Belantamab mafodotin, bortezomib and dexamethasone - BVd (Myeloma)

Please note this protocol has been produced in a new format that is currently being piloted. Any feedback on this new format should be sent to SSGMeetings@uhbw.nhs.uk

Index

Indication

Second line treatment of relapsed or refractory myeloma in patients who received lenalidomide as part of their first line systemic therapy.
(CDF)

Response Rates

Phase 3 DREAMM-7 trial

- Belantamab mafodotin, bortezomib & dexamethasone (BVd, n=243) vs daratumumab, bortezomib & dexamethasone (DVd, n=251)
- Median PFS: 36.6 months BVd vs 13.4 months DVd
- Median PFS if lenalidomide refractory: 25 months vs 8.6 months DVd
- OS at 18 months:

Treatment related mortality

~3%

Regimen details

Cycles 1-8

ONCE weekly bortezomib schedule (preferred schedule):

Day	Drug	Dose	Route
1	Belantamab mafodotin	2.5mg/kg	IV infusion
1, 8 & 15	Bortezomib	1.3mg/m^2	Subcutaneous
1, 2, 8, 9, 15 & 16	Dexamethasone*	20mg	Oral

* Reduce dexamethasone to 20mg on day 1 and 8 only for patients > 75 years old or low BMI or if previous glucocorticoid toxicity

TWICE weekly bortezomib schedule (to consider if rapid disease control is required):

Day	Drug	Dose	Route
1	Belantamab mafodotin	2.5mg/kg	IV infusion
1, 4, 8 & 11	Bortezomib	1.3mg/m^2	Subcutaneous
1, 2, 4, 5, 8, 9, 11 & 12	Dexamethasone*	20mg	Oral

* Reduce dexamethasone to 20mg on day 1 and 8 only for patients > 75 years old or low BMI or if previous glucocorticoid toxicity

Cycle 9 onwards:

Day	Drug	Dose	Route
1	Belantamab mafodotin	2.5mg/kg	IV infusion

Cycle frequency

21 days

In the DREAMM-7 study, extending the dose interval to mitigate side effects (see section below on managing ocular toxicity) was common, with the average dose interval being approximately 6 weeks between months 3-9, approximately 8 weeks between months 9-15, and 9-12 weeks between months 15-30.

Number of cycles

Until disease progression or unacceptable toxicity.

Pre-medication

The cycle 1, day 1 dexamethasone dose should be administered 1-3 hours prior to the first belantamab mafodotin infusion. Premedication with chlorphenamine and paracetamol is not routinely required unless previous infusion related reaction.

Supportive medication

Cycle 1, Days 1-7: Allopurinol 300 mg OD (100mg OD if CrCl < 20mL/min)
Cycles 1-3: Levofloxacin 500mg OD (reduced dose if CrCl <50mL/min)
Hypromellose eye drops should be administered at least 4 times daily during belantamab mafodotin treatment.
Consider use of a cooling eye mask from the start of each belantamab mafodotin infusion for as long as tolerated
Antiviral prophylaxis as per local policy
Proton pump inhibitor or H2 antagonist on steroid days or continuously (as per local policy)
Loperamide as required
Bisphosphonates as per local policy.

Emetogenicity

This regimen has low emetic potential – refer to local policy

Administration

Belantamab mafodotin

Administration by intravenous infusion in 250mL sodium chloride 0.9% over 30 minutes.

Bortezomib

Administration by subcutaneous bolus injection into the thigh or abdomen. Rotate sites, avoid injecting into the same site in the same cycle e.g., alternate between right and left abdomen, and right and left thigh. Patient should be encouraged to drink 2 – 3 litres over the 24 hours after each dose of bortezomib in the first cycle, to reduce the risk of tumour lysis syndrome. At least 72 hours must elapse between doses of bortezomib. If a planned dose of bortezomib is delayed, adjust the dosing schedule accordingly, to maintain the treatment interval.

