DRUG NAME: Tislelizumab

SYNONYM(S): BGB-A317[1]

COMMON TRADE NAME(S):

CLASSIFICATION: immunotherapy

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

MECHANISM OF ACTION:

Tislelizumab is a humanized IgG4 monoclonal antibody known as a programmed cell death-1 (PD-1) immune checkpoint inhibitor. The PD-1 pathway is an immune control checkpoint that may be exploited by tumour cells to escape active T-cell surveillance. Tislelizumab binds to the extracellular domain of PD-1 on activated T-cells with high specificity and affinity, thus competitively blocking the binding of both PD-L1 and PD-L2 ligands expressed on tumour cells. By disrupting PD-1 signalling, tislelizumab acts to restore antitumour immunity and halt progression of tumour growth.[1]

USES:

Primary uses:

Other uses:
Lymphoma, cutaneous T-cell (investigational)[2]
Esophageal cancer (investigational)[1]:
Gastric cancer (investigational)[1]:
Liver cancer (investigational)[1]:
Lung cancer, non-small cell (investigational)[1]:
Lymphoma, Hodgkin's (investigational)[1]:

*Health Canada approved indication

SPECIAL PRECAUTIONS:

- ***immune related adverse reactions*** may involve one or more body systems; reactions can be life threatening or fatal[1]
- ***fetal harm*** may occur if tislelizumab is administered during pregnancy; contraception is recommended during treatment and for 3 months following treatment[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	anemia (8-21%, severe 1-8%)
	leukopenia (5-12%, severe 2%)

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
neutropenia	lymphopenia (<1%)
	neutropenia (3-9%, severe 1-3%)
	thrombocytopenia (1-9%, severe 1%)
cardiac	***immune-mediated myocarditis*** (1%, severe <1%)
endocrine	***immune-mediated adrenal insufficiency*** (<1%)
	immune-mediated hyperthyroidism (3-4%, severe <1%)
	immune-mediated hypothyroidism (6-21%, severe 1%)
	immune-mediated thyroiditis (1%)
eye	***immune-mediated uveitis*** (<1%)
gastrointestinal	*emetogenic potential:* low[3]
	colitis, ***immune-mediated colitis*** (1%, severe 1%)
	constipation (13%, severe <1%)
	diarrhea (5-13%, severe 1%)
	nausea (4-13%, severe <1%)
	immune-mediated pancreatitis (1%, severe 1%)
	stomatitis, aphthous ulcer (3%, severe <1%)
	vomiting (10%, severe 1%)
general disorders and administration site conditions	*extravasation hazard:* none[4]
	chills (1%, severe 0%)
	fatigue, asthenia (1-23%, severe 2%)
	pyrexia (5-33%, severe 1%)
hepatobiliary	***immune-mediated hepatitis*** (1-3%, severe 1-2%)
immune system	***immune-mediated adverse events*** (21-22%, severe 5-11%); see paragraph following **Side Effects** table
infections and infestations	pneumonia (3%)
injury, poisoning, and procedural complications	***infusion-related reactions*** (2-29%, severe <2%); see paragraph following **Side Effects** table
investigations	alkaline phosphatase increase (6%, severe 1%)
	ALT increase (1-16%, severe 2%)
	AST increase (1-17%, severe 3%)
	bilirubin increase (5-12%, severe 2%)
	creatine phosphokinase increase (1-6%, severe 1%)
	hyperglycemia (2-5%, severe 1%)
	hyponatremia (1%, severe 1%)
	lipase increase (1%, severe 1%)

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	proteinuria (1-6%)
	thyroid hormone (free triiodothyronine and thyroxine) decrease (1%)
	thyroid stimulating hormone (TSH) increase (1-7%)
metabolism and nutrition	appetite decrease (1-15%, severe <1%)
	diabetes mellitus, type 1 (1%, severe 1%)
	diabetic ketoacidosis (<1%)
musculoskeletal and connective tissue	arthralgia (2-6%)
	immune-mediated myositis/rhabdomyolysis (1%, severe 1%)
renal and urinary	***immune-mediated nephritis, renal dysfunction*** (1%, severe 1%)
respiratory, thoracic and mediastinal	cough (13%)
	dyspnea (6%, severe 1%)
	immune-mediated pneumonitis, interstitial lung disease (2-7%, severe 1-6%)
skin and subcutaneous tissue	***immune-mediated dermatitis*** (1%, severe <1%)
	immune-mediated pruritus (2-4%)
	immune-mediated rash (3%, severe <1%)
	immune-mediated vitiligo (1%)
	pruritus (8-14%, severe <1%)
	rash (6-18%, severe 1%)
	skin reaction, undefined (1%, severe <1%)

Adapted from standard reference[1] unless specified otherwise.

