the first line setting could affect the effectiveness of BmBd in clinical practice. The PBAC also considered that the incremental cost-effectiveness ratio (ICER) and financial estimates presented in the submission were high.

7.2 The PBAC considered that the primary reason for this outcome was the proposed place in therapy. The PBAC noted that restricting BmBd to the second line setting did not align with the clinical trial or with how clinicians would like to use MM therapies. The Multiple Myeloma Stakeholder meeting (July 2025)[20] advised that treatment sequencing could be improved if determined by prior drug exposure rather than lines of therapy and that optimal care was an individualised approach. The PBAC considered that the listing BmBd as a second line treatment only would restrict patient access not only to BmBd, but to other therapies (i.e., daratumumab and other BCMA-directed therapies). The PBAC also noted feedback from health professionals via the consumer comments portal which stated that restricting BmBd to the second line setting would make the treatment choice scenario in first relapse significantly worse and that flexibility in when these medications are used is needed. The PBAC considered that

[20] Multiple Myeloma Stakeholder Meeting Outcome Statement. July 2025. Available at: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/pbac-stakeholder-meetings/Multiple-Myeloma-Meeting-Outcome-Statement.pdf

BmBd should be listed for the treatment of RRMM (consistent with the proposed TGA indication) to allow physician discretion as to when in the clinical pathway it is used.

7.3 For the proposed second-line listing, the PBAC considered that the nomination of DBd as the comparator was appropriate. The PBAC noted that as DLd was recently PBS listed for use in the first line setting for transplant ineligible patients, the use of DBd in the second-line setting will likely reduce but considered that it would take a number of years for this change to affect the prevalent patient population. The PBAC also advised that if it were to consider a broader RRMM listing, a mixed comparator that consisted of daratumumab, carfilzomib, pomalidomide, selinexor and elotuzumab would be reasonable.

7.4 The PBAC noted that the submission was based the DREAMM-7 trial, which was a randomised trial comparing BmBd with DBd in patients who had received at least one prior line of therapy. The PBAC noted that the economic evaluation and financial estimates were based on the results of a subgroup of patients who had received lenalidomide in any prior line of therapy. The PBAC considered that the use of the intention to treat (ITT) population would have been more robust as although the majority of first-line therapy in Australia includes lenalidomide, the lenalidomide-exposed subgroup did not reflect the proposed second-line population in terms of prior lines of therapy (67% of patients had received more than one prior line of therapy).

7.5 In terms of effectiveness, the PBAC noted that the results of the DREAMM-7 trial supported the claim that BmBd was superior compared to DBd. BmBd was associated with statistically significant improvement over DBd in progression-free survival in the ITT population (HR = 0.46; 95% CI 0.35, 0.50) after approximately 40 months follow-up. BmBd was also associated with statistically significant improvement in overall survival (HR = 0.58; 95% CI: 0.43, 0.79).

7.6 The PBAC also accepted that claim that BmBd was inferior in term of safety compared to DBd noting that BmBd was associated with more serious adverse events, Grade 3 or 4 adverse events and more adverse events that resulted in discontinuation, dose reductions and dose interruptions. The PBAC also noted that BmBd was associated with any Grade ocular events that resulted in blurred vision, visual impairment, dry eye and photophobia. The PBAC noted that it was recommended that patients be assessed by an optometrist or ophthalmologist before commencing treatment and then again before the next 3 doses. The PBAC also noted that dose modifications were recommended to manage and reverse ocular adverse events and were concerned that this could affect the effectiveness of BmBd in the real world compared to in the clinical trial setting.

7.7 Given the issues with the proposed place in therapy, the PBAC considered that the economic model presented in the submission was largely uninformative. For the second-line only population, the PBAC considered that the ICER of $55,000 to < $75,000 per quality adjusted life year (QALY) was high and likely underestimated.

The PBAC considered that the following inputs were optimistic:

- The use of the lenalidomide-exposed subgroup, which was not adequately justified in the submission. The PBAC noted that use of the more robust ITT population increased the ICER to approximately $115,000 to < $135,000 per QALY;
- The use of the exponential function appeared to underestimate overall survival for patients in the DBd arm. Further, the modelled survival of patients in the BmBd arm was implausibly high, with 11% of patients remaining alive at 20 years; and
- Extrapolation of the trial data, from a median follow-up of 37.5 months in the DREAMM-7 trial to 20 years, was associated with a substantial amount of uncertainty. Further, the PBAC considered that the 20-year time horizon was long as the mean age of patients diagnosed with MM in Australia was 71.5 years.

7.8 Additionally, the PBAC considered that the economic model did not adequately capture the costs and quality of life impacts associated with severe ocular toxicity events.

7.9 The PBAC considered that the utilisation and financial impact estimates were largely uninformative, given the proposed place in therapy issues. The PBAC considered that a standard market share approach, accounting for increased survival, would have provided more accurate estimates of the initial population than the combined epidemiological/market share approach used as the submission assumed that BmBd will replace DBd. The PBAC noted that with the listing of DLd in the first line setting, the use of other drugs, such as BmBd would likely increase in the second and later line settings in approximately 3 to 4 years. Conversely, the potential PBS listing of the near market comparator, elranatamab, which is also an antibody targeting B-cell maturation antigen (BCMA), may reduce BmBd use.

7.10 In terms of a future restriction, the PBAC advised that:

- An Authority Required (telephone/online) listing for both the initial and continuing restrictions would be appropriate;
- Initial treatment of belantamab mafodotin should be in combination with bortezomib and dexamethasone, i.e. monotherapy should not be allowed;
- The listing should be consistent with the current daratumumab listing in terms of not including an ECOG score and being age agnostic;
- A cautionary note regarding ocular toxicity should be included and reference the need for eye exams prior to the first four doses of belantamab mafodotin; and
- The restriction should prevent use in patients who have received a prior BCMA therapy.

7.11 The PBAC considered a resubmission for belantamab mafodotin should address the following issues:

- Revise the place in therapy and present a resubmission based on a broader RRMM

listing;

- The comparator should be updated to a mixed basket of drugs (see paragraph 7.3);
- Provide a new economic model;
- Provide new financial estimates; and
- Provide a revised restriction that incorporates the advice presented in paragraph 7.10.

The resubmission may be lodged at any future standard due date for PBAC submissions using the standard re-entry pathway.

7.12 The PBAC noted the outcome from the Multiple Myeloma Stakeholder meeting stated that the assessment of sustained minimal residual disease (MRD) negativity may deliver substantial clinical and economic benefits by enabling treatment decisions that support treatment cessation, reduce unnecessary medication use and minimise toxicity. The PBAC noted that equitable access to funded technology to measure MRD would be required.

7.13 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:
Not recommended

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

GSK is disappointed by the decision not to recommend belantamab mafodotin (Blenrep®), in combination with bortezomib and dexamethasone (BVd). Equitable access to BVd for relapsed and/or refractory multiple myeloma (RRMM) is a priority for GSK, noting that the current PBS listings of drugs for RRMM create challenges in practice for the optimal sequencing of RRMM treatments. GSK will work with the PBAC to ensure such barriers to optimal care are resolved in a future resubmission.