# DRUG NAME: Epcoritamab

**SYNONYM(S):** GEN3013[1]; epcoritamab-bysp[2]

**COMMON TRADE NAME(S):** EPKINLY® (USA)

**CLASSIFICATION:** immunotherapy

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

## MECHANISM OF ACTION:

Epcoritamab is a humanized immunoglobulin G1 (IgG1) manufactured in Chinese hamster ovary cells. It is a T-cell engaging bispecific antibody that binds to the T-cell antigen CD3 and the B-cell antigen CD20 on malignant cells. By co-engaging CD3 and CD20, epcoritamab induces the activation of T cells which then causes the release of proinflammatory cytokines and the subsequent lysis of CD20 expressing B cells and tumour cells.[1-3]

## USES:

***Primary uses:***

Lymphoma, B-cell[2]

***Other uses:***

*Health Canada approved indication

## SPECIAL PRECAUTIONS:

***Caution:***

- to reduce the incidence and severity of ***cytokine release syndrome*** (CRS), epcoritamab is administered using a step-up dosing schedule[2]
- ***premedication*** is required before each dose in cycle 1 and in patients who experience any grade 2 or 3 CRS with a previous dose[2]
- ***antimicrobial/antiviral prophylaxis*** is recommended for *Pneumocystis jirovecii* pneumonia and herpes virus prior to starting epcoritamab[2]
- epcoritamab-induced immune activation (T-cell activation and cytokine release) may compromise ***pregnancy maintenance***; infants exposed to epcoritamab *in utero* may develop ***B-cell lymphocytopenia***[2]

## 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.



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| ORGAN SITE | SIDE EFFECT |
|---|---|
| Clinically important side effects are in ***bold, italics*** | |
| blood and lymphatic system/ febrile neutropenia | ***anemia*** (12%) |
| | ***febrile neutropenia*** (3%) |
| | ***neutropenia*** (32%) |
| | ***thrombocytopenia*** (12%) |
| cardiac | ***arrhythmias*** (10%, severe 1%); includes bradycardia, tachycardia, supraventricular extrasystole |
| | ***myocardial infarction*** (1%); fatalities have been reported |
| gastrointestinal | *emetogenic potential:* low[4] |
| | abdominal pain (23%, severe 2%) |
| | diarrhea (20%, severe 0%) |
| | nausea (20%, severe 1%) |
| | vomiting (12%, severe <1%) |
| general disorders and administration site conditions | fatigue (29%, severe 3%) |
| | injection site reactions (27%, severe 0%) |
| | pyrexia (24%, severe 0%) |
| hepatobiliary | ***hepatotoxicity*** (1%); fatalities have been reported |
| immune system | ***cytokine release syndrome*** (51%, severe 3%); see paragraph following **Side Effects** table |
| infections and infestations | COVID-19 (1%) |
| | pneumonia, including COVID-19 pneumonia (<10%) |
| | sepsis (<10%) |
| | upper respiratory tract infections (<10%) |
| investigations | ***ALT increase*** (45%, severe 5%) |
| | ***AST increase*** (48%, severe 5%) |
| | ***creatinine increase*** (24%, severe 3%) |
| | hemoglobin decrease (62%, severe 12%) |
| | lymphocyte count decrease (87%, severe 77%) |
| | magnesium decrease (31%) |
| | neutrophil decrease (50%, severe 32%) |
| | phosphate decrease (56%) |
| | platelet decrease (48%, severe 12%) |
| | potassium decrease (34%, severe 5%) |
| | potassium increase (21%, severe 1%) |
| | sodium decrease (56%, severe 3%) |
| | white blood cell decrease (53%, severe 22%) |



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| ORGAN SITE | SIDE EFFECT |
|---|---|
| Clinically important side effects are in ***bold, italics*** | |
| metabolism and nutrition | appetite decrease (12%, severe 1%) |
| musculoskeletal and connective tissue | musculoskeletal pain (28%, severe 1%) |
| nervous system | headache (13%, severe 1%) |
| | ***immune effector cell-associated neurotoxicity syndrome*** (1%); see paragraph following **Side Effects** table |
| respiratory, thoracic and mediastinal | pleural effusion (<10%) |
| | ***pulmonary embolism*** (1%); fatalities have been reported |
| skin and subcutaneous tissue | rash (15%, severe 1%) |

Adapted from standard reference[2] unless specified otherwise.

***Cytokine release syndrome*** (CRS) is reported in approximately 50% of patients, with the majority of patients experiencing grade 1 or 2 reactions. Serious or life-threatening reactions can occur. Reported signs and symptoms include pyrexia, hypotension, hypoxia, dyspnea, chills, and tachycardia. Concurrent neurological reactions associated with CRS include headache, confusional state, tremours, dizziness, and ataxia. Most events occur during the first cycle, and the majority of those occur after the first full dose on day 15. Recurrent CRS is reported in 16% of patients. The median time to onset is 24 hours after epcoritamab is administered (range 0 to 10 days). CRS resolves in 98% of patients and the median duration of CRS events is 2 days (range 1 to 27 days). To reduce the incidence and severity of CRS, epcoritamab treatment is initiated in a step-up dosing regimen. Premedicate with corticosteroid, antihistamine, and acetaminophen prior to each dose in the first cycle. Patients experiencing grade 2 or higher CRS with a previous dose should be premedicated with corticosteroids for subsequent cycles. If CRS is suspected, withhold epcoritamab until symptoms resolve and manage according to severity. Permanently discontinue epcoritamab for grade 4 or recurrent grade 3 reactions. Refer to protocol by which patient is being treated.[2] For further information about the management of CRS, see BC Cancer Protocol SCCRS Cytokine Release Syndrome Management.

