Indication	For 2nd line treatment of relapsed or refractory myeloma in patients who have previously received lenalidomide as part of 1st line systemic therapy that has had to be discontinued due to disease progression whilst on treatment or intolerance of lenalidomide. Patients with amyloidosis or POEMS syndrome are not eligible for Belantamab mafodotin. NB lenalidomide treatment to have been given either as commissioned by NHS England or is part of a 1st line treatment regimen in a NIHRbadged clinical trial.
Treatment Intent	Disease Modification
Frequency and number of cycles	Repeat every 21 days. Cycle 1 to 8 combination therapy. Bortezomib and dexamethasone should be stopped after 8 cycles. Cycle 9 onwards belantamab mafodotin monotherapy. Continue belantamab mafodotin until disease progression or unacceptable toxicity or patient choice. A formal medical review as to how belantamab mafodotin is being tolerated and whether treatment with belantamab mafodotin should continue or not will be scheduled to occur **after each of the first 4 cycles** of treatment. NB this indication is exempt from NHS England's treatment break policy due to the potentially necessary frequency and duration of treatment breaks during treatment. If there is disease progression during a treatment break, treatment with belantamab mafodotin must be discontinued.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • Consider flu and pneumococcal vaccination pre-therapy. • **Ophthalmology assessment:** o An ophthalmic examination including visual acuity and slit lamp examination must be performed by an eye care professional prior to each of cycles 1, 2, 3 and 4 and then during treatment as indicated. o Arrangements must be in place for eye care professionals to categorize both the degree of any corneal damage and the best corrected visual acuity in the most severely affected eye and for these results to be communicated to the myeloma team. o Patients should avoid using contact lenses until the end of belantamab mafodotin treatment unless bandage contact lenses are used under the direction of an ophthalmologist. o Dose modification may be required. After a dose reduction is made for ocular adverse reactions do not re-escalate the dose (see table 2). • **Haematological monitoring and parameters:** o **Cycle 1 to 8:** Monitor FBC on Day 1, 8 and 15. If NEUTS >/= 1 and PLTS >/= 25 continue treatment. o If parameters not met see table 1 for belantamab mafodotin guidance and for bortezomib see guidance below*. o U&Es & LFTs at each cycle. o **Cycle 9 onwards:**

	○ Monitor FBC, LFTS, U&Es at each cycle. • **Hepatic impairment:** ○ **Belantamab mafodotin:** No dose modification recommended in mild impairment. Limited data in moderate impairment, treat with caution and monitor closely. No data in severe impairment. ○ **Bortezomib:** Consider dose reduction in moderate/severe hepatic impairment (Bilirubin >1.5ULN), reduce Bortezomib to 0.7 mg/m^2 in the first treatment cycle. Consider dose escalation to 1.0 mg/m^2 or further dose reduction to 0.5 mg/m^2 in subsequent cycles based on patient tolerability. • **Renal impairment:** ○ **Belantamab mafodotin:** no dose modification recommended. ○ **Bortezomib:** CrCl < 20ml/min discuss with consultant. • **Infusion-related reactions (IRRs):** • Belantamab mafodotin: Patients experiencing IRR may require a dose modification (delay and/or reduction) or treatment discontinuation (see table 1). • **Management of adverse reactions and dose adjustments:** • **Belantamab mafodotin:** If a dose reduction is required dose at 1.9mg/kg, if this dose is not tolerated no further dose reductions are recommended and treatment should be stopped. See table 1 for dose modification guidance. • **Bortezomib cycle 1 to 8 specific monitoring and guidance:** ○ Blood glucose every cycle. ○ BP baseline and if clinically indicated thereafter. ○ ECG baseline and if clinically indicated thereafter. ○ Use with caution in patients with pre-existing heart disease or with high risk factors. ○ Lung function assessment required in patients with pre-existing respiratory disease (COPD, asthma) and heavy smokers. Clinician to decide if further imaging required in patients with additional co-morbidities. ○ Patients should be advised to report any new or worsening respiratory symptoms. ○ At least 72 hours must elapse between consecutive Bortezomib doses. ○ Ensure patient is well hydrated (drinking ~3L/day) prior to treatment. ○ **Dose modification bortezomib:** If Hb < 65g/l transfuse patient and restart treatment when Hb >65g/l. ○ Bortezomib should be withheld for any grade 3 non-haematological (see below for guidance on managing neuropathic toxicities) or Grade 4 haematological toxicities (neutrophils < 0.5 x 10^9/L or platelets < 25 x 10^9/L); once toxicity has settled reinitiate at 75%, (ie 1.3mg/m^2 → 1.0mg/m^2 → 0.7mg/m^2). ○ For Neuropathic Pain and or Peripheral Sensory or Motor Neuropathy dose reductions see table 3. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ **Belantamab mafodotin:** no drug interaction studies have been performed. ○ **Bortezomib:** The concomitant use of bortezomib with strong CYP3A4 inducers (e.g., rifampicin, carbamazepine, phenytoin, phenobarbital and St. John's Wort) is not recommended, as efficacy may be reduced. CYP3A4 inhibitors (e.g. ketoconazole, ritonavir) should be used with caution and patients monitored for toxicity. • **Contraception:** To avoid exposure to the foetus, women of reproductive potential should use effective contraception and avoid becoming pregnant during treatment and for 8 months after cessation of bortezomib treatment and for 4 months after cessation of belantamab mafodotin treatment. Male patients should use effective contraceptive measures during treatment and be advised not to father a child while receiving bortezomib and for 6 months following completion of belantamab mafodotin treatment.

