SMC2727

belantamab mafodotin powder for concentrate for solution for infusion (Blenrep®)

GlaxoSmithKline

05 September 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission assessed under the orphan equivalent medicine process

belantamab mafodotin (Blenrep®) is accepted for restricted use within NHSScotland.

Indication under review: in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

SMC restriction: Patients with relapsed or refractory multiple myeloma eligible for second line treatment for whom lenalidomide is an unsuitable treatment option.

In an open-label phase III study in patients with relapsed or refractory multiple myeloma after at least one prior line of therapy, belantamab mafodotin in combination with bortezomib plus dexamethasone was associated with statistically significant improvements in progression-free survival compared with an anti-CD38 monoclonal antibody in combination with a proteasome inhibitor and a glucocorticoid.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Chair, Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Belantamab mafodotin is a humanised monoclonal antibody conjugated with a cytotoxic agent called maleimidocaproyl monomethyl auristatin F (mcMMAF). Belantamab mafodotin binds to cell surface B-cell maturation agent (BCMA) and is rapidly internalised. Once inside the tumour cell, the cytotoxic agent is released which leads to programmed cell death. The antibody also kills tumour cells by enhancing recruitment and activation of immune effector cells. In combination with bortezomib and dexamethasone, belantamab mafodotin is administered by intravenous infusion once every three weeks, at a starting dose of 2.5 mg/kg. Treatment should be continued until disease progression or unacceptable toxicity.[1]

1.2. Disease background

Multiple myeloma (MM) accounts for 2% of all new cancer cases every year in the UK, with 6,200 new cases each year.[2] The incidence of MM in Scotland is estimated to be 8.8 per 100,000 people.[3] MM predominantly affects older people and the median age at diagnosis is approximately 70 years, with more than 40% of new myeloma cases being diagnosed in those aged 75 years or above.[2] Patients with MM have a poor prognosis; based on data from 2015 to 2019, it is estimated that the 1-year and 5-year age-standardised net survival rates were 83% and 62% in Scotland, respectively.[4]

MM is a haematological cancer of plasma cells. This results in the destruction of bone and bone marrow, which can cause bone fractures, anaemia, increased susceptibility to infections, elevated calcium levels in the blood, kidney dysfunction and neurological complications. Despite being incurable current treatments can delay progression and improve quality of life. However, the condition is characterised by periods of remission and relapse (due to drug resistance), with each additional line of treatment being associated with reduced remission times and worse outcomes.[5, 6] Additionally, not all patients with MM are well enough to receive subsequent lines of therapy; in Europe around 95% of those diagnosed with MM receive first line (1L) treatment, of which 61% receive second line (2L) treatment, and around 38% receive third-line (3L).[7]

1.3. Company proposed position

Patients with relapsed or refractory multiple myeloma (RRMM) eligible for second line (2L) treatment for whom lenalidomide is an unsuitable treatment option.

1.4. Treatment pathway and relevant comparators

For MM, first line treatment is decided on a patient-by-patient basis and is dependent on various factors including age, symptoms, general health, and eligibility to receive high-dose induction chemotherapy with autologous stem cell transplantation (ASCT). There may also be geographical variation in prescribing patterns in Scotland. Multi-drug resistance is common, and class-switching between treatments is recommended upon disease progression and at each relapse. Treatment options for patients with MM include: glucocorticoids (dexamethasone, prednisolone), proteasome inhibitors (bortezomib, carfilzomib), histone deacetylase inhibitors (panobinostat),

immunomodulatory agents (thalidomide, lenalidomide, pomalidomide), anti-CD38 monoclonal antibodies (daratumumab, isatuximab), high-dose chemotherapy and ASCT.[6, 8, 9]

For patients with RRMM eligible for second line treatment for whom lenalidomide is an unsuitable treatment option, the submitting company state the relevant comparators are daratumumab in combination with bortezomib and dexamethasone (known as DVd) (SMC2180) and carfilzomib in combination with dexamethasone (known as Kd) (SMC1242/17). Clinical experts consulted by SMC agreed that DVd and Kd are the most relevant comparators and also highlighted that pomalidomide in combination with bortezomib plus dexamethasone (known as PVd) may be used.[10] Selinexor in combination with bortezomib and dexamethasone is accepted for restricted use by SMC for use in patients with lenalidomide-refractory MM where an anti-CD38 monoclonal antibody is not appropriate (SMC2674), however clinical expert responses suggest limited use.

