Belantamab mafodotin with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more treatments [ID6212]

Technology appraisal committee B [8 January 2025]

For PUBLIC – confidential information redacted

Chair: Charles Crawley

Lead team: Gabriel Rogers, Nigel Westwood, Andrew Makin

External assessment group: CRD and CHE Technology Assessment Group, University of York

Technical team: Lauren Elston, Nigel Gumbleton, Richard Diaz

Company: GlaxoSmithKline

© NICE 2025. All rights reserved. Subject to Notice of rights.

Belantamab mafodotin with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more treatments [ID6212]

- ✓ **Background and key issues**
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ❑ Summary

NICE National Institute for Health and Care Excellence

Relapsed or refractory multiple myeloma

Incurable, rare, relapsing, remitting cancer of plasma cells of unknown cause

- **Epidemiology**: 4,906 new cases in England in 2020 (Cancer registration statistics).
  - more common in elderly, men and the Black ethnic group.
- **Classification**
  - Relapsed/refractory: MM that is not responsive to treatment or for MM that has had minimal response or better, progression within 60 days of the last LoT.
- **Symptoms**: infections, bone pain, fractures, fatigue, hypercalcaemia, kidney issues.
- **Prognosis**: In 2019 in England, 5-year survival for adults diagnosed with MM was 54% (Baker and Mansfield 2023).
  - Survival likely worse for LEN-refractory MM.
  - Prognosis improving with more new and effective treatments.
- **Challenge of treatment**: as MM progresses, resistance to different classes of treatments.
  - In UK, 95% diagnosed with MM have 1L, 64% have 2L (company estimates ~3,400 eligible for 2L).

Abbreviations: 1L, first-line treatment; 2L, second-line treatment; LEN, lenalidomide; LoT, line of treatment; MM, multiple myeloma

Patient perspectives

Submission from Myeloma UK

- Complications of myeloma can be devastating, debilitating and painful and can have a severe impact on quality of life.
- The constant possibility of relapse completely disrupts the lives of patients and their families, and has a huge psychological impact.
- There is a clear need for innovative treatments which deliver deep, durable responses for relapsed and refractory myeloma
- Belamaf will be the first BCMA targeted treatment for myeloma on the NHS*; has potential to overcome treatment resistance and fulfil the unmet need.
- People who have received belamaf had a positive experience and would recommend it.
- BEL+BOR+DEX can deliver benefits that are most important to patients: high response rates and good remission times; view that the frequently reported eye side effects are manageable and don't negate the overall treatment benefit.

"Myeloma has had a major impact on my quality of life. No day is the same as you can wake up and find you are in chronic pain and unable to do anything for yourself and have to rely on your carers which has a really negative effect on your mental health…."

"There is a constant pressure of wondering what's going to happen to me next because myeloma is like that, it's not curable and it's going to come back, I'm sure every month there's the possibility of relapse and it's hard to ignore that…"

"Myeloma is currently incurable, so having a variety of available strategies/options gives me and my partner some hope and time."

*Available from 2L. Teclistimab and elranatamab are available from 4L+.

Abbreviations: Belamaf, belantamab mafadotin; BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; BCMA, B-cell maturation antigen; 2L, second line; 3L; third line

Clinical perspectives

Submissions from UK Myeloma Society & Royal College Physicians (joint), and clinical expert:

- Myeloma is incurable; RRMM is challenging to treat as patients often have worsening quality of life due to side effects of previous treatment and morbidity of relapse/refractoriness.
- Treatment aims to reduce symptoms by controlling the disease for as long as possible, and preventing significant morbidity caused by disease progression.
- BEL+BOR+DEX significantly improves outcomes (PFS) compared to standard of care (DAR+BOR+DEX) at second line; BEL has a novel target and mechanism of action in myeloma.
- BEL monotherapy is widely used through the compassionate use programme; belamaf would easily fit into current treatment algorithms and be easily delivered.
- BEL ocular side effects are manageable (indicated by DREAMM-7 low discontinuation rate); require access to specialist eye clinics for monitoring and may need dose reductions or longer dose intervals.

"Myeloma is incurable with current therapy for the majority of patients. There is a clear unmet need to provide better treatments to induce a longer and more durable period of remission and limit, or prevent, myeloma associated complications."

"Healthcare professional[sic] will have some experience of administration and dealing with potential complications. There will be additional health resource needed to access specialist eye clinics."

NICE

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; BCMA, B-cell maturation antigen; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone.

Belantamab mafodotin (Blenrep, GlaxoSmithKline)

Marketing authorisation	• belantamab mafodotin in combination with bortezomib and dexamethasone is indicated for the treatment of adult patients with multiple myeloma who have received at least one prior therapy • Date of UKMA: April 2025
Mechanism of action	• An antibody-drug that targets and binds to B-cell maturation antigen (BCMA), which is highly expressed on the surface of malignant plasma cells. • Bound belemaf is internalised by the malignant cell, where the cytotoxic drug is released and leads to cell cycle arrest and apoptosis. • While bound to BCMA, it enhances recruitment and activation of immune effector cells, inducing antibody-dependant cellular cytotoxity and phagocytosis.

Administration	• 3-week cycle:
	  • Belamaf: 2.5 mg/kg IV infusion on day 1
	  • Bortezomib: 1.3 mg/m^2 subcutaneously on days 1, 4, 8, and 11 (first 8 cycles only)
	  • Dexamethasone 20 mg IV or oral on both the day of and day after bortezomib (8 doses, first 8 cycles only)
	• Treatment should be continued until disease progression or unacceptable toxicity.

Price	• £16,848 per 100 mg vial. £11,784 per 70 mg vial • Patient access scheme in place.

Abbreviations: MM, multiple myeloma; IV, intravenous; UKMA, UK marketing authorisation.

