DRUG NAME: Mogamulizumab

SYNONYM(S):

COMMON TRADE NAME(S): POTELIGEO® (USA)

CLASSIFICATION: immunotherapy

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

MECHANISM OF ACTION:

Mogamulizumab is a first-in-class defucosylated, humanized IgG_1 κ monoclonal antibody which selectively binds to C-C chemokine receptor 4 (CCR4). CCR4 is involved in cell trafficking of lymphocytes to various organs, including skin, and is consistently expressed on the surface of tumour cells in T-cell malignancies. By binding to CCR4 on the cell surface, mogamulizumab causes the cell to be targeted for antibody-dependent cellular cytotoxicity (ADCC), resulting in the depletion of target cells.[1-3]

USES:

Primary uses:

Lymphoma, cutaneous T-cell[1]

*Health Canada approved indication

Other uses:

SPECIAL PRECAUTIONS:

Caution:

- life-threatening ***infusion reactions*** are reported; consider premedication with diphenhydramine and acetaminophen for the first infusion in all patients[1,2]
- ***immune-mediated complications*** are reported; patient with ***pre-existing autoimmune disease*** may experience a worsening of their condition during treatment with mogamulizumab[1]
- ***hepatitis B virus reactivation*** has been reported[1]
- serious ***infections*** are common and may be life-threatening; fatalities have been reported[1,3]
- patients receiving ***allogeneic HSCT*** after mogamulizumab may have a higher risk of transplant complications if mogamulizumab is administered within 50 days before HSCT[1]

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. When placebo-controlled trials are available, adverse events will generally be included if the incidence is ≥5% higher in the treatment group.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	anemia (12-35%, severe 2%)
	leukopenia (severe 1%)
	lymphopenia (severe 5%)

Developed: 15 March 2021
Revised: 1 May 2021

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	neutropenia (10%, severe 2%)
	thrombocytopenia (14-29%, severe 0%)
cardiac	arrhythmia (5%)
	cardiac failure (<1%)
	myocardial ischemia or infarction (<1%)
endocrine	***immune mediated hypothyroidism*** (1%)
eye	conjunctivitis (5%)
gastrointestinal	*emetogenic potential:* rare[4]
	abdominal pain (5%)
	constipation (13%)
	diarrhea (28%)
	mucositis (12%, severe 1%)
	nausea (16%)
	vomiting (7%)
general disorders and administration site conditions	*extravasation hazard:* none[5]
	chills (7%)
	edema (16%)
	fatigue (31%)
	pyrexia(17%, severe <1%)
hepatobiliary	hepatitis (2%)
immune system	***immune mediated complications***; see paragraph following **Side Effects** table
infections and infestations	candidiasis (9%)
	folliculitis (8%)
	herpes virus infection (5%)
	lower respiratory tract infection (2%)
	otitis (6%)
	pneumonia (severe 5-6%)
	sepsis (severe 4%)
	skin infection (19%, severe 3%)
	upper respiratory tract infection (22%, severe 0%)
	urinary tract infection (9%)
injury, poisoning, and procedural complications	***infusion reactions*** (33-35%, severe 2-8%); see paragraph following **Side Effects** table
investigations	alkaline phosphatase increase (17%, severe 0%)
	ALT increase (18%, severe 1%)

Developed: 15 March 2021
Revised: 1 May 2021

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	AST increase (25%, severe 2%)
	hyperglycemia (9-52%)
	hyperuricemia (8%)
	hypomagnesemia (6%)
	hypophosphatemia (severe 1%)
	weight changes (6-8%)
metabolism and nutrition	appetite decrease (8%)
	tumour lysis syndrome (<1%)
musculoskeletal and connective tissue	muscle spasms (5%)
	musculoskeletal pain (22%, severe <1%)
nervous system	dizziness (8%)
	headache (14%)
	peripheral neuropathy (7%)
psychiatric	depression (7%)
	insomnia (9%)
renal and urinary	renal insufficiency (9%)
respiratory, thoracic and mediastinal	cough (11%)
	dyspnea (7%)
skin and subcutaneous tissue	alopecia (7%)
	rash, including drug eruption (35%, severe 5%); see paragraph following **Side Effects** table
	Stevens Johnson syndrome (<1%); see paragraph following **Side Effects** table
	toxic epidermal necrolysis (<1%); see paragraph following **Side Effects** table
	xerosis (8%)
vascular	hypertension (10%)

Adapted from standard reference[1] unless specified otherwise.