1.5. Category for decision-making process

Eligibility for interim acceptance decision option

Belantamab mafodotin received an Innovation Passport allowing entry into the Innovative Licensing and Access Pathway.

Eligibility for a PACE meeting

Belantamab mafodotin meets SMC orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of belantamab mafodotin in combination with bortezomib plus dexamethasone for the treatment of patients who had progression of MM after at least one line of therapy comes from DREAMM-7. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant studies

Criteria	DREAMM-7[11]
Study design	International, randomised, open-label, phase III study.
Eligible patients	• Patients with MM who had received at least one line of therapy and had disease progression during or after the most recent therapy • Patients aged ≥ 18 years with Eastern Cooperative Oncology Group performance status of 0 to 2 • For patients who have undergone autologous stem cell transplant, they must have done so >100 days prior to initiating study treatment.
Treatments	• Belantamab mafodotin intravenously at a dose of 2.5 mg/kg on day 1 of 21-day cycles or • Daratumumab intravenously at a dose of 16 mg/kg every week in cycles 1 through 3 (total of nine doses), every 3 weeks in cycles 4 through 8 (total of five doses), and every 4 weeks in cycle nine and beyond. Both groups received bortezomib (administered subcutaneously at a dose of 1.3 mg/m^2 body surface area on days 1, 4, 8, and 11 of 21-day cycles) and dexamethasone (administered orally or intravenously at a dose of 20 mg on the day of and the day after bortezomib administration) for the first eight cycles. Treatment was continued until the

	occurrence of progressive disease, unacceptable toxic effects, withdrawal of consent, or death (whichever occurred first).
Randomisation	Patients were randomised in a 1:1 ratio. Randomisation was stratified according to Revised International Staging System stage at screening (I versus II or III), previous exposure to bortezomib (yes versus no), and the number of previous lines of therapy (one versus two or three versus. four or more).
Primary outcome	Progression-free survival, defined as the time from randomisation to the occurrence of documented disease progression or death from any cause. Disease progression was assessed by an independent review committee with the use of International Myeloma Working Group (IMWG) criteria.
Secondary outcomes	Overall survival, minimal residual disease-negative status, best overall response.
Statistical analysis	Efficacy analyses were performed in the intention-to-treat population, which included all patients who underwent randomisation. The familywise type I error was controlled at 2.5% (one-sided). Overall survival and duration of response were only allocated alpha upon successful rejection of the hypothesis for progression-free survival, and minimal residual disease would only be allocated alpha upon successful rejection of the hypothesis for overall survival.

In DREAMM-7, at data-cut October 2023, belantamab mafodotin in combination with bortezomib plus dexamethasone was associated with a statistically significant improvement in progression-free survival (PFS) compared with daratumumab in combination with bortezomib plus dexamethasone. The results for overall survival did not meet the significance criterion at this data-cut.[11] See Table 2.2 for details.

Table 2.2. Summary of DREAMM-7 study key results (ITT population; data-cut October 2023).[11]

	Belantamab mafodotin, bortezomib, dexamethasone (n=243)	**Daratumumab, bortezomib, dexamethasone (n=251)**
Median duration of follow-up	28.2 months	
Primary outcome: PFS (IRC, IMWG 2016 criteria)		
Events, n	91	158
Median PFS	36.6 months	13.4 months
Hazard ratio (95% CI)	0.41 (0.31 to 0.53) p<0.001	
12-month PFS estimate	78%	53%
Secondary outcome: overall survival		
Events, n	54	87
Median OS	NR	NR
Hazard ratio (95% CI)	0.57 (0.40 to 0.80)	
12-month OS estimate	87%	81%
Secondary outcome: minimal residual disease-negative status (IRC, IMWG 2016 criteria)*		
Patients with complete response or better	25% (60/243)	10% (24/251)
Secondary outcome: best overall response (IRC, IMWG 2016 criteria)		
Complete response or better	35% (84/243)	17% (42/251)
Partial response or better	83% (201/243)	71% (179/251)

*MRD-negative status was determined based on next-generation sequencing with a sensitivity of 10^{-5} or lower.