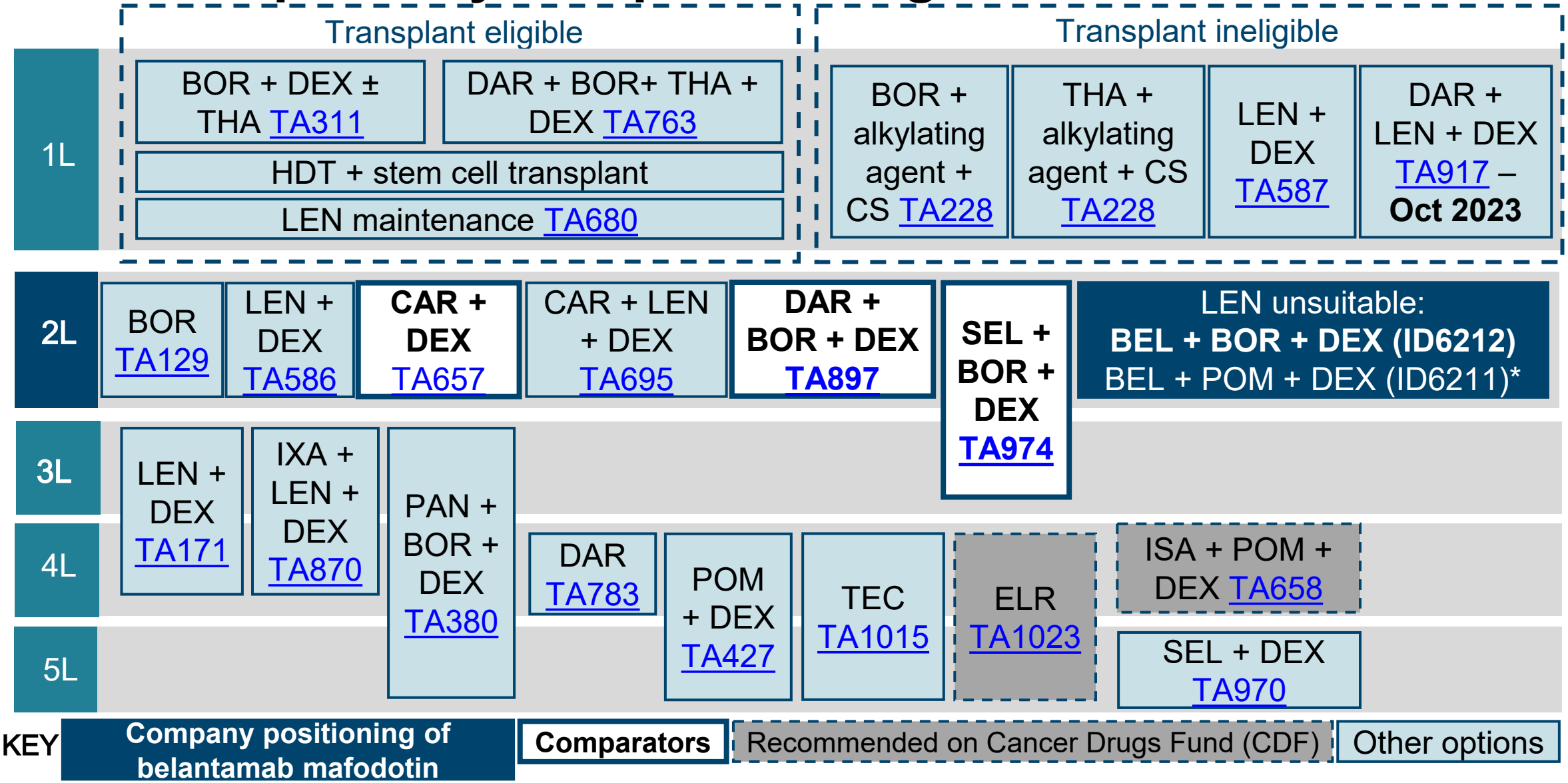
Key issues for discussion

Issue	ICER impact
Proposed position of BEL+BOR+DEX in the treatment pathway	Unknown
Lack of evidence for the proposed population: 2L-only in adults for whom lenalidomide is unsuitable	Unknown
Exposure to belamaf may be lower in NHS clinical practice than in the DREAMM-7 trial – unclear impact on effectiveness	Unclear
Uncertainty in the OS predictions for BEL+BOR+DEX due to immature data from DREAMM-7 and optimistic long-term survival extrapolations	Large
Uncertainty in the PFS and progressive disease health state utility values	Small?

Resolved issue	
Inconsistent descriptions of the populations of interest	Company have clarified the proposed population is narrower than the MA: eligible 2L patients for whom lenalidomide is unsuitable

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; ICER, incremental cost-effectiveness ratio; MA, marketing authorisation; PFS, progression free survival; 2L, second line

Treatment pathway and positioning of BEL+BOR+DEX



*BEL+POM+DEX is being appraised in the same committee meeting at the same proposed position (ID6212).

Abbreviations: BEL, belantamab mafodotin ; BOR, bortezomib; CAR, carfilzomib; CS, corticosteroid; DAR, daratumumab; DEX, dexamethasone ELR, elranatamab; ISA, isatuximab; IXA, ixazomib ; LEN, lenalidomide; PAN, panobinostat ; POM, pomalidomide; SEL, selinexor ; TEC, teclistamab ; THA, thalidomide

Key issues: Position of BEL+BOR+DEX in the pathway and relevant population

Background

- Decision problem population (as per NICE scope and proposed MA indication): people with RRMM who have had at least 1 previous therapy, therefore positioning BEL+BOR+DEX at 2L onwards.
- Company submission restricts to 2L only (i.e. adults with relapsed or remitting MM who have had 1 previous therapy) and where LEN is unsuitable – narrower than the MA.
- Company states most people at 2L are LEN-refractory and 2L highest area of unmet need.

EAG comments

- Clinical advice:
  - Expect LEN-eligible patients at 2L over next 3-5 years (30% transplant eligible, 15% transplant ineligible).
  - Clinicians would prefer BEL+BOR+DEX to also be included at 3L; treatment options at 3L limited, and may prefer a 'gentler' treatment over BEL+BOR+DEX at 2L due to side effects (e.g. ocular toxicity).
- Company does not present clinical evidence specific for proposed population (i.e. 2L and unsuitable for lenalidomide - see later key issue).
- Unclear why evidence for 3L-only and 3L+ has not been included; requested at FAC.

Company (at FAC)

- Evidence for 3L+ not provided – confirms proposed pop: 2L only and lenalidomide unsuitable.

Is the company proposed positioning and population for BEL + BOR + DEX appropriate? How would 'unsuitable' for LEN be defined in NHS practice? Should BEL + BOR + DEX at 3L+ be included? What is likely impact of BEL at 2L on subsequent treatments e.g. BCMA-targeted treatments TEC / ELR?

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; EAG, external assessment group; FAC, factual accuracy check; LEN, lenalidomide; MA, marketing authorisation; RRMM, relapsed/remitting multiple myeloma; 2L, second line; 3L third line

Belantamab mafodotin with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more treatments [ID6212]

- ❑ Background and key issues
- ✓ **Clinical effectiveness**
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ❑ Summary

NICE National Institute for Health and Care Excellence

Key clinical trial results – DREAMM-7 (2 October 2023 cut-off)

Compared to DAR+BOR+DEX, BEL+BOR+DEX significantly improves both PFS and OS

Table 1. Effectiveness evidence presented for the full ITT population (adult patients with RRMM who had 1+ prior therapy)

	BEL+BOR+DEX (n = 243)	DAR+BOR+DEX (n = 251)	HR (95% CI)
PFS, median months (95% CI)	36.6 (28.4, NR)	13.4 (11.1, 17.5)	0.41 (0.31; 0.53), p<0.001
OS, 1st quartile* months (95% CI)	[redacted]	[redacted]	0.57 (0.40; 0.80), p<0.001
DOR, median months (95% CI)	35.6 (30.5, NR)	17.8 (13.8, 23.6)	-
ORR, % (95% CI)	82.7 (77.4, 87.3)	71.3 (65.3, 76.8)	-

*Median endpoint not reached for OS, so 1st quartile months are presented

EAG comments

- All main analyses were conducted for the full ITT population of DREAMM-7 with one or more prior lines of therapy, including lenalidomide-exposed, not exposed, and lenalidomide-refractory patients