Dexamethasone

Tablets should be taken in the morning, with or immediately after food

Extravasation

Belantamab mafodotin - irritant
Bortezomib – neutral

Mandatory investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U&E (including creatinine)	14 days
LFT	14 days
Virology (Hep B, C and HIV serology)	3 months
Ophthalmic examination (including visual acuity and slit lamp examination)	Baseline

Additional investigations advised pre-first cycle

- HBA1C
- Serum protein electrophoresis
- Serum free light chains, immunoglobulins
- β2 microglobulin
- Bone profile (calcium, phosphate, magnesium, vitamin D)
- CRP, LDH
- Serum free light chains (SFLC)/Paraprotein (PP)/Immunoglobulins (Igs)
- Urine protein/creatinine ratio
- Bone marrow examination for cytogenetic analysis FISH
- Imaging as per local guidelines

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	96 hours
U&E (including creatinine)	7 days
LFT	7 days
Ophthalmic examination (including visual acuity and slit lamp examination)	Prior to each dose in cycles 1-4 then as clinically indicated

Additional investigations advised pre subsequent cycles

- SFLC, PP, Igs – results are not required prior to administration of cycle
- Bone profile (calcium, phosphate, magnesium)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer must be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 50 x 10^9/L
Bilirubin	< 1.5 x ULN
ALT/AST	≤ ULN

Dose modifications

Drug	Belantamab mafodotin	Bortezomib
Full dose	2.5mg/kg	1.3mg/m^2
Dose level -1	1.9mg/kg	1.0mg/m^2
Dose level -2	Discontinue belantamab mafodotin	0.7mg/m^2
Dose level -3		Discontinue bortezomib

Haematological toxicity

Belantamab mafodotin:

If neutrophils < 1.0x 10^9/L, delay until count recovery. Consider GCSF support as indicated. For recurrent neutropenia despite GCSF support, consider one level dose reduction.

Thrombocytopenia:

Platelet count (x10^9/L)	Action
25-49 (no bleeding)	If no active bleeding treatment may proceed at a reduced belantamab mafodotin dose of 1.9mg/kg or for patients already on 1.9mg/kg, continue with same dose
25-49 (with bleeding)	Withhold belantamab mafodotin until platelets > 50 x 10^9/L. Reduce belantamab mafodotin to 1.9mg/kg or for patients already on 1.9mg/kg, continue with same dose.
< 25	Withhold belantamab mafodotin until platelets > 25 x 10^9/L and no active bleeding. Reduce belantamab mafodotin to 1.9mg/kg or for patients already on 1.9mg/kg, continue with same dose. If thrombocytopenia is considered to be disease related, is not accompanied by bleeding and recovers with transfusion to > 25 x 10^9/L, continuing at same dose may be considered – consultant decision.

Bortezomib: Interrupt dosing for Grade 4 toxicity (neutrophils < 0.5 x 10^9/L or platelets < 25 x 10^9/L). Bortezomib may be reintroduced at next dose reduction level once toxicity has resolved (neutrophils > 1.0 x 10^9/L and platelets > 70 x 10^9/L).

Renal impairment

No dose modification is required for renal impairment.

For dialysis patients, bortezomib should be given after dialysis and bortezomib mafodotin may be given before or after dialysis as it is not expected to be dialysed due to its molecular size.

Hepatic impairment

Belantamab mafodotin: No dose modification is required in mild hepatic impairment (bilirubin ≤ 1.5 x ULN or Bilirubin < ULN and ALT/AST > ULN). There is limited data in moderate hepatic impairment (bilirubin 1.5-3 x ULN with any ALT), but no significant pharmacokinetic changes are expected. There is no data in severe impairment.

Bortezomib: If bilirubin > 1.5 x ULN consider starting dose of 0.7mg/m^2 for cycle 1. For subsequent cycles consider increasing dose to 1mg/m^2 or reducing to 0.5mg/m^2 according to tolerability.

Other toxicities

Belantamab mafodotin

Ocular toxicity

Dose modifications are based on corneal examination findings and/or changes in best corrected visual acuity (BCVA). Belantamab mafodotin dosing should be based on the highest grading from the most severely affected eye as both eyes may not be affected to the same degree. The belantamab mafodotin dose should not be re-escalated after a dose reduction for ocular adverse events.

Severity/Grade	Recommended dose modification
Grade 1 *Corneal examination findings:* 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 findings:* 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 findings:* severe superficial punctate keratopathy, diffuse microcyst-like deposits involving the central cornea, central subepithelial haze or a new central stromal opacity. *Change in BVCA:* 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 dose level -1.
Grade 4 *Corneal examination findings:* corneal epithelial defect *Change in BCVA:* Decline to Snellen Equivalent Visual Acuity worse than 20/200	Withhold treatment until improvement in both corneal examination findings and BCVA to Grade 1 or better. Resume treatment at dose level -1. For worsening symptoms that are unresponsive to dose reductions or withholding of treatment, consider permanent discontinuation of belantamab mafodotin.

