DRUG NAME: Belantamab mafodotin

SYNONYM(S): GSK2857916[1]

COMMON TRADE NAME(S):

CLASSIFICATION: miscellaneous

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Belantamab mafodotin is a humanized immunoglobulin IgG1 antibody-drug conjugate that binds specifically to B-cell maturation antigen (BCMA). The monoclonal antibody component (belantamab) is conjugated to the active cytotoxic drug (monomethyl auristatin F or MMAF) via a stable protease-resistant maleimidocaproyl linker to create the antibody-drug conjugate. Belantamab mafodotin targets both dividing and non-dividing BCMA-expressing tumour cells. The antibody-drug conjugate is rapidly internalized by the tumour cell following binding to the cell surface. Inside the cell, free MMAF is released via proteolysis of the monoclonal antibody component. MMAF disrupts the microtubule network, which leads to cell cycle arrest and apoptosis. MMAF is cell cycle phase-specific for the G2/M phase. In addition to the cytotoxic mechanism of MMAF, belantamab also mediates the killing of tumour cells through antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular-mediated phagocytosis (ADCP) by enhancing the recruitment and activation of immune effector cells.[1]

USES:

Primary uses:

Multiple myeloma[2]

Other uses:

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Caution:

- ***hepatitis B screening*** (HBsAg) is recommended prior to initiation of treatment[3]; for recommended HBV screening and prophylaxis, see BC Cancer Protocol SCHBV ***Hepatitis B Virus Reactivation Prophylaxis***[4]
- ***corneal events*** are reported; a baseline ophthalmic examination is recommended prior to starting treatment[3]
- avoid use of ***contact lenses*** during treatment with belantamab mafodotin; use may be restarted 45 days after discontinuation of belantamab mafodotin[3]

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	anemia (24-37%, severe 14-25%)
	bleeding (5-17%)
	leucopenia (7-9%, severe 2-4%)
	lymphocytopenia (12-13%; severe 8-12%)
	neutropenia (13-27%, severe 9-15%)
	thrombocytopenia (35-58%, severe 20-34%)
eye (see paragraph following **Side Effects** table)	***blurry vision*** (22-46%, severe 2-4%)
	dry eye (13-34%, severe 1-3%)
	keratitis, ***keratopathy*** (70-75%, severe 20-27%)
	lacrimation increase (11%, severe 0%)
	night blindness (3%, severe 0%)
	pain (6%, severe 3%)
	photophobia (23%, severe 0%)
	pruritus (3%, severe 0%)
gastrointestinal	*emetogenic potential:* low[5]
	constipation (9-13%)
	diarrhea (13-15%, severe 1%)
	nausea (23-32%, severe 1%)
	vomiting (7-20%, severe 2%)
general disorders and administration site conditions	*extravasation hazard:* none[1,6]
	chills (23%, severe 0%)
	fatigue (16-26%, severe 2-5%)
	pyrexia (22-25%, severe 3-4%)
infections and infestations	pneumonia (4-13%, severe 4-11%)
	sepsis (1-3%)
	upper respiratory tract infection (7-17%, severe 1%)
injury, poisoning, and procedural complications	***infusion related reaction*** (16-23%, severe 1-9%)
investigations	alkaline phosphatase increase (8-12%, severe 1%)
	AST increase (20-29%, severe 2-6%)
	creatinine increase (10-11%, severe 1-3%)
	gamma glutamyltransferase increase (8-13%, severe 3-8%)
	LDH increase (4-7%, severe 1%)
metabolism and nutrition	appetite decrease (12-18%, severe 2%)
	hypercalcemia (13-16%; severe 3-7%)

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
renal and urinary	acute kidney injury (3-5%, severe 1-2%)
	renal impairment, failure (1%, severe 1%)
respiratory, thoracic and mediastinal	cough (7-26%, severe 0%)
	epistaxis (7-19%, severe 1-2%)

Adapted from standard reference[2,7] unless specified otherwise.

Corneal events are a class effect associated with antibody drug conjugates containing MMAF and are the most frequently reported adverse event with belantamab mafodotin.[3] The reason for the increased sensitivity of the eye is not known, but may be related to the nonspecific uptake of the antibody-drug conjugate into actively dividing cells of the cornea.[2] Keratopathy, blurred vision, dry eyes, and photophobia are the main symptoms reported. Corneal events are typically mild to moderate in severity and resolve or improve with dose modifications or delays. Once symptoms resolve to grade 1 or better, the dose can be increased to the starting dose. To minimize corneal events, artificial tears may be administered prophylactically 4-8 times daily starting on day 1 of the first cycle and continued daily until belantamab mafodotin is discontinued. Artificial tears may be increased up to every two hours as needed if ocular symptoms such as dry eye develop.[3,7] Corticosteroid eye drops were found to be ineffective as prophylaxis against the development of changes to the corneal epithelium.[2] Contact lens use is not recommended during treatment with belantamab mafodotin, but may be restarted 45 days after treatment has been discontinued if the patient is not experiencing ocular symptoms and has stopped using corticosteroid eye drops.[3]

Infusion reactions have been reported in approximately 20% of patients without premedication. The majority of reactions have been grade 1 or 2 and non-serious; however, serious reactions characterized by tachycardia, hypertension, and pyrexia have been reported after the first dose. Subsequent premedication prevents recurrence in most patients.[1]

INTERACTIONS: none known[1]

SUPPLY AND STORAGE:

Injection:
GlaxoSmithKline supplies belantamab mafodotin as 30 mg single-use (preservative free) vials of aqueous solution (as a frozen liquid) in a concentration of 20 mg/mL. Keep frozen at -50°C to -15°C. Protect from light.[1,8]

GlaxoSmithKline supplies belantamab mafodotin as 100 mg single-use (preservative free) vials of lyophilized powder. Refrigerate. Protect from light.[9,10]

Additional information (frozen liquid):
- vials may be thawed for up to 4 hours prior to use at room temperature or in the refrigerator if protected from light; swirl gently to ensure uniformity of solution[8]
- once thawed, drug cannot be refrozen; if not punctured, a thawed vial is stable for up to 10 days if refrigerated and protected from light[8]

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

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SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BC Cancer administration guideline noted in ***bold***, ***italics***

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous	no information found
Intermittent infusion[1,2,8]	***30***-60 ***minutes***
Continuous infusion	no information found
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

Adults:

BC Cancer usual dose noted in ***bold, italics***

	Cycle Length:	
Intravenous:	***3 weeks***[1,2,8]:	***2.5 mg/kg IV for one dose on day 1*** (total dose per cycle 2.5 mg/kg)

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3. GlaxoSmithKline. GSK2857916 Safety Considerations for Compassionate Use (version 2). Collegeville, Pennsylvania, USA; 23 October 2018
4. BC Cancer Supportive Care Tumour Group. (SCHBV) BC Cancer Protocol Summary for Hepatitis B Virus Reactivation Prophylaxis . Vancouver, British Columbia: BC Cancer; September 1 2023
5. BC Cancer. Provincial Pharmacy Directive Number II-20: Chemotherapy Preparation Chart. Vancouver, British Columbia: BC Cancer; December 5 2018
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8. GlaxoSmithKline. Belantamab mafodotin (GSK2857916) Investigational Product Information for Compassionate Use - Version 5.0. Collegeville, Pennsylvania, USA; 25 September 2019
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