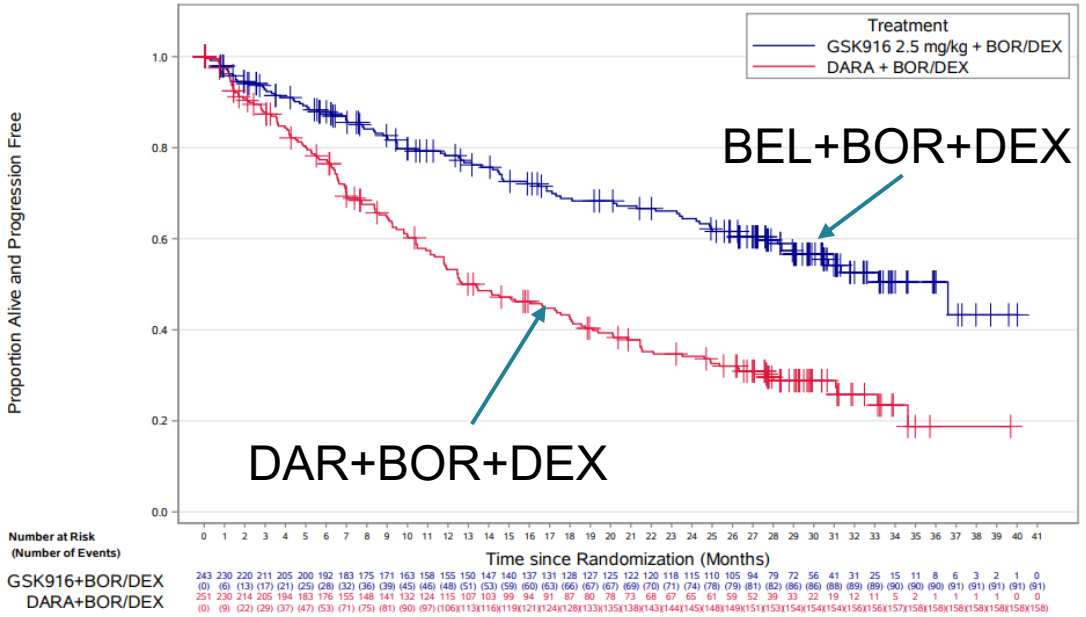
NICE

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CI, confidence interval; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; DOR, duration of response; EAG, external assessment group; HR, hazard ratio; ITT, intention to treat; NR, not reported; OS, overall survival; ORR, overall response rate; PFS, progression free survival; RRMM, relapsed/remitting multiple myeloma

Key clinical trial results – DREAMM-7 (full ITT population)

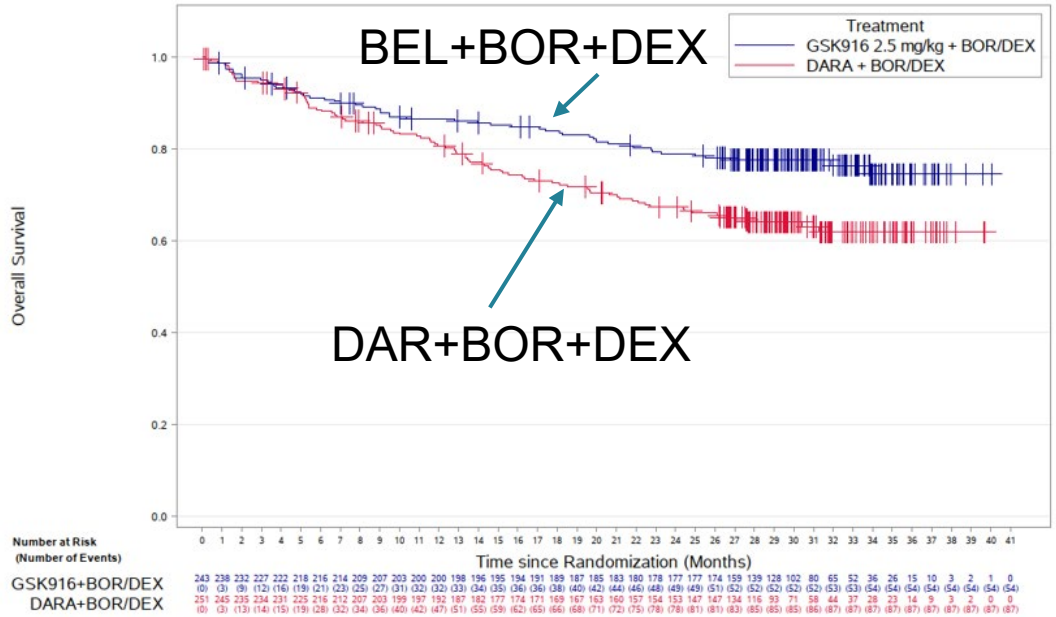
Compared to DAR+BOR+DEX, BEL+BOR+DEX significantly improves both PFS and OS

Figure 1. KM PFS - BEL+BOR+DEX versus DAR+BOR+DEX



HR (95% CI; p-value)	0.41 (0.31, 0.53), p<0.001

Figure 2. KM OS - BEL+BOR+DEX versus DAR+BOR+DEX



HR (95% CI; p-value)	0.57 (0.40; 0.80), p<0.001

NICE

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CI, confidence interval; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; HR, hazard ratio; ITT, intention to treat; KM, Kaplan-Meier; OS, overall survival; PFS, progression free survival.

Key clinical trial results – additional subgroup results

Evidence of benefit of BEL+BOR+DEX on PFS in 2L-only and lenalidomide-refractory subgroups, and OS in the lenalidomide-refractory subgroup only

- At clarification, EAG requested efficacy data for company proposed population - 2L only and lenalidomide not suitable
- Company provided results for the following subgroups:
  - 2L only (prespecified stratification factor from the DREAMM-7 protocol).
  - Lenalidomide refractory (not a prespecified stratification factor).

	2L only (BEL+BOR+DEX=125, DAR+BOR+DEX=123)	Lenalidomide-refractory only (all lines, BEL+BOR+DEX=79, DAR+BOR+DEX=87)
PFS	[redacted]	HR 0.31 (0.19; 0.48) median 25.0 vs 8.6 months
OS	[redacted]	[redacted]

EAG comments

- Unclear whether lenalidomide would be an effect modifier for OS (not the case in CASTOR study)
- Baseline characteristics for lenalidomide refractory only subgroup not provided; comparability across treatment not be assessed.

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CI, confidence interval; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; HR, hazard ratio; ITT, intention to treat; OS, overall survival; PFS, progression free survival; 2L, second line

Key issues: Lack of evidence for the 2L-only population where lenalidomide is unsuitable

Background

- Company submission restricts to 2L-only adults with relapsed or remitting MM unsuitable for lenalidomide.
- Evidence for DREAMM-7 ITT population is used to inform effectiveness and company base case: adults with relapsed or refractory MM (2L+, proposed full MA population).
- Analyses for other subgroups, e.g. 3L only or 3L+, requested at clarification (not provided).

Company (Clarification)

- Using ITT data is the best approach; 2L-only lenalidomide-refractory subgroup from DREAMM-7 small and would introduce uncertainty (n = 22 for BEL+BOR+DEX and n = 27 for DAR+BOR+DEX)
- Clinical data for 2L-only and lenalidomide-refractory subgroups provided, but not used in cost-effectiveness analysis; [redacted]
- Retains that strongest clinical case is for 2L.

EAG comments

- In the absence of clinical data for the company's proposed population, EAG acknowledges the reasoning to use the DREAMM-7 ITT population; however, this is a limitation of the evidence.

Is it appropriate to use clinical effectiveness data from DREAMM-7 ITT population to inform decision making for the company proposed population: 2L only and lenalidomide unsuitable?

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CI, confidence interval; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; HR, hazard ratio; ITT, intention to treat; OS, overall survival; PFS, progression free survival; 2L, second line; 3L, third line

Company NMA methodology

Company

- No direct evidence comparing BEL+BOR+DEX with all relevant comparators in NICE scope (CAR+DEX, SEL+BOR+DEX) – NMA conducted
- NMA used a global perspective (including comparators not in NICE scope).
- Bayesian framework using R (company reported WinBUGS)
- Both fixed and random effects analyses were done; fixed preferred.
- Informative Turner priors used for between-study standard deviation of treatment effects in the random effects models.