Other toxicities

Toxicity	Definition	Action/Dose adjustment
Infusion related reactions	Grade 2	Interrupt infusion and provide supportive treatment. Once symptoms resolve to Grade 1 or better, resume at 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 2-4 hours. Use premedication for future infusions
	Grade 4	Permanently discontinue belantamab mafodotin

Toxicity	Definition	Action/Dose adjustment
Other adverse reactions	Grade 3	Withhold belantamab mafodotin until improvement to Grade 1 or better. Reduce belantamab mafodotin to 1.9mg/kg or for patients already on 1.9mg/kg, continue with same dose.
	Grade 4	Consider permanent discontinuation of belantamab mafodotin. If continuing treatment, withhold belantamab mafodotin until improvement to Grade 1 or better. Reduce belantamab mafodotin to 1.9mg/kg or for patients already on 1.9mg/kg, continue with same dose.

Bortezomib:

Neuropathy grade	Action and bortezomib dose
Grade 1 with no pain	100%
Grade 1 with pain or grade 2 but not interfering with daily living	Reduce to 1.0mg/m^2
Grade 2 with pain or grade 3	Withhold until symptoms resolved. Restart at 0.7mg/m^2
Grade 4	Discontinue

Any other ≥ grade 3 non-haematological toxicity withhold bortezomib until recovered to ≤ grade 1. Recommence with dose reduction of one level.

Side Effects

DREAMM-7 study:

Toxicity		Any grade (%)	Grade 3 or 4 (%)
Haematological	Thrombocytopenia	69	55
	Anaemia	19	8
Non-haematological	Infections	70	31
	Blurred vision	66	22
	Dry eye	51	7
	Photophobia	47	2
	Foreign-body sensation in eye	44	3
	Eye irritation	43	5
	Diarrhoea	32	4
	Eye pain	32	1
	Peripheral sensory neuropathy	25	1
	Peripheral neuropathy	21	1
	Cataract	20	7
	Upper respiratory tract infection	20	0
	Constipation	19	1
	Fatigue	19	4
	Increased alanine aminotransferase level	19	6
	Pyrexia	19	<1
	Pneumonia	18	12
	Nausea	16	1
	Insomnia	16	1
	Increased aspartate aminotransferase level	15	1
	Increased γ-glutamyltransferase level	15	9
	Back pain	9	1
	Infusion related reactions	3	<1

Specific drug related side effects:

Belantamab mafodotin - refer to SPC for full details

Common (>10%)	Uncommon (1-10%)	Rare (<1%)
Visual acuity reduced	Diplopia	Corneal ulcer
Corneal examination findings	Infusion related reactions	Hepatitis B reactivation
Blurred vision, dry eye	Albuminuria	
Eye irritation, eye pain	Vomiting	
Thrombocytopenia, anaemia, neutropenia		
Diarrhoea		
Nausea		
Infections		
Deranged LFTs		
Fatigue		

- **Ocular adverse reactions**

79% of patients experienced ocular adverse events in the DREAMM-7 trial. Patients should have ophthalmic examination (including visual acuity and slit lamp examination) before each of the first four doses of belantamab mafodotin and as clinically indicated thereafter. Patients should be encouraged to report any ocular symptoms and to administer preservative free artificial tears at least 4 times a day beginning on the first day of infusion until treatment completion as this may reduce ocular symptoms. Dose modifications and/or delays, when needed due to ocular toxicity, resulted in resolution of ocular side effects in almost all patients on study, with evidence of ongoing response thereafter.

Bortezomib – refer to SPC for full details

Common (>10%)	Uncommon (1-10%)	Rare (<1%)
Thrombocytopenia, neutropenia, anaemia	Infections	Posterior Reversible Encephalopathy Syndrome
Peripheral sensory neuropathy	Motor neuropathy	Pneumonitis, acute respiratory distress syndrome
Orthostatic hypotension	Rash	Stevens-Johnson syndrome, toxic epidermal necrolysis
Fatigue, asthenia		
Nausea, vomiting		Hepatitis, hepatic failure
Diarrhoea, constipation		Heart failure

- **Peripheral neuropathy**

Patients should be advised to report pain, hypersensitivity, prickling, burning sensation, numbness and paraesthesia. If these occur see above dose reductions for bortezomib and consider use of amitriptyline or gabapentin. Caution in patients with existing peripheral neuropathy.