	• **Driving:** Both bortezomib and belantamab mafodotin can have significant effects on a patient's ability to drive and operate machinery, patients should be advised to use caution when driving or operating machinery.
References	https://pubmed.ncbi.nlm.nih.gov/38828933/ https://clinicaltrials.gov/study/NCT04246047 SPC belantamab mafodotin accessed online 04.07.2025 SPC bortezomib accessed online 09.07.2025 CDF list V1.367 Blueteq form accessed online 08.07.2025

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1 Recommended dose modifications for belantamab mafodotin for other adverse reactions[a]

Adverse Reaction	Severity	Recommended dose modifications
Thrombocytopenia	Grade 3	No bleeding: • For patients on 2.5 mg/kg, reduce to 1.9 mg/kg. For patients on 1.9 mg/kg continue at same dose.[b] With bleeding: • Withhold until improvement to Grade 2 or better. For patients previously on 2.5 mg/kg, resume at 1.9 mg/kg. For patients on 1.9 mg/kg resume at same dose. Consider additional supportive treatment (e.g., transfusion), as clinically indicated and per local practice.
	Grade 4	Withhold the dose. Consider restarting if recovered to Grade 3 or better, and only if there is no active bleeding at time of treatment restart. For patients previously on 2.5 mg/kg, resume at 1.9 mg/kg. For patients on 1.9 mg/kg resume at same dose. If thrombocytopenia is considered disease-related, is not accompanied by bleeding, and recovers with transfusion to >25 x10^9/L, continuing treatment at the same dose may be considered.
Infusion-related reactions	Grade 2	Interrupt infusion and provide supportive treatment. Once symptoms resolve to Grade 1 or better, resume at a decreased infusion rate by at least 50%.
	Grade 3	Interrupt infusion and provide supportive treatment. Once symptoms resolve to Grade 1 or better, resume with premedication and at lower infusion rate extended to 2 to 4 hours. Any future infusion requires premedication.
	Grade 4	Permanently discontinue. If anaphylactic or life-threatening infusion reaction, permanently discontinue the infusion and institute appropriate emergency care.
Other adverse reactions	Grade 3	Withhold until improvement to Grade 1 or better. For patients previously on 2.5 mg/kg, resume at 1.9 mg/kg. For patients on 1.9 mg/kg resume at same dose.
	Grade 4	Consider permanent discontinuation. If continuing treatment, withhold until improvement to Grade 1 or better. For patients previously on 2.5 mg/kg, resume at 1.9 mg/kg. For patients on 1.9 mg/kg resume at same dose.

[a] Other adverse reactions were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE).
[b] For belantamab mafodotin with bortezomib and dexamethasone, may consider reverting to previous dose, if appropriate once thrombocytopenia recovers to Grade 2 or better.

Table 2: Recommended dose modifications for belantamab mafodotin for ocular adverse reactions

Severity[a]	**Recommended dose modifications**
Grade 1 *Corneal examination finding(s)* Mild superficial punctate keratopathy with worsening from baseline, with or without symptoms. *Change in BCVA* Decline from baseline of 1 line on Snellen Equivalent Visual Acuity.	Continue treatment at current dose.
Grade 2 *Corneal examination finding(s)* Moderate superficial punctate keratopathy, patchy microcyst-like deposits, peripheral sub-epithelial haze, or a new peripheral stromal opacity. *Change in BCVA* Decline from baseline of 2 lines (and Snellen Equivalent Visual Acuity not worse than 20/200). Or Grade 3 *Corneal examination finding(s)* Severe superficial punctate keratopathy, diffuse microcyst-like deposits involving the central cornea, central sub-epithelial haze, or a new central stromal opacity. *Change in BCVA* Decline from baseline of 3 or more lines (and Snellen Equivalent Visual Acuity not worse than 20/200).	Withhold treatment until improvement in both corneal examination findings and BCVA to Grade 1 or better. Resume treatment at reduced dose level 1.
Grade 4 *Corneal examination finding(s)* Corneal epithelial defect.[c] Or *Change in BCVA* Decline to Snellen Equivalent Visual Acuity of worse than 20/200.	Withhold until improvement in both corneal examination findings and BCVA to Grade 1 or better. Resume treatment at reduced dose level 1 For worsening symptoms that are unresponsive to dose reductions or withholding of treatment, consid*er permanent discontinuation*.