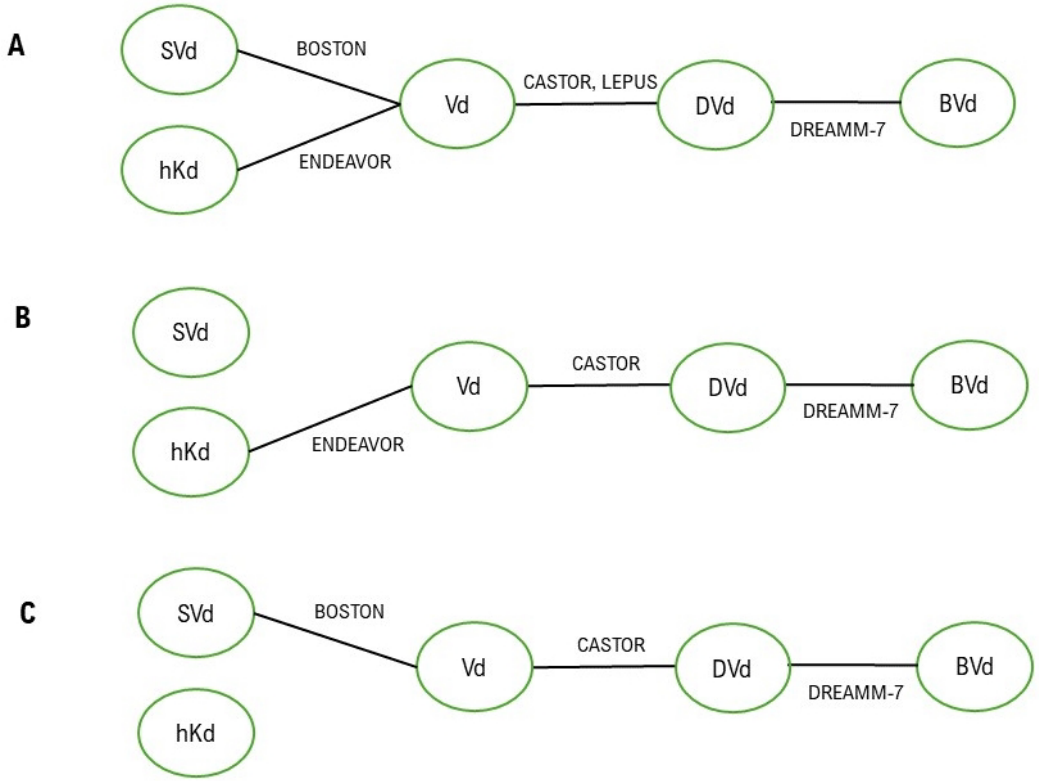
EAG comments

- Methods are appropriate but poorly described in the company submission.
- No loops – inconsistency between direct and indirect evidence cannot be checked.
- Code/dataset provided by company with unexplained differences; EAG could not replicate the company's PFS NMA results. EAG base case applies updated results (minor discrepancies).
- Few studies; heterogeneity could not be adequately assessed.
- Agree with use of fixed effect model; fits data well.
- Company used earlier data cut-off for LEPUS study for OS NMA than what is available; EAG prefer use of the later cut-off (although does not change conclusions).

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CAR+DEX, carfilzomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; NMA, network meta analysis; OS, overall survival; PFS, progression free survival; SEL+BOR+DEX, Selinexor with bortezomib and dexamethasone

Network meta-analysis results

Figure 3. Simplified network diagrams for different outcomes and populations for the comparators of interest



A. Network for the ITT population for PFS, OS, and ORR and the 1 prior line of therapy population for PFS.
B. Network for the lenalidomide-refractory population for PFS (comparisons to SEL+BOR+DEX are not possible)
C. Network for the lenalidomide-refractory population for ORR (comparisons to CAR+DEX are not possible).

Table 3. Results of EAGs fixed effect NMAs for ITT population

Outcome	BEL+BOR+DEX vs. DAR+BOR+DEX	BEL+BOR+DEX vs. CAR+DEX	BEL+BOR+DEX vs. SEL+BOR+DEX	BEL+BOR+DEX vs.BOR+DEX
PFS, HR (95% CrI)	[redacted]	[redacted]	[redacted]	[redacted]
OS, HR (95% CrI)	[redacted]	[redacted]	[redacted]	[redacted]
ORR, OR (95% CrI)	[redacted]	[redacted]	[redacted]	[redacted]

Company

- NMA results for comparison of BEL+BOR+DEX with DAR+BOR+DEX are aligned with the DREAMM-7 in terms of PFS, OS and ORR.
- NMA results used to inform clinical effectiveness for CAR+DEX and SEL+BOR+DEX in the model.

Should the EAG updated NMA results for PFS and OS be used in the economic model?

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CAR+DEX, carfilzomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; NMA, network meta analysis; OS, overall survival; PFS, progression free survival; SEL+BOR+DEX, Selinexor with bortezomib and dexamethasone

Key issues: Exposure to belamaf in NHS clinical practice

Background

- Belamaf SmPC = initial dose 2.5mg/kg. If moderate corneal adverse events occur withold treatment until improvements in corneal examination findings and BCVA is mild or better; then resume at 1.9mg/kg.
- In DREAMM-7: patient exposure to belamaf reduced due to dose reductions / delays following AEs .
- Company base case:
  - Belamaf acquisition and administration costs applied based on IPD dose information [redacted] from the DREAMM-7 trial to the proportion on treatment in each weekly cycle.
  - All other drugs in the model use RDI.

EAG comments

- Use of IPD dosing from DREAMM-7 to calculate belamaf costs reasonable approach given dosage modelled is consistent with actual dosage received in trial.
- Clinical advice: dosing may be reduced more in clinical practice to reduce number/severity of ocular side effects.
- Clinical and cost-effectiveness analyses include dose reductions based on DREAMM-7, but do not include further reductions anticipated in NHS practice.
- The costs of belamaf are sensitive to whether delays are accounted for (lower costs) or not (higher costs), but the impact of delays on safety and effectiveness are uncertain as they cannot be explored within the model.

Is it appropriate to use IPD dosing from DREAMM-7 to inform acquisition and administration costs of Belamaf ?

Abbreviations: AE, adverse events; BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; EAG, external assessment group; IPD, individual patient-level data; RDI, relative dose intensity;

Belantamab mafodotin with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more treatments [ID6212]

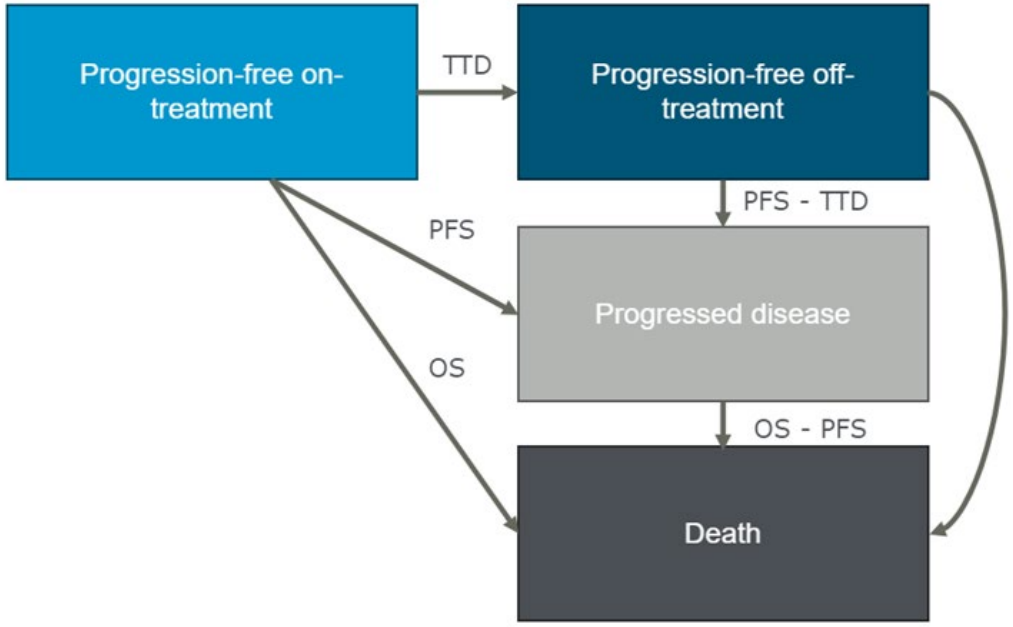
- ❑ Background and key issues
- ❑ Clinical effectiveness
- ✓ **Modelling and cost effectiveness**
- ❑ Other considerations
- ❑ Summary