Immune-mediated adverse events are a spectrum of side effects caused by general immunologic enhancement that can occur at any time during tislelizumab treatment or months after discontinuation. Immune-mediated events associated with tislelizumab are primarily low grade events and are generally considered manageable with established treatment algorithms. Symptoms can be severe or escalate quickly if not recognized and treated. Some fatalities have been reported. Consider the etiology of any adverse event to be immune-mediated until another etiology is confirmed for any reported diarrhea/colitis, endocrinopathy, hepatitis, myocarditis, nephritis, pneumonitis, rash, and uveitis. Strongly advise patients to promptly report symptoms and to avoid self-treatment without medical advice. Management of symptoms depends on the severity of the reaction and may require treatment interruption and/or administration of systemic corticosteroids. Corticosteroids should be appropriately tapered following resolution of symptoms to grade 1 or less. Depending on the severity of the initial reaction, tislelizumab may be restarted following completion of the steroid taper. Referral to appropriate medical specialty may be required to manage other immune-mediated complications related to treatment.

Permanently discontinue tislelizumab for:

- life-threatening (grade 3 or 4) reactions; excluding endocrinopathies controlled with replacement hormones,
- persistent reactions that do not improve to grade 0 or 1, even with corticosteroids, or
- recurrent grade 3 reactions.[1]

For further information on management of immune-mediated adverse reactions, see BC Cancer Protocol SCIMMUNE ***Management of Immune-Mediated Adverse Reactions to Checkpoint Inhibitors Immunotherapy***.

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Infusion related reactions are uncommon with tislelizumab treatment of solid tumours, but incidence may be higher in hematological malignancies. Reactions are sometimes life-threatening. Symptoms may include fever, chills/rigor, nausea/vomiting, pruritus, rash, angioedema, hypo or hypertension, headache, dizziness, bronchospasm, and myalgias. Reactions may be managed by grade as follows:

- grade 1: reduce infusion rate by 50%
- grade 2: stop infusion until reaction resolves to grade 1 or less in severity; may restart infusion at 50% of previous rate if clinically appropriate
- grade 3 or 4: permanently discontinue tislelizumab

Following a grade 1 or 2 reaction, standard premedications will be required for subsequent infusions, and the previously reduced infusion rate should be maintained.[1]

INTERACTIONS:

No information found; however, drug-drug interactions are not anticipated given that the primary elimination pathways are protein catabolism via the reticuloendothelial system or target-mediated disposition.[1]

SUPPLY AND STORAGE:

Injection: BeiGene, Ltd. supplies tislelizumab as 100 mg ready-to-use, single-use (preservative free) vials in a concentration of 10 mg/mL. Refrigerate. Store in original carton.[1,5]

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	no information found
Intramuscular	no information found
Direct intravenous	no information found
Intermittent infusion[6]	***over 30-60 min*** (initial infusion over 60 min; if well tolerated, subsequent infusions can be given over 30 min); administer using 0.2-0.22 micron inline 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

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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*[1,6]:**	***200 mg IV for one dose on day 1*** (total dose per cycle 200 mg)

REFERENCES:

1. BeiGene Ltd. Tislelizumab (BGB-A317) Investigator's Brochure - Edition 8.0. San Mateo, California, USA; 10 September 2020.
2. BeiGene Ltd. Clinical Study Pharmacy Manual Protocol BGB-A317-207: An phase 2, open-label study of BGB-A317 in patients with relapsed or refractory mature T- and NK-cell neoplasms. San Mateo, California, USA; 8 November 2019; Version 5.0.
3. BC Cancer. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; 1 July 2020.
4. 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.
5. Lillian Phan. Senior Manager, Medical Affairs US, EU & New Markets. Personal communication. BeiGene Ltd.; 15 January 2021.
6. BeiGene Ltd. Tislelizumab (BGB-A317) Product Information for Investigator Sponsored Research (ISR) Investigators. San Mateo, California, USA; 19 May 2020; Version 0.0.

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