Abbreviations: CI = confidence interval; IMWG = International Myeloma Working Group; IRC = independent review committee; ITT = intention-to-treat; NR = not reached; OS = overall survival; PFS = progression-free survival

Since submitting to SMC, a subsequent data-cut (October 2024) of DREAMM-7 has been made available. At this data-cut, a statistically significant overall survival benefit favouring belantamab mafodotin in combination with bortezomib plus dexamethasone has been reported; hazard ratio = 0.58 (95% CI: 0.43 to 0.79). The number of events (deaths) in the belantamab mafodotin combination group and the daratumumab combination group were 68 (28%) and 103 (41%) respectively. Median OS was not reached in either treatment group.[12]

2.2. Evidence to support the positioning proposed by the submitting company

The submitting company consider the ITT population to be the most representative of the proposed positioning, however they note that the lenalidomide-refractory subgroup is of particular interest. In the belantamab mafodotin combination and daratumumab combination groups, 79 (33%) patients and 87 (35%) patients had disease refractory to lenalidomide, respectively; the hazard ratio for PFS (independent review committee assessed) was 0.37 (95% CI: 0.24 to 0.56).[11]

2.3. Health related quality of life outcomes

Health Related Quality of Life (HRQoL) was assessed using the global health status and quality of life domains of the European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30). For the global health status domain, no substantial differences between treatment groups were observed.[11]

2.4. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence comparing belantamab mafodotin in combination with bortezomib plus dexamethasone with several comparators, the submitting company presented an indirect treatment comparison. This has been used to inform the economic base case for the comparison versus carfilzomib plus dexamethasone.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Bayesian Network Meta Analysis (NMA)
Population	Adults (aged ≥18 years) with documented MM, previously treated with at least one prior line of therapy, and with documented disease progression during or after most recent therapy.
Comparators	The company considered carfilzomib plus dexamethasone (56 mg/m^2 body surface area twice weekly) and daratumumab plus bortezomib plus dexamethasone to be the relevant comparators. Other treatments were included in the NMA, including pomalidomide plus bortezomib plus dexamethasone.
Studies included	DREAMM-7[11], CASTOR[13, 14], ENDEAVOUR[15], OPTIMISMM[16], and LEPUS[17, 18].
Outcomes	PFS, overall survival.
Results	Results of the indirect treatment comparison suggest a PFS and OS benefit for belantamab mafodotin in combination with bortezomib plus dexamethasone versus the relevant comparators: daratumumab in combination with bortezomib plus dexamethasone, carfilzomib in combination with dexamethasone and pomalidomide in combination with bortezomib plus dexamethasone.

*Other data were also assessed but remain confidential.**

3. Summary of Safety Evidence

Evidence from DREAMM-7 supports the relative safety of belantamab mafodotin in combination with bortezomib plus dexamethasone compared with daratumumab in combination with bortezomib plus dexamethasone in patients with relapsed or refractory MM after at least one line of therapy. Daratumumab plus bortezomib plus dexamethasone is a relevant comparator in this setting. At data-cut October 2023, the median total duration of exposure to any study medicine was 15.9 months in the belantamab mafodotin combination group and 12.9 months in the daratumumab combination group.[11]

The percentage of patients with a grade 3 or higher adverse event (AE) was 95% in the belantamab mafodotin plus bortezomib plus dexamethasone group and 78% in the daratumumab plus bortezomib plus dexamethasone group; the percentage of patients with serious AEs was 50% and 37% respectively; AEs leading to discontinuation of any study treatment (considered treatment related by investigator) was 26% versus 15% respectively; 10% and 7.7% died from serious AEs.[11]