NICE National Institute for Health and Care Excellence

Company's model overview

Company model is a cohort-based partition survival model

Figure 4. Diagram of model structure



Cost-effectiveness analyses covered for 2 subpopulations:

- DAR+BOR+DEX-eligible population (BEL+BOR+DEX compared with DAR+BOR+DEX and CAR+DEX)
- DAR+BOR+DEX-ineligible population (BEL+BOR+DEX compared with SEL+BOR+DEX and CAR+DEX.

- Technology affects **costs** by:
  - Increasing the time on treatment.
  - Decreasing the proportion with progressive disease and associated costs of subsequent therapies upon progression.
  - Incurring the costs of monitoring for and managing ocular adverse events.

- Technology affects **QALYs** by:
  - Increasing the proportion of patients who are alive and progression-free over time
  - Conferring a higher utility value for patients who are progression-free on the technology compared to patients who are progression-free on the comparator.

- Assumption(s) with greatest ICER effect:
  - Preferred distribution for the extrapolation of OS for BEL+BOR+DEX .

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CAR+DEX, carfilzomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; ICER, incremental cost-effectiveness ratio; OS, overall survival; PFS, progression-free survival; QALY, quality-adjusted life-year SEL+BOR+DEX, Selinexor with bortezomib and dexamethasone; TTD, time to treatment discontinuation.

Key issues: Uncertainty in OS predictions due to immature data – BEL+BOR+DEX extrapolation

Background

- OS data extrapolated by fitting independent parametric models to observed data:
  - DAR+BOR+DEX - Bayesian approach to provide informative prior distribution for shape parameter of OS curve estimated from CASTOR trial. Weibull considered best fit → EAG consider appropriate.
  - BEL+BOR+DEX – no external data source with more mature data. Weibull distribution to DREAMM-7 data
- Company clinical advice considered exponential fit for BEL+BOR+DEX more plausible
- Independent fits due to concerns that the PH assumption might not hold; log-cumulative hazard plot curves cross multiple times and empiric hazard plot indicates hazards not constant over time

EAG comments

- OS from DREAMM-7 highly uncertain (particularly BEL+BOR+DEX) due to immaturity of trial data and optimistic long-term predictions; likely to favour BEL+BOR+DEX over comparators.
- EAG base case:
  - DAR+BOR+DEX – Independent Weibull, informative prior (same as company base case)
  - BEL+BOR+DEX – Independent Exponential

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; HR, hazard ratio; OS, overall survival; PH, proportional hazards.

OS extrapolation for DAR+BOR+DEX

Figure 5. DAR+BOR+DEX OS from DREAMM-7 and CASTOR

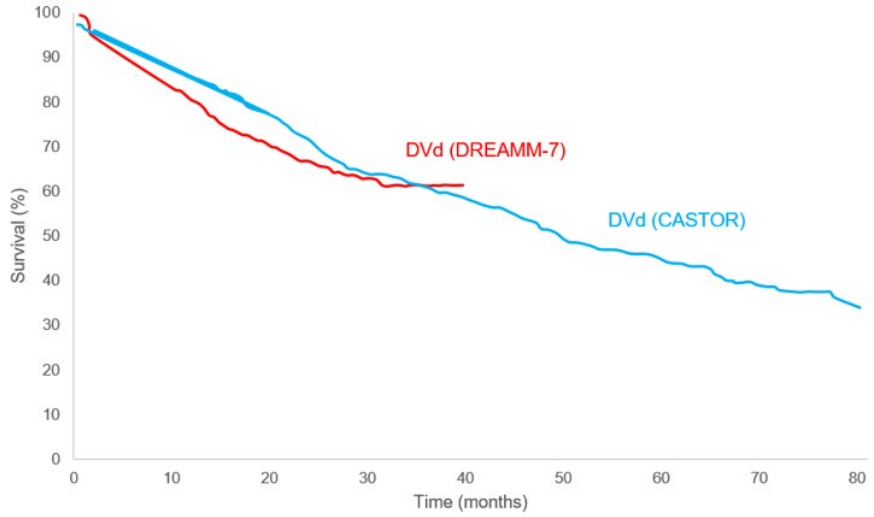


Figure 6. DAR+BOR+DEX OS extrapolation using CASTOR (company base case)

[redacted]

EAG comments

- Using more mature external trial evidence to inform DAR+BOR+DEX OS appears appropriate.
- Difficult to judge which study characteristics would influence shape parameter of distributions fitted to DAR+BOR+DEX OS data, but CASTOR and DREAMM-7 study designs and populations are broadly similar.
- DAR+BOR+DEX OS predictions with Weibull and informative prior on shape parameter appear consistent with observed data in CASTOR and DREAMM-7, and considered clinically valid by company's experts.
- EAG reassured that DAR+BOR+DEX OS extrapolation in company's base-case provides an appropriate survival baseline for comparison with treatments for which the PH assumption holds.

NICE

Abbreviations: DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; OS, overall survival; PH, proportional hazards.

Key issues: Uncertainty in OS predictions due to immature data – BEL+BOR+DEX extrapolation

Figure 7. Time varying OS HR for BEL+BOR+DEX vs. DAR+BOR+DEX implied by alternative extrapolations

Figure 8. Long-term OS parametric extrapolations company and EAG base case

EAG comments

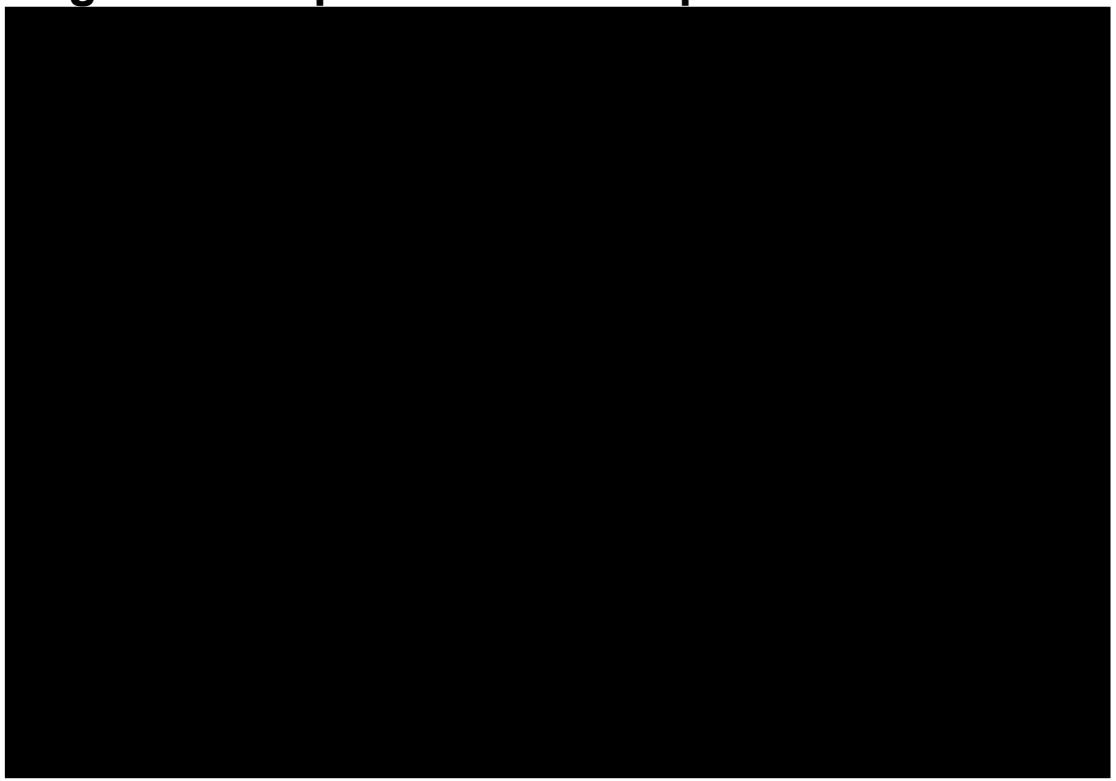
- Company base case implies decreasing HR over time (increasing treatment effect over time) for BEL+BOR+DEX versus DAR+BOR+DEX that is not supported by DREAMM-7 evidence; optimistic long-term OS predictions for BEL+BOR+DEX.

