DRUG NAME: Ixabepilone

SYNONYM(S):

COMMON TRADE NAME(S): IXEMPRA®

CLASSIFICATION: miscellaneous

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

MECHANISM OF ACTION:

Ixabepilone is a semi-synthetic analog of epothilone B that binds to beta-tubulin subunits on microtubules, leading to suppression of microtubule dynamics; specifically, the dynamic instability of alpha-beta-II and alpha-beta-III microtubules, which leads to apoptosis. Ixabepilone is cell cycle phase-specific.

USES:

Primary uses:
*Breast cancer

*Health Canada approved indication

Other uses:

SPECIAL PRECAUTIONS:

Caution:

- premedication with H_1 and H_2 antagonists is recommended
- dosage adjustment may be necessary for hepatic dysfunction and for concomitant use with strong CYP 3A4 inhibitors

Fertility: impaired fertility in animal studies[1]

Pregnancy: FDA Pregnancy Category D.[1] There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk(e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).

Breastfeeding is not recommended due to potential secretion into breast milk.[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, and/or determined to be clinically important.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
allergy/immunology	***hypersensitivity reactions*** (5%)
auditory/hearing	vertigo (4%)
blood/bone marrow/ febrile neutropenia	anemia (6%)
	febrile neutropenia (3%)
	leukopenia (36%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	neutropenia (23%)
	thrombocytopenia (2%)
cardiovascular (general)	myocardial ischemia (2%)
constitutional symptoms	fatigue (56%)
	hot flush (6%)
dermatology/skin	*extravasation hazard: none*[2]
	alopecia (48%)
	nail disorder (9%)
	palmar-plantar erythrodysesthesia (8%)
	pruritis (6%)
	skin rash (9%)
gastrointestinal	*emetogenic potential: low*[3]
	abdominal pain (13%)
	anorexia (19%)
	diarrhea (22%)
	nausea (42%)
	stomatitis/mucositis (29%)
hepatobiliary/pancreas	acute hepatic failure, jaundice
infection	upper respiratory tract infection (6%)
musculoskeletal	myalgia/arthralgia (49%)
neurology	headaches (11%)
	peripheral neuropathy (62%)
ocular/visual	lacrimation increased (4%)
pain	musculoskeletal pain (20%)
	pain (8%)
pulmonary	cough (2%)
	dyspnea (9%)

Adapted from standard reference[1] unless specified otherwise.

SUPPLY AND STORAGE:

Injection[1]: Bristol-Myers Squibb supplies ixabepilone as a kit containing a 15 mg or 45 mg vial of ixabepilone for injection together with an 8 mL or 23.5 mL vial of supplied diluent which both provide ixabepilone 2 mg/mL solution after reconstitution. Refrigerate. Retain in original package until time of use.

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

SOLUTION PREPARATION AND COMPATIBILITY:

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

Additional information[1]: Administer using an in-line filter with a microporous membrane of 0.2 to 1.2 microns. Non-DEHP infusion containers and administration sets must be used.

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in ***bold***, ***italics***

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous[1]	not to be used
Intermittent infusion[1]	***over 3 hours*** (use non-DEHP administration set)
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*:**

BCCA usual dose noted in ***bold, italics***

Intravenous:	Cycle Length: 3 weeks[1]:	***40 mg/m^2* IV for one dose on day 1** If calculated BSA is greater than 2.2 m^2, use BSA of 2.2 m^2

REFERENCES:

1. Bristol-Myers Squibb. IXEMPRA® product monograph. Princeton, New Jersey; 01 October 2007.
2. BC Cancer Agency Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer Agency; 1 September 2006.
3. BC Cancer Agency. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer Agency; 1 November 2005.