SMC2747

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 not recommended for use within NHSScotland.

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

In an open-label phase III study in patients with relapsed or refractory multiple myeloma who had previously received lenalidomide, belantamab mafodotin in combination with pomalidomide plus dexamethasone was associated with statistically significant improvements in progression-free survival compared with an immunomodulatory agent in combination with a proteasome inhibitor and a glucocorticoid.

The submitting company's justification of the treatment's cost in relation to its health benefits was not sufficient and in addition the company did not present a sufficiently robust economic analysis to gain acceptance by SMC.

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 pomalidomide and dexamethasone, belantamab mafodotin is administered by intravenous infusion once every four weeks, with a starting dose of 2.5 mg/kg given once in cycle 1 (each cycle is a 28-day period). From cycle 2 onwards, belantamab mafodotin is dosed at 1.9 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 pomalidomide plus dexamethasone for the treatment of patients with lenalidomide exposed relapsed or refractory MM comes from DREAMM-8. Details are summarised in table 2.1.

Table 2.1. Overview of relevant studies

Criteria	DREAMM-8[11, 12]
Study design	International, randomised, open-label, phase III study.
Eligible patients	• Patients with MM who had been treated with at least one line of therapy that included lenalidomide and who had progressive disease during or after the most recent therapy • Eastern Cooperative Oncology Group performance status of 0 to 2 • Patients with a history of autologous stem cell transplant must have undergone transplant at least 100 days prior to enrolment.
Treatments	• 28-day cycles of belantamab mafodotin 2.5 mg/kg intravenously on day 1 of cycle 1 and 1.9 mg/kg on day 1 of cycle 2 onward combined with pomalidomide and dexamethasone or • bortezomib 1.3 mg/m^2 body surface area subcutaneously on days 1, 4, 8, and 11 of cycles 1 through 8 and days 1 and 8 of cycle 9 onward combined with pomalidomide and dexamethasone. Treatment was to continue until the occurrence of progressive disease, unacceptable adverse effects, withdrawal of consent, or death (whichever occurred first).
Randomisation	Patients were randomised in a 1:1 ratio. Randomisation was stratified according to the number of previous lines of therapy they had received (one, two or three, or four or more), previous exposure to bortezomib (yes or no), and whether anti-CD38 antibodies had been received previously (yes or no).

Primary outcome	Progression-free survival, defined as the time from randomisation to the earliest date of disease progression based on assessment by an independent review committee (per International Myeloma Working Group 2016 criteria) or death from any cause.
Secondary outcomes	Overall survival, minimal residual disease (MRD)-negative status, best overall response.
Statistical analysis	Efficacy analyses were performed in the intention-to-treat population, which included all patients who underwent randomisation. A hierarchical statistical testing strategy was applied in the study with no formal testing of outcomes after the first non-significant outcome in the hierarchy. Therefore, the results reported for these outcomes are descriptive only and not inferential (no p-values reported). Outcomes were tested sequentially in the following order: progression-free survival, overall survival and MRD-negative status.

In DREAMM-8, at data-cut 29 January 2024, belantamab mafodotin in combination with pomalidomide plus dexamethasone was associated with a statistically significant improvement in progression-free survival (PFS) compared with pomalidomide in combination with bortezomib plus dexamethasone. See Table 2.2 for details.

Table 2.2. Summary of DREAMM-8 study key results (ITT population).[11]

	Belantamab mafodotin, pomalidomide, dexamethasone (n=155)	**Pomalidomide, bortezomib, dexamethasone (n=147)**
Median duration of follow-up	22.4 months	20.5 months
Primary outcome: progression-free survival (IRC, IMWG 2016 criteria)		
Events, n	62	80
Median PFS	NR	12.7 months
Hazard ratio (95% CI)	0.52 (0.37 to 0.73) p<0.001	
12-month PFS estimate	71%	51%
Secondary outcome: overall survival		
Events, n	49	56
Median OS	NR	NR
Hazard ratio (95% CI)	0.77 (0.53 to 1.14)	
12-month OS estimate	83%	76%
Secondary outcome: minimal residual disease-negative status (IRC, IMWG 2016 criteria)*		
Patients with complete response or better	24%	4.8%
Secondary outcome: best overall response (IRC, IMWG 2016 criteria)		
Complete response or better	40%	16%
Partial response or better	77%	72%