- **Dizziness/Orthostatic hypotension**

Patients should be advised that bortezomib may cause orthostatic hypotension and they should sit upright for a few minutes prior to standing up from a recumbent position. Caution is advised when treating patients with a history of syncope receiving medications known to be associated with hypotension or in those who are dehydrated. Management of orthostatic hypotension may include adjustment of antihypertensives, rehydration or administration of mineralocorticosteroids and/or sympathomimetics.

Dexamethasone

Common (>10%)	Uncommon (1-10%)	Rare (<1%)
*High blood sugars	Blurred vision	Headache
Insomnia	Cataracts	Heart failure
Mood disturbance (depression, anxiety, euphoria)	Osteopenia	
Fluid retention	Acne	
Gastro-oesophageal reflux disease (GORD)	Abnormal fat deposits	
Increased appetite		

*pre-treatment HBA1C levels should be checked with monitoring for treatment emergent hyperglycaemia when HBA1C levels are >42mmol/mol. Patients with known diabetes/borderline diabetes should be referred to their diabetic nurse for close monitoring upon commencing dexamethasone

Additional information

Nil

Significant drug interactions – for full details consult product literature/ reference texts

Belantamab mafodotin: no interaction studies have been performed. Based on available data there is a low risk of pharmacokinetic or pharmacodynamic drug interactions.

Bortezomib:

Antihypertensives: Risk of additive hypotensive effect. Close monitoring of BP is required.

Oral antidiabetic agents: Hyper- and hypoglycaemia has been reported. Close monitoring of blood glucose is required.

Ciclosporin: increased risk of severe neuropathy: avoid concomitant use.

High dose vitamin C: reduced efficacy of bortezomib: avoid concomitant use.

Cytochrome P34A inhibitors (ketoconazole and other azole antifungals, clarithromycin, erythromycin) may increase bortezomib levels: avoid concomitant use. Cytochrome P34A inducers (rifampicin, carbamazepine, phenytoin, St John's Wort) may reduce bortezomib levels: avoid concomitant use.

References

- Summary of Product Characteristics: Belantamab mafodotin (GSK) accessed 10 July 2025 via www.medicines.org.uk
- Summary of Product Characteristics: Bortezomib (Aspire Pharma) accessed 10 July 2025 via www.medicines.org.uk
- National Institute for Health and Care Excellence ID6212. Accessed 10 July 2025 via www.nice.org.uk
- Hungria, V. et al. Belantamab mafodotin, bortezomib and dexamethasone for Multiple Myeloma. N Engl J Med 2024;391:393-407
- Hungria, V. et al. Belantamab mafodotin plus bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma (DREAMM-7): updated overall survival analysis from a global, randomised, open-label, phase 3 trial. Lancet Oncology. Published online 15 July 2025.

Version	Issue date	Review date	Revision	Written/Checked/Authorised
1	Jul 2025	Jul 2028	New protocol	**Written/reviewed:** Dr J Crowe (Consultant Haematologist, RUH NHS Trust), Dr S Moore (Consultant Haematologist, UHBW NHS Trust), Dr A Whiteway (Consultant Haematologist, NBT NHS Trust) **Checked:** Kate Gregory (Lead Pharmacist for SACT Protocols, SWAG Cancer Alliance) **Authorised:** Dr J Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)

Schedule of investigations and treatment plan

Activity	Pre-tx	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5+	Ongoing
Informed consent	X						
Clinical assessment	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	Every cycle
U&E, LFTs & bone profile	X	X	X	X	X	X	Every cycle
Ophthalmic examination	X	X	X	X	X	X	Repeat as clinically indicated
B2 microglobulin, LDH	X						
SFLC, Igs, PP	X	X	X	X	X	X	Every cycle
HbA1c	X						If clinically indicated
Blood pressure	X	X					Monitor during cycle 1. Continue for subsequent cycles only if infusion related reaction
Temperature, RR, pulse		X					
Weight recorded	X	X	X	X	X	X	Repeat if necessary
Height recorded	X						Repeat if necessary
Blood glucose	X						If clinically indicated
Imaging as per clinical guidance	X						If clinically indicated