***Immune effector cell-associated neurotoxicity syndrome*** (ICANS) has been reported with epcoritamab and may be life-threatening or fatal. Signs and symptoms of ICANS include: confusional state, lethargy, tremour, dysgraphia, aphasia, and non-convulsive status epilepticus. The majority of ICANS events occur during cycle 1, with a median time to onset of 16.5 days (range 8 to 141 days). The median duration is 4 days (range 0-8 days). ICANS can occur concurrent with CRS, following the resolution of CRS, or in the absence of CRS. Patients should be advised to report symptoms immediately if they occur. Withhold epcoritamab at the first signs of neurotoxicity. Neurology consult may be required. Management of ICANS may include anti-seizure medications for seizure prophylaxis and corticosteroids for symptom management. Provide supportive care as required. Withhold epcoritamab until ICANS resolves and permanently discontinue epcoritamab for grade 4 reactions and recurrent grade 3 reactions. Patients experiencing signs and symptoms of ICANS should refrain from driving or operating machinery until symptoms have resolved.[2]

## INTERACTIONS:

Epcoritamab causes release of cytokines that may suppress the activity of CYP enzymes, resulting in increased exposure of CYP substrates. Substrates of CYP450 enzymes with a narrow therapeutic index may require dose adjustment and monitoring for toxicity if given concurrently with epcoritamab. Interactions with CYP substrates are most likely to occur after the first dose of epcoritamab (Cycle 1, day 1) and up to 14 days after the first full dose (Cycle 1, day 15), as well as during/after a CRS event.[2]



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## SUPPLY AND STORAGE:

***Injection***:

AbbVie Inc. supplies epcoritamab (via Health Canada Special Access Program) as a single dose (preservative free) vial in two vial sizes: 4 mg vials in a concentration of 5 mg/mL and 48 mg vials in a concentration of 60 mg/mL Non-medicinal ingredients: sorbitol (provides 21.9 mg of sorbitol with epcoritamab 48 mg dose)[5]; clinical significance is unknown. Refrigerate. Keep in original carton to protect from light. Do not shake.[5]

AbbVie Corporation supplies epcoritamab as a single dose (preservative free) vial in two vial sizes: 4 mg vials in a concentration of 5 mg/mL and 48 mg vials in a concentration of 60 mg/mL Refrigerate. Keep in original carton to protect from light. Do not shake.[6]

***Additional information:***

- ***Caution:*** epcoritamab vials are supplied as two different concentrations (5 mg/mL and 60 mg/mL); ensure selection of appropriate vial size for dose preparation[6]

***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:***

- ***Caution:*** epcoritamab vials are supplied as two different concentrations; ensure selection of appropriate vial size for dose preparation
- 4 mg vials must be further diluted prior to use for step-up doses[6]
- do not use if particulates are present[5]
- for SAP supply: do not use closed system transfer devices for preparation or administration[7]; filtered venting needles (such as Chemo-Vent®) will be used for preparation instead of CSTD
- for commercial supply: closed system transfer devices may be used for preparation and administration[8]
- for prepared solutions: minimize exposure to daylight and protect from light during periods of refrigerated storage prior to use[6]

***Compatibility:*** consult detailed reference

## PARENTERAL ADMINISTRATION:

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

| | |
|---|---|
| Subcutaneous | injection into the lower abdomen is preferred; may be administered into the thigh[2] |
| Intramuscular | do not use |
| Direct intravenous | do not use |
| Intermittent infusion | do not use |
| Continuous infusion | do not use |
| Intraperitoneal | do not use |
| Intrapleural | do not use |
| Intrathecal | do not use |



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

| | |
|---|---|
| Intra-arterial | do not use |
| Intravesical | do not use |

## 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***

*Subcutaneous:* Cycle Length: 4 weeks[2]:

**Cycle 1:**

| Dosing Schedule | | Day of treatment | Dose (SC) |
|---|---|---|---|
| Step-up dosing schedule | Step-up dose 1 (priming) | 1 | 0.16 mg |
| | Step-up dose 2 (intermediate) | 8 | 0.8 mg |
| | First full treatment dose | 15 | 48 mg |
| | Second full treatment dose | 22 | 48 mg |

(total dose per cycle 96.96 mg)

**Cycles 2 and 3:**
48 mg SC given once weekly on days 1, 8, 15, and 22
(total dose per cycle 192 mg)

**Cycles 4 to 9:**
48 mg SC given once on days 1 and 15
(total dose per cycle 96 mg)

**Cycles 10 and beyond**:
48 mg SC given once on day 1
(total dose per cycle 48 mg)

**Following dose delays**: for instruction about restarting epcoritamab, refer to protocol by which patient is being treated as the step-up regimen may need to be repeated[2]



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## REFERENCES:

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3. AbbVie Inc. Protocol for Study M20-638 Relapsed/Refractory Follicular Lymphoma: Epcoritamab in Combination with Rituximab and Lenalidomide. Version 1.0. North Chicago, Illinois, USA; April 22 2022
4. BC Cancer. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; December 1 2018
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8. Adi Klil-Drori. Medical Advisor, Oncology. AbbVie Inc. Personal Communication - epcoritamab (CSTD use with commercial supply). February 14,2024



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