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

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 a post-hoc subgroup analysis in the lenalidomide-refractory subgroup, similar PFS results were observed with belantamab mafodotin in combination with pomalidomide plus dexamethasone versus pomalidomide plus bortezomib plus dexamethasone. Another potential subgroup of interest is patients with one prior line of therapy, which was consistent with the primary findings (HR = 0.52, 95% CI: 0.31 to 0.88).[11, 13]

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). These showed no clinically meaningful change from baseline in either treatment group over time. Similar results were also observed in physical and role functioning, fatigue and pain.[11]

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

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

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. Patients had also prior exposure to lenalidomide.
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-8[11], CASTOR[14], ENDEAVOR[15] and OPTIMISMM[16].
Outcomes	Progression-free survival, overall survival.
Results	Results of the indirect treatment comparison suggest a PFS benefit for belantamab mafodotin in combination with pomalidomide plus dexamethasone versus carfilzomib plus dexamethasone and pomalidomide plus bortezomib plus dexamethasone; versus daratumumab plus bortezomib plus dexamethasone credible intervals spanned one meaning the results are uncertain and there may not be a difference between the treatments . For OS, central estimates of treatment effect favoured belantamab mafodotin plus pomalidomide plus dexamethasone versus relevant comparators however credible intervals spanned one, meaning the results are uncertain and there may not be a difference between the treatments.

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

3. Summary of Safety Evidence

Evidence from DREAMM-8 supports the relative safety of belantamab mafodotin in combination with pomalidomide plus dexamethasone compared with pomalidomide in combination with bortezomib plus dexamethasone in lenalidomide exposed patients who had relapsed or refractory myeloma after at least one line of therapy. Pomalidomide plus bortezomib plus dexamethasone is a relevant comparator in this setting. At data-cut 29 January 2024, the median total duration of exposure was 16.5 months for the belantamab mafodotin plus pomalidomide plus dexamethasone group and 8.5 months for the pomalidomide plus bortezomib plus dexamethasone group.[11]

The percentage of patients with grade 3 or higher adverse events (AEs) was 94% in the belantamab mafodotin plus pomalidomide plus dexamethasone group and 76% in the pomalidomide plus bortezomib plus dexamethasone group; the percentage of patients with serious AEs was 63% and 45% respectively; AEs leading to permanent discontinuation of any study treatment was 15% versus 12% respectively; fatal AEs was 11% in both groups.[11]

The most frequent adverse reactions (≥20%) in belantamab mafodotin plus pomalidomide plus dexamethasone included reduced visual acuity (91%), corneal examination findings (87%), blurred vision (79%), neutropenia (63%), foreign body sensation in eyes (61%), dry eye (61%), thrombocytopenia (55%), eye irritation (50%), photophobia (44%), eye pain (33%), fatigue (27%), upper respiratory tract infection (27%), pneumonia (24%), anaemia (23%), and diarrhoea (23%).[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-8 provides direct data for belantamab mafodotin in combination with pomalidomide plus dexamethasone versus pomalidomide in combination with bortezomib plus dexamethasone, which is a relevant active comparator in this setting.
- In DREAMM-8, belantamab mafodotin in combination with pomalidomide plus dexamethasone was associated with a statistically significant and clinically relevant improvement in PFS compared with pomalidomide plus bortezomib plus dexamethasone; median PFS was not reached in the belantamab mafodotin combination group versus 12.7 months in the pomalidomide combination group; 12-month PFS estimates were 71% and 51% respectively.[11]

4.2. Key uncertainties

- There are no direct data comparing belantamab mafodotin in combination with pomalidomide plus dexamethasone with other relevant comparators, namely

daratumumab in combination with bortezomib plus dexamethasone or carfilzomib 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. There were notable between-study differences in 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, and there was a paucity of data in the daratumumab combination study for the lenalidomide exposed population which adds further uncertainty. Overall, given the limitations described the results of the NMA were highly uncertain.