Rash (including drug eruption) is one of the most common adverse reactions associated with mogamulizumab, occurring in approximately 35% of patients. The affected areas and appearance vary. The more common presentations include papular or maculopapular rash, morbilliform rash, and lichenoid, spongiotic, or granulomatous dermatitis, but other presentations such as scaly plaques, pustular eruptions, folliculitis, and non-specific dermatitis are also reported. Life threatening dermatologic toxicity, including Stevens-Johnson syndrome and toxic epidermal necrolysis, has been reported with mogamulizumab. Onset of dermatologic toxicity is variable. Median time to onset is 15 weeks, but a quarter of reported cases have occurred after 31 weeks. Monitor for rash throughout the treatment course. Management of dermatologic toxicity includes topical corticosteroids plus either interruption or permanent cessation of mogamulizumab depending on the severity of the toxicity. Following a moderate to severe reaction, mogamulizumab may be restarted after at least 2 weeks of topical steroids, if the rash has improved to grade 1 or better. Mogamulizumab should not be restarted following a life-threatening reaction. Skin biopsy may be required to distinguish drug eruption from disease progression.[1]

Developed: 15 March 2021
Revised: 1 May 2021

Immune-mediated complications have been reported with mogamulizumab. Grade 3 or higher reactions have included myositis, myocarditis, polymyositis, hepatitis, pneumonitis, and Guillain-Barre syndrome. Systemic immunosuppressants may be necessary to manage symptoms and mogamulizumab should be held or discontinued as appropriate. Patients with a history of autoimmune disease may experience a worsening of their pre-existing condition during treatment with mogamulizumab and this should be considered prior to commencing mogamulizumab. New onset hypothyroidism (grade 1 or 2) has been reported rarely, and can be managed with observation or levothyroxine if required.[1]

Infusion reactions are reported in more than a third of patients and are sometimes life-threatening. Most reactions (~90%) occur during or shortly after the first infusion. The most commonly reported symptoms include chills, nausea, fever, tachycardia, rigors, headache, and vomiting. It is still unclear whether premedication reduces the risk or severity of infusion reactions as premedicated patients may still experience an infusion-related reaction; however, premedication with diphenhydramine and acetaminophen is suggested for the first mogamulizumab infusion in all patients. Infusions should be interrupted for any grade reaction and symptoms treated. Permanently discontinue mogamulizumab for life-threatening reactions. When restarting the infusion after symptoms resolve, the infusion rate should be reduced by at least 50%. Premedication with diphenhydramine and acetaminophen should be used for all subsequent infusions. If symptoms recur and are unmanageable, discontinue mogamulizumab.[1]

SUPPLY AND STORAGE:

Injection: Kyowa Kirin Inc. supplies mogamulizumab as 20 mg vials of ready-to-use, single-use (preservative free) solution in a concentration of 4 mg/mL. Refrigerate. Protect from light in original packaging. Do not shake.[1]

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

SOLUTION PREPARATION AND COMPATIBILITY:

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

Additional information:

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

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

Subcutaneous	do NOT use[1]
Intramuscular	no information found
Direct intravenous	do NOT use[1]
Intermittent infusion[1]	***over 60 min***; administer using a 0.22 micron (or equivalent) ***in-line filter***
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

Developed: 15 March 2021
Revised: 1 May 2021

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:	4 weeks[1,2]:	Cycle 1: ***1 mg/kg IV for one dose on days 1, 8, 15, and 22*** (total dose per cycle 4 mg/kg) Cycle 2 and subsequent cycles: ***1 mg/kg IV for one dose on days 1 and 15*** (total dose per cycle 2 mg/kg)

REFERENCES:

1. Kyowa Kirin Inc. POTELIGEO® full prescribing information. Bedminister, New Jersey, USA; August 2018.
2. Kim YH, Bagot M, Pinter-Brown L, et al. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomized, controlled phase 3 trial. Lancet Oncol 2018;19(9):1192-1204.
3. Kyowa Hakko Kirin Co Ltd. Mogamulizumab: Canadian Med-Info Dossier in Support of Clinical Enquiries by Canadian Healthcare Providers. Version 1.0. Gunma, Japan; January 2021.
4. BC Cancer. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; 1 July 2020.
5. BC Cancer Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer; January 2016.

Developed: 15 March 2021
Revised: 1 May 2021