BCVA = best corrected visual acuity; BVd = Belantamab mafodotin with bortezomib and dexamethasone.

[a] Ocular adverse reaction severity is defined by the most severely affected eye as both eyes may not be affected to the same degree.

[c] A corneal defect may lead to corneal ulcers. These should be managed promptly and as clinically indicated by an eye care professional.

Table 3: Dose modification of bortezomib for neuropathic toxicities

Severity of Peripheral Neuropathy Signs and Symptoms*	**Modification of Dose and Regimen**
Grade 1 (asymptomatic; loss of deep tendon reflexes or paraesthesia) without pain or loss of function	No Action
Grade 1 with pain or Grade 2 (moderate symptoms; limiting instrumental Activities of Daily Living (ADL)**)	Reduce bortezomib to 1 mg/m^2
Grade 2 with pain or Grade 3 (severe symptoms; limiting self-care ADL ***)	Withhold bortezomib therapy until toxicity resolves. When toxicity resolves, reinitiate with a reduced dose of bortezomib at 0.7 mg/m^2 once per week
Grade 4 (life-threatening consequences; urgent intervention indicated)	Discontinue bortezomib
*Grading based on NCI Common Terminology Criteria for Adverse Events (CTCAE) v4.0 **Instrumental ADL: refers to preparing meals, shopping for groceries or clothes, using telephone, managing money etc; ***Self care ADL: refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.	

Cycle 1 to 8: Repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**BELANTAMAB MAFODOTIN**	**2.5mg/kg**	IV	30minutes	In 250ml sodium chloride 0.9%
	BORTEZOMIB	**1.3mg/m²**	SC	bolus	Inject in to the thigh or abdomen at a 45-90° angle. Injection sites should be rotated from left to right.
8 and 15	**BORTEZOMIB**	**1.3mg/m²**	SC		Inject in to the thigh or abdomen at a 45-90° angle. Injection sites should be rotated from left to right.
TTO	Drug	Dose	Route	Directions	
Day 1	**DEXAMETHASONE**	**20mg**	PO	OM on days 1, 2, 8, 9, 15 and 16 Take with or after food. When taken on d1 take prior to belantamab mafodotin.	
	Hypromellose Preservative free	0.3%	Eye drops	1 drop both eyes QDS for the duration of treatment.	
	Aciclovir	400mg	PO	BD continuously (plus 3 more months after completion of last treatment dose)	
	Co-trimoxazole	480mg	PO	TWICE daily on Mondays, Wednesdays and Fridays (plus 3 more months after completion of last treatment dose)	
	Allopurinol	300mg	PO	OD and review after 3 weeks. Cycle 1 only, then prescribe only if required.	
	Omeprazole	20mg	PO	OD	
	Metoclopramide	10mg	PO	Take 10mg TDS for 3 days after bortezomib then up to TDS when required. Do not take for more than 5 days continuously. On Cycle 1 only, then prescribe as required	
	Loperamide	2mg	PO	Take two capsules (4mg) after first loose stool, then one capsule (2mg) after each loose stool when required. (Maximum 16mg per day). Dispense on Cycle 1 only, and then prescribe as required.	
	Consider the use of prophylactic anti-fungals				

Cycle 9 onwards repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**BELANTAMAB MAFODOTIN**	**2.5mg/kg**	IV	30minutes	In 250ml sodium chloride 0.9%
TTO	Drug	Dose	Route	Directions	
Day 1	Hypromellose Preservative free	0.3%	Eye drops	1 drop both eyes QD for the duration of treatment.	
	Aciclovir	400mg	PO	BD continuously (plus 3 more months after completion of last treatment dose)	
	Co-trimoxazole	480mg	PO	TWICE daily on Mondays, Wednesdays and Fridays (plus 3 more months after completion of last treatment dose)	
	Consider the use of prophylactic anti-fungals				