- Overall survival data from DREAMM-8 are immature. At data-cut January 2024, data have reached 35% (105/302 patients) overall maturity.[17] Further data are awaited.
- In the pomalidomide, bortezomib, and dexamethasone treatment group, 24% were refractory to proteasome inhibitors (bortezomib [5%], carfilzomib [16%], ixazomib [7%]) at baseline.[11] For some of these patients, retreatment with bortezomib may have been suboptimal, and consequently the treatment effect of belantamab mafodotin, pomalidomide, dexamethasone relative to this treatment group could be overestimated.
- There are some uncertainties regarding the generalisability of the DREAMM-8 study to proposed positioning in the NHSScotland population: for second line treatment in patient whom lenalidomide is an unsuitable option. The profile of prior treatments is unlikely to align: in DREAMM-8 approximately 53% of patients had one prior line of therapy, approximately 26% had previously received daratumumab (a commonly used first line option in NHSScotland). The treatment pathway has changed considerably since DREAMM-8 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-8 study. Lastly, Black patients were not represented in the study which is not reflective of the epidemiologic profile for MM.[11, 18]
- There were imbalances in patient baseline characteristics, namely patients aged 75 years or older (12% versus 24%); patients with baseline extramedullary disease (13% versus 7.5%); male patients (64% versus 56%); previous ASCT (64% versus 56%); previous chemotherapy (70% versus 59%); refractory to lenalidomide (81% versus 76%). It is unclear how these imbalances impacted the primary results.[11]
- DREAMM-8 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 pomalidomide plus dexamethasone appeared less favourable than pomalidomide in combination with bortezomib plus dexamethasone: grade 3 or higher AEs 94% versus 76%, serious AEs 63% and 45% 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.[19]

4.3. Innovative Licensing and Access Pathway (ILAP)

A subsequent data-cut of DREAMM-8 is expected in the near 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 pomalidomide 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 pomalidomide plus dexamethasone) is initially administered as an intravenous infusion once every four 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 pomalidomide 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 mafodotin 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. Both belantamab mafodotin and pomalidomide are not used in the first line and would be particularly useful to have this combination as a treatment option in the second-line, and could be useful for patients who are unable to take bortezomib (for example patients with peripheral neuropathy).
- 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 pomalidomide 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 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	33.9 years
Population	Patients with relapsed or refractory MM eligible for second line (2L) treatment for whom lenalidomide is an unsuitable treatment option.
Comparators	Belantamab mafodotin in combination with pomalidomide plus dexamethasone (BPd) was compared to daratumumab in combination with bortezomib plus dexamethasone (DVd) and carfilzomib (56mg/m^2 twice weekly) in combination with dexamethasone (Kd).
Model description	A cohort-based partitioned survival model was used with four health states: progression-free on treatment, progression-free off treatment, progressed disease and death. The separate health states for patients on and off treatment in the progression-free state were included to reflect some patients in DREAMM-8 withdrawing from active treatment before disease progression. Different utility values were applied in the progression-free health states depending on whether patients were on or off treatment.
Clinical data	Data on PFS, overall survival, time to treatment discontinuation (TTD) and AEs for BPd and pomalidomide in combination with bortezomib plus dexamethasone (PVd) were from DREAMM-8. For DVd and Kd, PFS and overall survival hazard ratios were applied from the NMA to extrapolated PVd PFS and overall survival data from DREAMM-8. For DVd and Kd TTD, respective PFS hazard ratios from the NMA were applied to extrapolated PVd TTD data.
Extrapolation	The company extrapolated long-term overall survival, PFS and TTD for BPd and PVd for use in the economic model using parametric survival modelling with independently fitted distributions. Curve selection was based on goodness of fit statistics (AIC/BIC), visual fit and clinical expert opinion. This resulted in the selection of independently fitted: Weibull distributions for BPd and PVd PFS; exponential distributions for BPd and PVd overall survival; Weibull distributions for BPd and PVd TTD. The relative efficacy of Kd and DVd was estimated by applying hazard ratios from the NMA that compared each to PVd. These hazard ratios were applied to extrapolated PVd survival curves for the economic analysis. DVd and Kd TTD were estimated by applying each medicine's respective PFS hazard ratio from the NMA comparison to PVd to the extrapolated PVd TTD curve.
Quality of life	EQ-5D-3L data from DREAMM-8 were used to derive health state utility values for use in the economic model: for progression-free on treatment with BPd; progression-free on treatment with DVd and Kd, which was assumed to be equal to progression-free on treatment utility derived from the PVd arm of DREAMM-8; progression-free off treatment; and progressed disease. Utility values were adjusted for age. AE disutilities were also included except for ocular adverse events as the submitting company viewed these as captured in the treatment-specific health state utilities for patients on treatment.
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 relative dose intensity (RDI) 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-8.