The most frequent adverse reactions (≥20%) with belantamab mafodotin in combination with bortezomib plus dexamethasone included reduced visual acuity (89%), thrombocytopenia and/or platelet count decrease (87%), corneal examination findings (86%), blurred vision (66%), dry eye (51%), photophobia (47%), foreign body sensation in eyes (44%), eye irritation (43%), eye pain (32%), diarrhoea (32%), and upper respiratory tract infection (20%).[1]

Patients should have an ophthalmic examination (including visual acuity and slit lamp examination) performed by an eye care professional before each of the first four doses of belantamab mafodotin, and as clinically indicated thereafter. Patients are advised to administer preservative-free artificial tears during treatment as this may reduce ocular symptoms.[1]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Belantamab mafodotin has a novel mechanism of action and is the first antibody-drug conjugate that targets BCMA for patients with relapsed or refractory MM.
- Evidence from DREAMM-7 provides direct data for belantamab mafodotin in combination with bortezomib plus dexamethasone versus daratumumab in combination with bortezomib plus dexamethasone, which is a relevant active comparator in this setting.
- In DREAMM-7, belantamab mafodotin in combination with bortezomib plus dexamethasone was associated with a statistically significant and clinically relevant improvement in PFS compared with daratumumab plus bortezomib plus dexamethasone; median PFS was 36.6 months in the belantamab mafodotin combination group versus 13.4 months in the daratumumab combination group; 12-month PFS estimates were 78% and 53% respectively.[11]

4.2. Key uncertainties

- There are no direct data comparing belantamab mafodotin in combination with bortezomib plus dexamethasone with other relevant comparators, namely carfilzomib plus dexamethasone, or pomalidomide in combination with bortezomib plus dexamethasone. The indirect treatment comparison had several important limitations: the population used in the NMA does not reflect the proposed positioning; patients at later treatment lines were included and the proportions of patients with prior lenalidomide exposure were unknown or lower than what might be expected. There was clear heterogeneity in the baseline characteristics of patients, including notable differences in prior treatments, and length of follow-up. The network consisted of mainly single studies to support treatments, and there were no closed loops, which adds uncertainty. Overall survival data from included studies can also be considered immature. Given the limitations described the results of the NMAs were highly uncertain.
- Overall survival data from DREAMM-7 are immature. Data from the latest data-cut (October 2024) have reached 35% (171/494 patients) overall maturity.[12] Further data are awaited.
- There are some uncertainties regarding the generalisability of the DREAMM-7 study to proposed positioning in the NHSScotland population: for second line treatment in patients whom lenalidomide is an unsuitable option. The profile of prior treatments is unlikely to align: in DREAMM-7 approximately 51% of patients had one prior line of therapy, approximately 52% had previous treatment with lenalidomide and 1.4% had previously received daratumumab (a commonly used first line option in NHSScotland). The treatment pathway has changed considerably since DREAMM-7 started recruitment which may partially explain the differences in prior treatments. Real-world evidence submitted by the company suggest the relevant population seen in practice may be older and less fit than those in the DREAMM-7 study. [11, 19]
- DREAMM-7 was an open-label study, which may bias some outcomes such as safety and HRQoL outcomes. Furthermore, HRQoL was not adjusted for multiplicity and should therefore be interpreted with caution.
- The toxicity profile of belantamab mafodotin in combination with bortezomib plus dexamethasone appeared less favourable than daratumumab in combination with bortezomib plus dexamethasone: grade 3 or higher AEs 95% versus 78%, serious AEs 50% and 37% respectively.[11] Most patients treated with belantamab mafodotin develop ocular symptoms that can impact their quality of life. However, overall the safety profile is considered manageable with additional risk minimisation measures in place.[20]

4.3. Innovative Licensing and Access Pathway (ILAP)

Further data-cuts of DREAMM-7 are expected in the future, which will provide further overall survival data but is unlikely to address the other key uncertainties identified.

