Eribulin: Drug information

(For additional information see "Eribulin: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Brand Names: US

Halaven

Brand Names: Canada

Halaven

Pharmacologic Category

Antineoplastic Agent, Antimicrotubular

Dosing: Adult

Note: ***International Considerations:*** Some products available internationally may have vial strength and dosing expressed as the base (instead of as the salt). Refer to prescribing information for specific dosing information.

Breast cancer, metastatic: IV: Eribulin mesylate: 1.4 mg/m^2 on days 1 and 8 of a 21-day treatment cycle

Liposarcoma, unresectable or metastatic: IV: Eribulin mesylate: 1.4 mg/m^2 on days 1 and 8 of a 21-day treatment cycle

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

Note: ***International Considerations:*** Some products available internationally may have vial strength and dosing expressed as the base (instead of as the salt). Refer to prescribing information for specific dosing information.

CrCl ≥50 mL/minute: No dosage adjustment necessary.

CrCl 15 to 49 mL/minute: Reduce dose to eribulin mesylate 1.1 mg/m^2.

ESRD (*Canadian labeling*): Use is not recommended.

Dosing: Hepatic Impairment

Note: ***International Considerations:*** Some products available internationally may have vial strength and dosing expressed as the base (instead of as the salt). Refer to prescribing information for specific dosing information.

Mild hepatic impairment (Child-Pugh class A): Reduce dose to eribulin mesylate 1.1 mg/m^2.

Moderate hepatic impairment (Child-Pugh class B): Reduce dose to eribulin mesylate 0.7 mg/m^2.

Severe hepatic impairment (Child-Pugh class C): There are no dosage adjustments provided in the manufacturer's US labeling (has not been studied); use is not recommended in the Canadian labeling.

Dosing: Obesity

ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer:

Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012).

Dosing: Adjustment for Toxicity

Note: ***International Considerations:*** Some products available internationally may have vial strength and dosing expressed as the base (instead of as the salt). Refer to prescribing information for specific dosing information.

ANC <1,000/mm^3 or platelets <75,000/mm^3 or grade 3 or 4 nonhematologic toxicity on day 1 or 8: Withhold dose; may delay day 8 dose up to 1 week. If toxicity resolves to ≤ grade 2 by day 15 administer a reduced dose and wait at least 2 weeks before beginning the next cycle. Omit dose if not resolved to ≤ grade 2 by day 15. Do not re-escalate dose after reduction.

Permanently reduce dose from eribulin mesylate 1.4 mg/m^2 to 1.1 mg/m^2 for the following:

ANC <500/mm^3 for >7 days

ANC <1000/mm^3 with fever or infection

Platelets <25,000/mm^3

Platelets <50,000/mm^3 requiring transfusion

Nonhematologic toxicity of grade 3 or 4

Dose omission or delay due to toxicity on day 8 of prior cycle

Permanently reduce dose from eribulin mesylate 1.1 mg/m^2 to 0.7 mg/m^2 for occurrence of any of the above events; discontinue treatment if the above toxicities occur at the 0.7 mg/m^2 dose level.

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous, as mesylate:

Halaven: 1 mg/2 mL (2 mL) [contains alcohol, usp]

Generic Equivalent Available (US)

No

Administration

IV: Infuse over 2 to 5 minutes. May be administered undiluted or diluted. Do not administer other medications through the same IV line, or through a line containing dextrose.

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological

safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

Use

Breast cancer, metastatic: Treatment of metastatic breast cancer in patients who have received at least 2 prior chemotherapy regimens for the treatment of metastatic disease (prior treatment should have included an anthracycline and a taxane in either the adjuvant or metastatic setting)

Liposarcoma, unresectable or metastatic: Treatment of unresectable or metastatic liposarcoma in patients who have received a prior anthracycline-containing regimen

Medication Safety Issues

Sound-alike/look-alike issues:

EriBULin may be confused with epiRUBicin, erlotinib

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

International Issues:

Some products available internationally may have vial strength and dosing expressed as the base (instead of as the salt). Refer to prescribing information for specific strength and dosing information.