	Median OS, months
Exponential (EAG base case)	[redacted]
Weibull (Company base case)	[redacted]

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; HR, hazard ratio; OS, overall survival.

Key issues: Uncertainty in OS predictions due to immature data

Figure 9. Empiric OS hazard plot



EAG comments

- Considers empiric hazard plot does not support use of independent Weibull.
- PH assumptions cannot be excluded due to conflicting statistical tests. Extrapolations assuming PH holds should not be excluded.

BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CAR+DEX, carfilzomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; NMA, network meta analysis; OS, overall survival; PFS, progression free survival; SEL+BOR+DEX, Selinexor with bortezomib and dexamethasone

Key issues: Uncertainty in OS predictions due to immature data – BEL+BOR+DEX extrapolation

EAG comments

- Weibull extrapolation overly optimistic; company clinical advice preferred more conservative exponential fit.
- Weibull in company base case suggests treatment effect increases over time; not supported by empiric hazard plots
- EAG considers exponential extrapolation for BEL+BOR+DEX more plausible based on implied hazards over time – EAG base case
- EAG scenario analyses assuming PH holds → applying empirical HR for BEL+BOR+DEX vs. DAR+BOR+DEX from DREAMM-7 (HR=0.57; 95% CI: 0.40, 0.80) to the DAR+BOR+DEX OS curve baseline (termed PH Weibull) - more clinically plausible over independent Weibull
- Additional EAG scenario: BEL+BOR+DEX OS based on company's absolute median PFS:OS surrogacy estimate ([redacted] months) – most conservative scenario.

What is the committees preferred approach to extrapolate OS in BEL+BOR+DEX arm? Independent Weibull? Independent exponential? PH holds Weibull? PFS:OS surrogacy estimate? Other?

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; PH, proportional hazards

Key issues: Uncertainty in progression-free and progressive disease health state utility

Background

- PF utilities for BEL+BOR+DEX higher than DAR+BOR+DEX [redacted]; supported by DREAMM-7 trial; PF utilities for SEL+BOR+DEX and CAR+DEX assumed to be same as DAR+BOR+DEX
- Company included a higher utility value for progressive disease than progression-free for the comparator treatments [redacted].

EAG comments

- Company utilities not explicitly conditional on the line of therapy; TA974 requested utilities based on treatment line, supported by external evidence (Hatswell et al. 2019).
- PF benefit for BEL+BOR+DEX versus DAR+BOR+DEX is supported by trial. Company has not given evidence to support higher utility in BEL+BOR+DEX PF state versus SEL+BOR+DEX and CAR+DEX; explored in scenario where PF utility values equal for BEL+BOR+DEX, CAR+DEX and SEL+BOR+DEX.
- Higher utility value for progressive disease not clinically plausible; considers estimates from Hatswell 2019 to be more appropriate with moving to subsequent line of therapy.
- EAG base case: PD utility same for all treatments – used DAR+BOR+DEX PF utility from DREAMM-7 and applied utility decrement based on average decrement across treatment lines beyond 2L from Hatswell 2019.

What is the committees preferred approach to applying PF and PD utilities?

Abbreviations: 2L, second line; BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; PD, progressed disease; PF, progression free; PH, proportional hazards

Key issues: Uncertainty in progression-free and progressive disease health state utility

	Intervention	PF	PD	Progression decrement	Data source
Company base case	BEL+BOR+DEX	[redacted]	[redacted]	[redacted]	DREAMM-7 trial (directly from EQ-5D-3L data)
	DAR+BOR+DEX, CAR+DEX, SEL+BOR+DEX	[redacted]	[redacted]	[redacted]	
EAG base case	BEL+BOR+DEX	[redacted]	[redacted]	[redacted]	PF: DREAMM-7 trial PD: same for all treatments, calculated average utility decrement across treatment lines beyond 2L (from Hatswell 2019) and deduct this from DREAMM-7 PF utility estimate for DAR+BOR+DEX
	DAR+BOR+DEX, CAR+DEX, SEL+BOR+DEX	[redacted]	[redacted]	[redacted]	

What is the committees preferred approach to applying PF and PD utilities?

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; PD, progressed disease; PF, progression free.

Subsequent treatment costs

Background

- Company applied differential costs for subsequent treatments, as a one-off cost to the proportion of patients entering the progressed disease health state each cycle.
- Company considered 3 distributions:
  - Likely future pathway aligned
  - Current patient pathway aligned – company base case.
  - NICE pathway aligned

EAG comments

- The EAG considered that the key driver of differences in the costs of subsequent treatments across the interventions compared was the delay to disease progression rather than the distribution of treatments. Therefore, the cost of subsequent treatments was based on the same PD treatment distribution across all interventions.

What is the committees preferred approach to applying subsequent treatment costs?

Abbreviations: EAG, external assessment group; PD, progressed disease

Summary of company and EAG base case assumptions

Assumptions in company and EAG base case

Assumption	Company base case	EAG base case
OS modelling approach	Weibull (both arms)	Exponential (BEL+BOR+DEX); Weibull (DAR+BOR+DEX)
NMA	Original NMA results	Updated results for PFS/OS
PD utility for comparator arms	DREAMM-7	Same PD utility for all treatments
Subsequent treatment costs	Costs for subsequent treatments differ in the DAR+BOR+DEX arm compared with other treatments under comparison	Same distribution across treatments

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; NMA, network meta-analysis; OS, overall survival; PD, progressed disease.

Cost-effectiveness results

All ICERs are reported in PART 2 slides

because they include confidential

comparator PAS discounts

Belantamab mafodotin with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more treatments [ID6212]

- ❑ Background and key issues
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ✓ **Other considerations**
- ❑ Summary

NICE National Institute for Health and Care Excellence

Other considerations

Severity modifier

- Does not meet severity weighting threshold

Uncaptured benefits

- No uncaptured benefits raised by stakeholders

Equality considerations

- No potential issues raised by stakeholders
- But, MM is more common in men, older people (≥75 years) and people of African and Caribbean family background

Managed access

- Company has not submitted a managed access proposal but notes in its submission that “managed access could be considered if this was an appropriate route to ensure patient access”.