4.4. Clinical expert input

Clinical experts consulted by SMC considered that belantamab mafodotin in combination with bortezomib plus dexamethasone fills an unmet need and is a therapeutic advance in this area since the clinical evidence suggests it is an effective treatment regimen which includes a different class of medicine compared to currently available treatments.

4.5. Service implications

Clinical experts consulted by SMC considered that the introduction of this medicine may impact on the patient and the service. Patients require ophthalmic examinations performed by eye care professionals before the first four doses and as clinically indicated thereafter.[1] Belantamab mafodotin (in combination with bortezomib plus dexamethasone) is initially administered as an intravenous infusion once every three weeks which will likely be administered at chemotherapy day units; intervals between doses may increase over time to manage adverse events. Management of other adverse events, such as grade 3 or above infections, may also require additional resource from the service.

5. Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of **belantamab mafodotin**, as an **orphan equivalent** medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- MM is a highly individual, rare and complex cancer originating from abnormal plasma cells in the bone marrow. The condition is most prevalent in older age, however there is a spectrum of ages at diagnosis, including relatively young adults being affected. Patients with myeloma have a poor prognosis and the complications of myeloma can be significant, debilitating and painful; they include severe bone pain, bone destruction (which is often disabling), kidney damage (sometimes requiring dialysis), fatigue and a depleted immune system that can lead to increased infections. It is an incurable cancer that is defined by periods of disease remissions and relapses. The constant possibility of relapse completely disrupts the lives of patients and their families and has a huge psychological impact.
- Current treatments for myeloma can halt its progress and improve quality of life, however there is no cure and for each relapse the condition generally becomes more resistant to treatment and patients' quality of life reduces. Myeloma remains a challenging cancer to treat, particularly for relapsed patients. In the first line, patients are commonly started on three or four medicines with different mechanisms of action and can become refractory to treatment or unable to tolerate treatments, leaving patients with unsatisfactory treatment options in the second line. There is therefore a high unmet need for additional effective treatment options at the second line and beyond. Additional treatment options are essential for myeloma, as one size does not fit all.
- Belantamab mafodotin in combination with bortezomib plus dexamethasone is expected to deliver higher response rates and longer remission times compared to the most widely used,

currently available treatments. Patients value treatments which control their myeloma, keep them in remission for as long as possible, prolong their life and allow them to enjoy a stable, normal, day-to-day life. Achieving the best possible response and reaching remission improves quality of life in several ways; it slows disease progression, reduces symptom burden and lessens anxiety about the future. Belantamab mafodotin is the first BCMA targeted antibody-drug conjugate to be licensed for relapsed or refractory myeloma. With its novel mechanism of action, belantamab as a new treatment option would be highly valued by clinicians and patients as it offers greater choice. It would also provide benefits for families and carers; increased remission times can give families longer, higher-quality time together and reduced hospital visits would be beneficial for patients, families/carers, and oncology units.

- Belantamab mafodotin is known to be associated with ocular side effects. However, PACE participants agreed that these side effects were generally manageable, reversible and tend to occur close to initiation of treatment and may improve over time. Although patients perceive the eye-related side effects of this treatment as a disadvantage, they do not believe that this takes away from its overall benefit and are willing to accept side effects in exchange for long-term benefits. Both clinicians and patients feel that side effects of belantamab mafodotin can be effectively managed through suitable ophthalmological care and careful dosing.
- PACE participants would like belantamab mafodotin in combination with bortezomib plus dexamethasone to be made available in NHSScotland as per the licensed indication: for the treatment of adult patients with MM who have received at least one prior therapy. They highlighted that many patients have not received the currently recommended first line medicines due to the rapidly evolving development of the pathway, and as a result there may be patients who are not eligible to receive this treatment because they have not previously received lenalidomide. Clinicians would also value the flexibility of being able to prescribe belantamab mafodotin in later lines of therapy.