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 prices.

6.2. Results

The company presented results comparing belantamab mafodotin in combination with pomalidomide plus dexamethasone (BPd) 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.

The company provided probabilistic sensitivity analysis, deterministic sensitivity analysis (DSA) and scenario analysis. In the DSA, the parameters with the greatest impact on the incremental cost-effectiveness ratio were the overall survival hazard ratios from the NMA. The company also conducted scenario analyses to test the impact of several assumptions.

Table 6.2 Key scenario analyses

	Parameter	Base Case	Scenario
1a	Time horizon	33.9 years	20 years
1b			10 years
2	PFS – BPd	Weibull	Exponential
3	PFS – PVd	Weibull	Loglogistic
4	OS – BPd	Exponential	Gompertz
5	OS – PVd	Exponential	Weibull
6	Baseline comparator curve for parametric survival modelling	PVd	BPd
7	BPd TTD	Weibull	Lognormal
8a	hKd/DVd treatment duration	PFS HRs applied to PVd TTD	TTD = PFS
8b			PVd TTD as proxy
9	RDI	IPD-based dosing belantamab mafodotin	DREAMM-8 mean RDI for belantamab mafodotin
10	Utilities	DREAMM-8 (on treatment PF utility varied by treatment arm)	ENDEAVOR (PF = 0.74, PD = 0.67)
11	Ocular AE disutilities	Excluded	Included
12	Population	DREAMM-8 ITT	DREAMM-8 2L

13a	NMA HR used for DVd and hKd PFS	Point estimate NMA HR applied to the PVd PFS curve	DVd and hKd: PFS HR = 1 applied to PVd PFS curve
13b			DVd PFS HR = 1 applied to BPd PFS curve; hKd PFS HR = 1.5 (lower bound of credible interval) applied to BPd PFS curve
14a	NMA HR used for DVd and hKd OS	Point estimate NMA HR applied to the PVd OS curve	OS HR = 1 applied to PVd OS curve
14b			OS HR = 1 applied to BPd OS curve
15	Pomalidomide cost	PAS discount	National framework contract price
C1	Scenarios 13b + 14b + PFS HRs applied to BPd TTD for DVd and hKd TTD		
C2	Scenario 10 + C1		
C3	Scenario 9 + C2		

Abbreviations: AE = adverse event; BPd = belantamab mafodotin in combination with pomalidomide plus dexamethasone; DVd = daratumumab in combination with bortezomib plus dexamethasone; Kd = carfilzomib (56mg/m^2 twice weekly) in combination with dexamethasone; HR = hazard ratio; ICER = cost-effectiveness ratio; IPD = individual patent level data; ITT = intention to treat; OS = overall survival; PD = progressed disease; PF = progression-free; 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.

6.5. Key uncertainties

- The company did not provide a comparison of the cost-effectiveness of BPd compared to all relevant comparators in Scottish clinical practice identified by clinical experts consulted by SMC. This included not providing a comparison to PVd, which was the only comparator that had direct evidence of relative clinical efficacy. While some SMC experts noted low patient uptake of PVd, this was not unanimous, reflecting the complexity of the treatment pathway.
- Direct evidence was not available for the relative clinical efficacy of BPd compared to DVd or Kd. This meant that relative efficacy in the economic analysis relied on an indirect treatment comparison, and this added uncertainty to the cost-effectiveness results.
- The immaturity of the overall survival data from DREAMM-8 necessitated extensive extrapolation over the modelled time horizon. Selecting long-term survival extrapolations for patients receiving BPd using the Gompertz distribution was considered plausible by a clinical expert consulted by the company and resulted in much higher estimates of cost effectiveness (Scenario 4).
- The population in DREAMM-8 did not match the target population for the economic analysis. A proportion of patients in the study were >2L and was not reflective of the

company's proposed positioning. An analysis that used the results of a subgroup analysis for DREAMM-8 patients who were 2L only (Scenario 12) resulted in much higher estimates of cost-effectiveness in both comparisons.