- Are there any uncaptured benefits?
- Are there any equality issues to consider?
- What are the uncertainties and can they be resolved with further data collection?

Belantamab mafodotin with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more treatments [ID6212]

- ❑ Background and key issues
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ✓ **Summary**

NICE National Institute for Health and Care Excellence

Key issues for discussion

Issue	ICER impact	Slide
Proposed position of BEL+BOR+DEX in the treatment pathway	Unknown 	9
Lack of evidence for the proposed population: 2L-only in adults for whom lenalidomide is unsuitable	Unknown 	14
Exposure to belamaf may be lower in NHS clinical practice than in the DREAMM-7 trial – unclear impact on effectiveness	Unclear 	17
Uncertainty in the OS predictions for BEL+BOR+DEX due to immature data from DREAMM-7 and optimistic long-term survival extrapolations	Large 	20 - 24
Uncertainty in the PFS and progressive disease health state utility values	Small? 	25 - 26

Abbreviations: 2L, second line; BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; ICER, incremental cost-effectiveness ratio; OS, overall survival; PFS, progression-free survival.

Belantamab mafodotin with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more treatments [ID6212]

Supplementary appendix

NICE National Institute for Health and Care Excellence

Decision problem (1/2)

Population, intervention, comparators and outcomes from the scope

	Final scope	Company	EAG comments
Population	People with relapsed or refractory multiple myeloma who have had at least one prior line of therapy.	Adults (> 18 years) with relapsed or refractory multiple myeloma who have had one prior line of therapy (2L patients). - High level of unmet need. - RCT evidence for 2L strongest clinical case.	Clinical advisors indicated BEL+BOR+DEX being available in 3L offers a chance to hold it back in favour of a 2L treatment with more tolerable side effects.
Intervention	Belantamab mafodotin	As per scope	N/A

Abbreviations: 2L, second line; BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; RCT, randomised controlled trial.

Decision problem (2/2)

Population, intervention, comparators and outcomes from the scope

	Final scope	Company	EAG comments
Comparators	NICE approved treatments for relapsed or refractory multiple myeloma and 2L+ (see scope)	2L only: Carfilzomib plus dexamethasone Daratumumab plus bortezomib and dexamethasone Selinexor plus bortezomib and low-dose dexamethasone (if refractory to daratumumab and lenalidomide) - Company proposed population 2L only - Bortezomib mono not used in practice - Lenalidomide not suitable – most patients will be refractory.	Agrees bortezomib mono is not relevant (with clinical advice). Clinical advice indicates that lenalidomide based therapy may still be used 2L
Outcomes	OS, PFS, RR, AEs, HRQoL	As per scope	N/A

Abbreviations: 2L, second line; AE, adverse event; HRQoL, health-related quality of life; ICER, incremental cost-effectiveness ratio; OS, overall survival; PFS, progression-free survival; RR, response rate.

Key clinical trial characteristics – DREAMM-7

DREAMM-7 trial design	Phase 3, randomised, multicentre, open-label trial
Population	Adults with RRMM who have had at least 1 previous therapy
Interventions	BEL+BOR+DEX (n = 243) versus DAR+BOR+DEX (n = 251)
Data cut-off	2 October 2023; median follow-up 28.2 months
Primary outcome	PFS
Key secondary outcomes	OS, RR, HRQoL (measured by EQ-5D-3L, EORTC QLQ-C30 and EORTC IL52), AEs
EAG comments	**Baseline characteristics:** Not fully representative of population in NHS clinical practice; participants younger and fitter, mainly ECOG PS 0/1. Approx. half study sample had 1 previous therapy (proposed population). [redacted] recruited from UK. **Study withdrawals/discontinuations:** [redacted] **Exposure to treatment:** [redacted]

Abbreviations: 2L, second line; AE, adverse event; BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; EAG, external assessment group; HRQoL, health-related quality of life; ICER, incremental cost-effectiveness ratio; OS, overall survival; PFS, progression-free survival; RR, response rate; RRMM, relapsed/remitting multiple myeloma.

DREAMM-7 baseline characteristics

Characteristics	BEL+BOR+DEX (N=243)	DAR+BOR+DEX (N=251)
Age, median (range), years	65.0 (34 -86)	64.0 (32 -89)
Sex, n (%)		
Male	128 (53)	144 (57)
Female	115 (47)	107 (43)
Race, n (%)		
White	206 (85)	203 (81)
Black	8 (3)	12 (5)
Asian	28 (12)	33 (13)
East Asian	[redacted]	[redacted]
Japanese		
Southeast Asian		
Central/South Asian		
Mixed race*		
ECOG PS ≤1, n/N (%)	232/242 (96)	235/246 (96)
Time since diagnosis, median (range), years	4.28 (0.2-26.0)	3.94 (0.1-23.4)
Prior lines of therapy, n (%)		
1	125 (51)	125 (50)
2 or 3	88 (36)	99 (39)
4+	30 (12)	27 (11)

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone

DREAMM-7 baseline characteristics (continued)

Characteristics	BEL+BOR+DEX (N=243)	DAR+BOR+DEX (N=251)
Time to relapse on latest prior line of therapy, n (%) *		
≤12 months	[redacted]	[redacted]
>12 months		
Prior proteasome inhibitor, n (%)	218 (90)	216 (86)
Prior immunomodulatory drugs, n (%)	198 (81)	216 (86)
Prior daratumumab, n (%)	3 (1)	4 (2)
Prior ASCT, n (%)	164 (67)	173 (69)
Chemotherapy, n (%)	[redacted]	[redacted]
Steroids, n (%)		

*Patients could be included in more than 1 category

NICE

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone

DREAMM-7: ITT population and subgroups

ITT population, N = 494
(BEL+BOR+DEX = 243, DAR+BOR+DEX = 251)
Adults with MM, ≥ 1 prior line of MM therapy and documented PD during or after most recent therapy, no prior treatment with anti-BCMA, not refractory to or intolerant of daratumumab or bortezomib

Second line only, N = 248
(BEL+BOR+DEX =125,
DAR+BOR+DEX =123)

Lenalidomide-refractory only, all lines, N = 166
(BEL+BOR+DEX =79,
DAR+BOR+DEX = 87)

Company proposed population: Second line and unsuitable for lenalidomide – No clinical evidence presented
(small patient numbers BEL+BOR+DEX = 22, DAR+BOR+DEX = 27)

NICE

Abbreviations: BCMA, B-cell maturation antigen; BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; ITT, intention-to-treat; MM, multiple myeloma

Network meta analysis: subgroup results

		HR/OR (95% CrI)			
Outcome	**Population**	**BEL+BOR+DEX vs. DAR+BOR+DEX**	**BEL+BOR+DEX vs. CAR+DEX**	**BEL+BOR+DEX vs. SEL+BOR+DEX**	**BEL+BOR+DEX vs. BOR+DEX**
PFS	Lenalidomide-exposed	[redacted]	[redacted]	[redacted]	[redacted]
	Lenalidomide-refractory	[redacted]	[redacted]	[redacted]	[redacted]
	1 Prior LoT	[redacted]	[redacted]	[redacted]	[redacted]
ORR	Lenalidomide-exposed	[redacted]	[redacted]	[redacted]	[redacted]
	Lenalidomide-refractory	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CAR+DEX, carfilzomib and dexamethasone; CrI, credible interval; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; HR, hazard ration; LoT, line of therapy; OR, odds ratio; ORR, overall response rate; PFS, progression-free survival; SEL+BOR+DEX, Selinexor with bortezomib and dexamethasone

Adverse events – DREAMM-7

BEL+BOR+DEX is associated with common adverse events, leading to more delayed, reduced and interrupted doses

Table X Adverse events by study arm after adjusting for [redacted].