Additional Patient and Carer Involvement

We received a patient group submission from Myeloma UK which is a registered charity. Myeloma UK has received 4.8% pharmaceutical company funding in the past two years, including from the submitting company. A representative from Myeloma UK participated in the PACE meeting. The key points of their submission have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

An economic case was presented and is summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis.
Time horizon	A lifetime time horizon of 36 years.
Population	Patients with MM who have received one prior therapy.
Comparators	The comparators were daratumumab in combination with bortezomib plus dexamethasone (DVd) and carfilzomib (56mg/m^2 twice weekly) plus dexamethasone (Kd).

Model description	A four-state partitioned survival model was used with health states of progression-free (on treatment), progression-free (off treatment), progressed disease and death. All patients enter the model in the progression-free (on treatment) health state. Patients could thereafter transition to the progression-free (off treatment), progressed disease or death health states. Patients in the progression-free (off treatment) health state could transition to progressed disease or death. Progressed disease patients could transition to the death health state.
Clinical data	Data on PFS, overall survival, time to treatment discontinuation (TTD) and adverse events for belantamab mafodotin in combination with bortezomib plus dexamethasone (BVd) and DVd were sourced from DREAMM-7 (ITT population)[11]. For Kd, hazard ratios for PFS, overall survival and TTD (using a PFS proxy) were from the NMA. Adverse events were from the CANDOR study[21].
Extrapolation	BVd and DVd PFS were extrapolated using separately fitted exponential distributions. Kd PFS was extrapolated using the Kd versus DVd PFS hazard ratio. BVd and DVd overall survival were extrapolated using separately fitted Weibull distributions. Due to the immaturity of overall survival data in DREAMM-7, informative priors derived from the CASTOR study were used to inform the shape parameter in the extrapolation of overall survival for DVd. Kd overall survival was extrapolated using the Kd versus DVd overall survival hazard ratio. BVd and DVd TTD were extrapolated using separately fitted Weibull distributions. Kd TTD was extrapolated through a PFS proxy, by applying the Kd versus DVd PFS hazard ratio to the DVd TTD.
Quality of life	EQ-5D-3L data from DREAMM-7 were used to derive health state utility values for progression-free (both on treatment and off treatment) and progressed disease. Utility values were adjusted for age. Adverse event disutilities were also included. Ocular adverse event disutilities were not included in the base case as the submitting company viewed these as captured in the health state utilities.
Costs and resource use	Costs included in the model were medicine acquisition, administration costs, subsequent treatments, adverse events (ocular and non-ocular), disease management and terminal care costs. The submitting company applied an individual patient level data dosing approach for belantamab mafodotin which impacted the estimation of medicine acquisition costs. The approach was justified on the basis that it provided greater granularity in capturing dose modifications observed in DREAMM-7.
PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price. A PAS discount is in place for daratumumab and carfilzomib and these were included in the results used for decision-making by using estimates of the comparator PAS price.

6.2. Results

The company presented results comparing belantamab mafodotin in combination with bortezomib plus dexamethasone (BVd) to daratumumab in combination with bortezomib plus dexamethasone (DVd) and carfilzomib (56mg/m2 twice weekly) in combination with dexamethasone (Kd). SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present these results due to competition law issues.

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered for the comparators described in section 6.2 and descriptions of these key scenarios are provided in Table 6.2.