- The company's approach of applying respective hazard ratios from the NMA comparing DVd and Kd to the PVd OS and PFS extrapolations was uncertain. This approach anchored the relative efficacy of these medicines to PVd, despite the NMA results' wide credible intervals that crossed one in most comparisons.
- The only NMA comparison where the credible interval did not cross one was PFS for Kd compared with BPd. Scenarios were explored where efficacy in terms of OS and PFS for DVd or Kd was set to the highest of either the lower bound of the NMA hazard ratios or 1 (no difference between treatments) from the comparison to BPd (Scenario C1). In this scenario, TTD was based on BPd TTD instead of PVd TTD to avoid overestimating treatment duration for DVd nor Kd relative to efficacy. This scenario resulted in much higher estimates of cost effectiveness.
- Treatment duration in all arms of the model was uncertain. Treatment duration with BPd required extensive extrapolation. In an analysis where the best fitting extrapolation for BPd TTD from DREAMM-8 was used substantially increased BPd acquisition costs, so resulted in much higher estimates of cost effectiveness (Scenario 7). However, this was also 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 treatment with BPd.
- There was an absence of data for treatment duration with DVd or Kd to directly inform their treatment duration in the economic analysis. Although the treatment duration assumptions used within the company's base case could be considered plausible, alternative approaches to estimating treatment duration for the comparators in the economic analysis showed that the cost effectiveness results were highly sensitive to this parameter (Scenarios 8a and 8b).
- There was uncertainty in the use of the individual patient level data RDI 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-8. The company viewed that the mean 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 was no precedent for the individual patient level data RDI approach, using the more conventional mean RDI approach for BPd was considered in a scenario analysis. This increased the estimate of cost-effectiveness (Scenario 9).
- There were uncertainties in how HRQoL data were used on the model. The company selected treatment-specific utility scores in the progression-free on treatment health state

which resulted in considerably higher utility scores for patients treated with BPd in the model. The company did not explain why patients across the treatment arms of DREAMM-8 might be expected to have different HRQoL. The open-label design of DREAMM-8 cast further uncertainty on the reliability of these estimates. A scenario that used utility scores for the progression-free health state that did not depend on treatment resulted in a higher estimate of cost-effectiveness (Scenario 10).

Also, the company did not include disutility associated with ocular adverse events that occurred at notably high rates exclusively in the BPd arm of DREAMM-8 despite including disutilities for other adverse events in the model. The company argued that ocular adverse event disutility would be included in the treatment specific health state utilities while patients were on treatment. This seemed uncertain as the company's approach was not consistent for all adverse events in the analysis. A scenario that included ocular adverse events resulted in a higher estimate of cost effectiveness (Scenario 11).

- A scenario that combined the scenario exploring the highest of either the lower bounds of the credible intervals or one from the NMA comparisons of DVd and Kd with BPd with health state utilities that did not vary by treatment in the progression-free health state resulted in much higher estimates of cost-effectiveness relative to the base case analysis. These estimates became even higher when these were combined with a more conventional approach to estimating RDI (Scenario C3).
- The cost of pomalidomide in NHS practice is lower than the price used in the economic model due to the existence of a national framework agreement for this medicine. Using the national framework contract price substantially improved the cost-effectiveness results as pomalidomide was included as a combination medicine (Scenario 15). The impact of the national framework contract price in a comparison to PVd on the cost-effectiveness results was unknown as the company did not provide this analysis.

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 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 was unable to accept belantamab mafodotin for 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.[20]

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.[21]

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.[22, 23]

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 pomalidomide plus dexamethasone)	**30-minute intravenous infusion once every four weeks, with a starting dose of 2.5 mg/kg given once in cycle 1 (each cycle is a 28-day period). From cycle 2 onwards, belantamab** mafodotin **is dosed at 1.9 mg/kg**	**Cycle 1: £23,568** **Cycle 2 onwards: £20,033**

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 budget impact due to commercial in confidence issues.

*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.