	BEL+BOR+DEX study arm	DAR+BOR+DEX study arm
Grade 3 or 4 adverse events (no. of events per 100 person years)	[redacted]	[redacted]
Adverse events leading to treatment discontinuation (no. of events per 100 patient years)	[redacted]	[redacted]
Any serious adverse event (no. of events per 100 patient years)	[redacted]	[redacted]

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone

Ocular adverse events – DREAMM-7

Corneal adverse events relating to study treatment were more common with BEL+BOR+DEX than DAR+BOR+DEX.

- Treatment-related corneal adverse events reported in [redacted]
- [redacted]
- [redacted]

KVA grade for BEL+BOR+DEX arm (safety population)

	BEL+BOR+DEX (n=242)
Eye-related events per overall KVA scale	
Any event, n (%)	[redacted]
Grade 2, n (%)	[redacted]
Grade ≥3, n (%)	[redacted]
Time to onset of first occurrence (≥ grade 2), median (range) days	[redacted]
Duration of first occurrence (≥ grade 2), median (range) days	[redacted]
First event resolved, n/N (%)[a]	[redacted]

EAG comments:

- [redacted] of BEL+BOR+DEX patients in DREAMM-7 experienced a keratopathy event grade 3 or more; however, company model applies [redacted] incidence of keratopathy, to the first model cycle only.

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; KVA, keratopathy visual acuity.

Best corrected visual acuity – DREAMM-7

- Of BEL+BOR+DEX patients who had normal BCVA at baseline (20/25 or better in at least one eye):
  - 34% reported a bilateral BCVA 20/50 or worse
  - 2% reported bilateral 20/200 or worse

- Median duration of occurrence was 3 weeks, regardless of severity.

Figure 10. Reference images for impact of best corrected visual acuity

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; BCVA, best visual acuity

Key issues: Uncertainty in OS predictions due to immature data – BEL+BOR+DEX extrapolation

EAG base case → Exponential

Company base case → Weibull

Table 4. Long-term observed and predicted OS over time - BEL+BOR+DEX

Source of survival predictions	Median	Years					
	Months	1	2	5	10	15	20
KM DREAMM-7	NR	[redacted]	[redacted]	-	-	-	-
Exponential	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Weibull	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Generalised gamma	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Gompertz	NR	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Log-logistic	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Lognormal	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; EAG, external assessment group; KM, Kaplan-Meier; OS, overall survival.

Health-related quality of life – DREAMM-7

Mean EQ-5D-3L utility scores were similar between BEL+BOR+DEX and DAR+BOR+DEX

Figure 11. European Quality of life-5 Dimensions 3 levels utility scores by visits: UK value set (mean, 95% CI)

Figure 12. Change in European Quality of life-5 Dimensions 3 levels Utility scores from baseline by visits recorded before progression UK value set (mean, 95% CI)

Abbreviations: BL, base line; CI, confidence interval; DARA; Daratumumab; EQ-5D-3L, European Quality of life-5 Dimensions 3 levels; GSK, GlaxoSmithKline belantamab mafadotin with bortezomib and dexamethasone; LFU, Last Follow-Up

Health-related quality of life – DREAMM-7

Table 1. Summary of Two-State EQ-5D-3L Utility scores Model - All Visits- UK Value Set

		Estimate	SE	95% CI (lower)	95% CI (Upper)	Z-Value	P-Value	QIC
Model Estimates								
Intercept		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
Baseline Utility Score		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Progression (IRC)	Progression Free	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
	Progressed	[redacted]	[redacted]	[redacted]	[redacted]	-	-	
Least Square Mean Estimates								
Progression (IRC)	Progression Free	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-
	Progressed	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CI, confidence interval; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; IRC, independent review committee; QIC, Quasi-likelihood under the Independence model Criterion; SE, standard error

Health-related quality of life – DREAMM-7

Table 2. Summary of Two-State EQ-5D-3L Utility scores Model with Treatment Arms - All Visits-UK Value Set

		Estimate	SE	95% CI (lower)	95% CI (Upper)	Z-Value	P-Value	QIC
Model Estimates								
Intercept		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Baseline Utility Score		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
Progression (IRC)	Progression Free	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
	Progressed	[redacted]	[redacted]	[redacted]	[redacted]	-	-	
Treatment	BEL+BOR+DEX	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
	DAR+BOR+DEX	[redacted]	[redacted]	[redacted]	[redacted]	-	-	
Least Square Mean Estimates								
Progression (IRC)	Progression (IRC)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-
	Progression (IRC)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
Treatment	BEL+BOR+DEX	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
	DAR+BOR+DEX	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CI, confidence interval; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; IRC, independent review committee; QIC, Quasi-likelihood under the Independence model Criterion; SE, standard error

Health-related quality of life – DREAMM-7

Table 3. Summary of Three-State EQ-5D-3L Utility scores Model with Treatment Arms - All Visits-UK Value Set

		Estimate	SE	Lower CL	Upper CL	Z-Value	P-Value	QIC
Model Estimates								
Intercept		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
Baseline Utility Score		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
Progression & Response (IRC)	Progression free, in response	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
	Progression free, no response	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Progressed	[redacted]	[redacted]	[redacted]	[redacted]	-	-	
Treatment	BEL+BOR+DEX	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
	DAR+BOR+DEX	[redacted]	[redacted]	[redacted]	[redacted]	-	-	
Least Square Mean Estimates								
Progression & Response (IRC)	Progression free, in response	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
	Progression free, no response	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-
	Progressed	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
Treatment	BEL+BOR+DEX	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
	DAR+BOR+DEX	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	

Abbreviations: BEL+BOR+DEX, belantamab mafadotin with bortezomib and dexamethasone; CI, confidence interval; CL, confidence limit; DAR+BOR+DEX, daratumumab with bortezomib and dexamethasone; IRC, independent review committee; QIC, Quasi-likelihood under the Independence model Criterion; SE, standard error

Health state utilities for PF and PD in previous submissions for RR MM

	Treatment line	PF	PD	Progression decrement
Selinexor with bortezomib and dexamethasone (TA974 2024) baseline scenario	2L & 3L	0.697	0.660	0.037
	2L	0.706	0.668	0.038
	3L	0.694	0.659	0.035
Selinexor with bortezomib dexamethasone (TA974 2024) scenario analysis using Hatswell et al. 2019	2L	0.620	0.550	0.070
	3L	0.590	0.520	0.070
Daratumumab with bortezomib (TA897 2023)	2L	0.737	0.665	0.072
Carfilzomib with dexamethasone and lenalidomide, (TA695 2021)	2L	0.714 (cycle 1 and 2), 0.761 (cycle 3 plus, CRd), 0.745 (cycle 3 plus, Rd)	0.698	0.055
Carfilzomib with dexamethasone, (TA657 2020)	2L	0.737 (cycle 1 and 2), 0.741 (cycle 3 plus, Cd), 0.714 (cycle 3 plus, BOR+DEX)	0.638	0.099 (cycle 1 and 2) 0.103 (cycle 3 plus, Cd) 0.076 (cycle 3 plus, Vd)
Panobinostat (TA380 2015)	3L	0.706 (PANO/BTZ/DEX), 0.725 (BTZ/DEX), 0.762 (off treatment)	0.64	0.066 (PANO/BTZ/DEX) 0.085 (BTZ/DEX) 0.122 (off treatment)

Abbreviations: 2L, second line, 3L, third line; BOR, bortezomib; DEX, dexamethasone; PANO, panobinostat