Table 6.2: Scenario analysis

	Parameter	Base case	Scenario
	Base case		
1a	Time horizon	36 years	30 years
1b			15 years
2a	PFS – BVd	Exponential	Weibull
2b			PFS HRs BVd versus DVd (DVd baseline)
3a	PFS – DVd	Exponential	Lognormal
3b			PFS HRs DVd versus BVd (BVd baseline)
4a	OS – BVd	Weibull	Exponential
4b			Weibull - subsequent treatment adjustment
4c			OS HRs BVd versus DVd (DVd baseline)
5a	DVd- OS	Informative prior Weibull	Informative prior log-logistic
5b			No informative prior Weibull
5c			Weibull - subsequent treatment adjustment
5d			OS HRs DVd versus BVd (BVd baseline)
6a	Method of OS survival analysis	Direct extrapolation	PFS:OS surrogacy (DVd baseline for Kd)
6b			PFS:OS surrogacy (BVd baseline for Kd)
7	BVd TTD	Weibull	Lognormal
8	Kd TTD	PFS HR proxy	TTD=PFS
9	Utilities	DREAMM-7	ENDEAVOR (PFS = 0.74 PD = 0.67)
10	RDI	IPD-based dosing belantamab mafodotin	Mean RDI from DREAMM-7 for belantamab mafodotin
11	Ocular AE disutilities	Excluded	Included
12a	Population	DREAMM-7 ITT	DREAMM-7 ITT lenalidomide refractory
12b			DREAMM- 7 second line only
13	Data-cut	DREAMM-7 IA1	DREAMM-7 IA2
C1	3a and 7. BVd OS exponential and BVd TTD lognormal.		
C2	C1 and 9 and 11. C1 with the inclusion of ocular disutilities and ENDEAVOR utility values.		
C3	C1 and C2 and 10. C1 and C2 with mean RDI used.		

Abbreviations: AE = adverse event; BVd = belantamab mafodotin in combination with bortezomib plus dexamethasone; C = combined scenario; DVd = daratumumab in combination with bortezomib plus dexamethasone; Kd = carfilzomib (56mg/m^2 twice weekly) in combination with dexamethasone; HR = hazard ratio; IA = interim analysis; ICER = cost-effectiveness ratio; Incr = incremental; IPD = individual patent level data; ITT = intention to treat; OS = overall survival; PD = progressed disease; PFS = progression-free survival; QALY = quality-adjusted life years; RDI = relative dose intensity; TTD = time to treatment discontinuation.

6.4. Key strengths

- A partitioned survival model was an appropriate choice for the economic model.
- The efficacy data for BVd and DVd were sourced from a randomised phase III study.
- The sources used to value medicine and resource use costs were appropriate.

6.5. Key uncertainties

- Pomalidomide in combination with bortezomib plus dexamethasone (PVd) was not included in the economic analysis. SMC clinical experts highlighted this regimen as a potential displaced comparator. While some SMC experts noted low patient uptake, this was not unanimous, reflecting the complexity of the treatment pathway. The submitting company was asked to provide exploratory cost-effectiveness analysis versus this comparator, but this was not provided.
- There were uncertainties in the relevance of the DREAMM-7 ITT population used in the economic model to the proposed positioning. The ITT population did not align with the proposed positioning, that of patients with relapsed or refractory MM eligible for second-line treatment for whom lenalidomide is an unsuitable treatment option. The submitting company highlighted that the most relevant subgroup, of second line-only patients who are lenalidomide refractory, had a low patient count in DREAMM-7 and would create a high degree of uncertainty in the economic analysis. Due to its large sample size and more complete NMA data, the ITT population was viewed as the most robust. Subgroup analyses were available for both lenalidomide refractory and second line only, but these were subject to additional limitations (Scenarios 12a and 12b). There was a lack of NMA data to inform overall survival for Kd extrapolations in these subgroups. Furthermore, the low proportion of lenalidomide refractory patients in DREAMM-7 increased concerns about the generalisability of the second line only subgroup's economic results to clinical practice. However, this concern would also be present in the ITT population. In summary, without robust data in the most relevant subgroup for the positioning, there remains uncertainty in the generalisability of the economic results to the proposed population.
- The overall survival data from DREAMM-7 were immature which led to uncertainties in the extrapolation of overall survival outcomes. Firstly, more conservative plausible overall survival curves of the exponential and log-logistic were considered to extrapolate BVd and DVd overall survival, respectively (Scenarios 4a and 5a). The exponential curve was considered for BVd as its landmark estimates were more consistent with the bounds of company clinical expert opinion. Secondly, as proportional hazards assessments for overall survival were inconclusive, scenario analysis considered applying the hazard ratios for BVd versus DVd (Scenario 5d). Thirdly, the submitting company used an informative prior method to reduce uncertainty in overall survival extrapolations for DVd. To consider uncertainty with this approach, it was removed in scenario analysis (Scenario 5b). Finally, an alternative overall survival extrapolation method of PFS:OS surrogacy was considered to account for overall survival data immaturity, in which hazard ratios derived from relapsed or refractory MM studies for each comparator were applied to the PFS curve to estimate overall survival for each comparator (Scenarios 6a and 6b). These issues highlight multiple challenges in extrapolating the overall survival data from DREAMM-7 and the resulting uncertainty in economic results.
- There was uncertainty in the extrapolation of TTD in the BVd arm. A more conservative plausible alternative curve, with landmark estimates within company clinical expert opinion, was the lognormal (Scenario 7). This increased BVd acquisition costs in the