Adverse Reactions

>10%:

Cardiovascular: Peripheral edema (≥5% to 12%)

Central nervous system: Fatigue (≤62%), peripheral neuropathy (29% to 35%; grades 3/4: 3% to 8%), headache (18% to 19%)

Dermatologic: Alopecia (35% to 45%)

Endocrine & metabolic: Hypokalemia (≥5% to 30%), hypocalcemia (28%), weight loss (21%), hypophosphatemia (20%)

Gastrointestinal: Nausea (35% to 41%), constipation (25% to 32%), abdominal pain (≥5% to 29%), anorexia (20%), decreased appetite (19%), vomiting (18% to 19%), diarrhea (17% to 18%), stomatitis (≥5% to 14%)

Genitourinary: Urinary tract infection (10% to 11%)

Hematologic & oncologic: Neutropenia (63% to 82%; grade 4: 29% grades 3/4: 12% to 57%; nadir:

13 days; recovery: 8 days), anemia (58% to 70%; grades 3/4: 2% to 4%)

Hepatic: Increased serum ALT (18% to 43%), increased serum AST (36%)

Neuromuscular & skeletal: Weakness (≤62%), arthralgia (≤22%), myalgia (≤22%), back pain (16%), ostealgia (12%), limb pain (11%)

Respiratory: Cough (14% to 18%), dyspnea (16%)

Miscellaneous: Fever (21% to 28%)

1% to 10%:

Cardiovascular: Hypotension (≥5% to <10%)

Central nervous system: Anxiety (≥5% to <10%), depression (≥5% to <10%), dizziness (≥5% to <10%), insomnia (≥5% to <10%), myasthenia (≥5% to <10%)

Dermatologic: Skin rash (≥5% to <10%)

Endocrine & metabolic: Hyperglycemia (≥5% to <10%)

Gastrointestinal: Dysgeusia (≥5% to <10%), dyspepsia (≥5% to <10%), xerostomia (≥5% to <10%), mucosal inflammation (9%)

Hematologic & oncologic: Thrombocytopenia (≥5% to <10%; grades ≥3: 1%), febrile neutropenia (≤5%)

Neuromuscular & skeletal: Muscle spasm (≥5% to <10%), musculoskeletal pain (≥5% to <10%),

Ophthalmic: Increased lacrimation (≥5% to <10%)

Respiratory: Oropharyngeal pain (≥5% to <10%), upper respiratory tract infection (≥5% to <10%)

<1%, postmarketing, and/or case reports: Dehydration, drug-induced hypersensitivity, hepatotoxicity, hypomagnesemia, interstitial pulmonary disease, lymphocytopenia, neutropenic sepsis, pancreatitis, pneumonia, prolonged Q-T interval on ECG, pruritus, sepsis, Stevens-Johnson syndrome, toxic epidermal necrolysis

Contraindications

There are no contraindications listed in the manufacturer's labeling.

Canadian labeling (not in US labeling): Hypersensitivity to eribulin mesylate, halichondrin B, or its chemical derivatives.

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: Hematologic toxicity, including severe neutropenia and neutropenic fever, has occurred. Neutropenic sepsis (fatal) has also been reported (case reports). May require treatment delay and dosage reduction. A higher incidence of grade 4 neutropenia and neutropenic fever occurred in patients with ALT or AST >3 x ULN or bilirubin >1.5 x ULN. Monitor complete blood counts prior to each dose; more frequently if severe cytopenias develop. Patients with baseline neutrophils <1,500/mm^3 were not included in clinical studies.

• Peripheral neuropathy: Peripheral neuropathy commonly occurs. Peripheral neuropathy may be prolonged (>1 year in 5% of metastatic breast cancer patients and >60 days in close to 60% of liposarcoma patients); over 60% of liposarcoma patients with peripheral neuropathy had not recovered within a median follow-up of ~6 months in one clinical trial. The median time to the first occurrence of peripheral neuropathy (any severity) in liposarcoma patients was 5 months (range: 3.5 to 9 months). Monitor for signs of peripheral motor or sensory neuropathy. May require treatment delay or discontinuation. Some patients may have preexisting neuropathy due to prior chemotherapy; monitor closely for worsening neuropathy.