economic model. However, it was subject to a limitation whereby the TTD and PFS curves crossed at approximately 10 years, with all progression-free patients from this point onwards receiving BVd treatment.

- There was uncertainty in the use of the individual patient level data dosing approach for belantamab mafodotin. The submitting company justified the approach on the basis that it provided greater granularity in reflecting dose modifications observed in DREAMM-7. The company viewed that the mean relative dose intensity (RDI) would be biassed toward earlier points in follow-up, when more patients remained on belantamab mafodotin, and would therefore overestimate belantamab mafodotin acquisition costs. SMC statistical support noted that given the RDI appeared to be decreasing over time, the general approach was potentially supportable. However, SMC statistical support emphasised that the approach lacked sufficient rigour to adequately characterise the uncertainty associated with it. As there is no precedent for the individual patient level dosing approach, the use of mean RDI, which is more commonly adopted, was considered in Scenario 10.
- There were uncertainties in the NMA, which in turn created uncertainty in the PFS and overall survival hazard ratios for Kd. As this affects the survival extrapolations for this comparator, their confidence interval bounds were considered in one-way deterministic sensitivity analysis. While this provides insight into the uncertainties, it may not comprehensively capture the extent of the limitations associated with the NMA.
- There were uncertainties in the utility values. Firstly, the progressed disease utility value was higher than previously seen in prior UK HTA submissions for MM with at least one prior therapy (SMC2290, SMC2180 and SMC 2301). Given this, a scenario applied the utility values from the ENDEAVOR study (Scenario 9). Secondly, ocular AE disutilities were excluded in the base case. However, given the ocular adverse events in the BVd arm of DREAMM-7, these were included as a scenario (Scenario 11). Finally, as DREAMM-7 was an open-label study, this may bias HRQoL outcomes.

7. Conclusion

The Committee considered the benefits of belantamab mafodotin in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that the as belantamab mafodotin is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, and after application of the appropriate SMC modifiers, the Committee accepted belantamab mafodotin for restricted use in NHSScotland.

8. Guidelines and Protocols

The British Society for Haematology (BSH) published “Guidelines on the diagnosis, investigation and initial treatment of myeloma: a British Society for Haematology/UK Myeloma Forum Guideline” in March 2021.[22]

The European Society for Medical Oncology (ESMO) and the European Haematology Association (EHA) published “Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up" in February 2021.[8]

The National Institute for Health and Care Excellence (NICE) published “Myeloma: diagnosis and management” (NG35) in February 2016, which was updated in October 2018.[23]

The European Myeloma Network published “European Myeloma Network guidelines for the management of multiple myeloma-related complications” in October 2015 and published “From transplant to novel cellular therapies in multiple myeloma: European Myeloma Network guidelines and future perspectives” in February 2018.[24, 25]

9. Additional Information

9.1. Product availability date

17 April 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per cycle (£)
Belantamab mafodotin (in combination with daratumumab plus dexamethasone)	**30-minute intravenous infusion once every three weeks, at a starting dose of 2.5 mg/kg**	**£23,568**

Costs from NHS Dictionary of Medicines and Devices Browser (dm+d) on 28 May 2025. Costs calculated using the full cost of vials assuming wastage and using a bodyweight of 70 kg. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 11 July 2025**.**

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A Patient Access Scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a Patient Access Scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.