• QT prolongation: QT prolongation was observed on day 8 of eribulin therapy (in an uncontrolled study). Monitor ECG in patients with heart failure, bradyarrhythmia, with concomitant medication known to prolong the QT interval, or with electrolyte imbalance. Correct hypokalemia and hypomagnesemia prior to treatment; monitor electrolytes periodically during treatment. Avoid use in patients with congenital long QT syndrome.

Disease-related concerns:

• Hepatic impairment: Dosage reduction required in patients with mild to moderate (Child-Pugh class A or B) hepatic impairment; use has not been studied in patients with severe hepatic impairment. Transaminase or bilirubin elevations are associated with a higher incidence of grade 4 neutropenia and neutropenic fever.

• Renal impairment: Dosage reduction required in patients with moderate or severe renal impairment (CrCl 15 to 49 mL/minute).

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Other warnings/precautions:

• International issues: Some products available internationally may have vial strength and dosing expressed as the base (instead of as the salt). Refer to prescribing information for specific dosing information.

Metabolism/Transport Effects

Substrate of CYP3A4 (minor); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Highest Risk QTc-Prolonging Agents: QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying) may enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. Management: Avoid such combinations when possible. Use should be accompanied by close monitoring for evidence of QT prolongation or other alterations of cardiac rhythm. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

MiFEPRIStone: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying). Management: Though the drugs listed here have uncertain QT-prolonging effects, they all have some possible association with QT prolongation and should generally be avoided when possible. *Risk D: Consider therapy modification*

Moderate Risk QTc-Prolonging Agents: QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying) may enhance the QTc-prolonging effect of Moderate Risk QTc-Prolonging Agents. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Pregnancy Implications Adverse effects were observed in animal reproduction studies. Based on its mechanism of action, eribulin would be expected to cause fetal harm if administered during pregnancy. Women of reproductive potential should use effective contraception to avoid pregnancy during eribulin treatment and for at least 2 weeks following the last eribulin dose; males with female partners of reproductive potential should use effective contraception during eribulin treatment and for 3.5 months following the last dose. The Canadian labeling recommends effective contraception during and for at least 3 months after treatment in women of reproductive potential.

Breast-Feeding Considerations It is not known if eribulin is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, breast-feeding is not recommended by the manufacturer during eribulin treatment and for 2 weeks after the last dose.

Monitoring Parameters CBC with differential prior to each dose (increase frequency with grades 3/4 cytopenias); renal and liver function tests; serum electrolytes, including potassium and magnesium. Assess for peripheral neuropathy prior to each dose. Monitor ECG in patients with heart failure, bradyarrhythmia, with concomitant medication known to prolong the QT interval, and electrolyte abnormalities (eg, hypokalemia, hypomagnesemia).

Mechanism of Action Eribulin is a non-taxane microtubule inhibitor which is a halichondrin B analog. It inhibits the growth phase of the microtubule by inhibiting formation of mitotic spindles causing mitotic blockage and arresting the cell cycle at the G_2/M phase; suppresses microtubule polymerization yet does not affect depolymerization.

Pharmacodynamics/Kinetics

Distribution: V_d: 43 to 114 L/m^2

Protein binding: 49% to 65%

Metabolism: Negligible

Half-life, elimination: ~40 hours

Excretion: Feces (~82%, predominantly as unchanged drug); urine (9%, primarily as unchanged drug)

Pricing: US

Solution (Halaven Intravenous)

1 mg/2 mL (2 mL): $1260.00

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Hal;aven (BR); Halaven (AE, AT, AU, BE, CH, CR, CY, CZ, DE, DK, DO, EE, ES, FI, FR, GB, GR, GT, HK, HN, HR, HU, IL, IS, IT, JO, JP, KR, LB, LT, LU, MT, MY, NI, NL, NO, PA, PH, PL, PT, RO, RU, SA, SE, SG, SI, SK, SV, TH, TR)

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