Adverse Events Grading Criteria

Common Terminology Criteria for Adverse Events*

In clinical studies, 2 of the most common adverse events reported with HALAVEN® were peripheral neuropathy and neutropenia.[1] With this card, you can help track and manage these adverse events by identifying their severity and adjusting the dose of HALAVEN as needed.

See Prescribing Information for additional adverse events.

Grading peripheral neuropathy[1,2]*

Monitor patients closely for signs of peripheral motor and sensory neuropathy.

Grade 1	• Asymptomatic • Motor: clinical or diagnostic observations only
Grade 2	• Moderate symptoms; limiting instrumental ADL
Grade 3	• Severe symptoms; limiting self-care ADL
Grade 4	• Life-threatening consequences; urgent intervention indicated
Grade 5	• Death (peripheral motor neuropathy)

ADL=activities of daily living.
*Adapted from Common Terminology Criteria for Adverse Events version 5.

Indications

Metastatic Breast Cancer

HALAVEN (eribulin mesylate) Injection is indicated for the treatment of patients with metastatic breast cancer (mBC) who have previously received at least 2 chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

Liposarcoma

HALAVEN is indicated for the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

Selected Safety Information

Warnings and Precautions

Neutropenia: Severe neutropenia (ANC <500/mm^3) lasting >1 week occurred in 12% of patients with mBC and liposarcoma or leiomyosarcoma. Febrile neutropenia occurred in 5% of patients with mBC and 2 patients (0.4%) died from complications. Febrile neutropenia occurred in 0.9% of patients with liposarcoma or leiomyosarcoma, and fatal neutropenic sepsis occurred in 0.9% of patients. Patients with mBC with elevated liver enzymes >3 × ULN and bilirubin >1.5 × ULN experienced a higher incidence of Grade 4 neutropenia and febrile neutropenia than patients with normal levels. Monitor complete blood cell counts prior to each dose, and increase the frequency of monitoring in patients who develop Grade 3 or 4 cytopenias. Delay administration and reduce subsequent doses in patients who experience febrile neutropenia or Grade 4 neutropenia lasting >7 days.

Peripheral Neuropathy: Grade 3 peripheral neuropathy occurred in 8% of patients with mBC (Grade 4=0.4%) and 22% developed a new or worsening neuropathy that had not recovered within a median follow-up duration of 269 days (range 25-662 days). Neuropathy lasting >1 year occurred in 5% of patients with mBC. Grade 3 peripheral neuropathy occurred in 3.1% of patients with liposarcoma and leiomyosarcoma receiving HALAVEN and neuropathy lasting more than 60 days occurred in 58% (38/65) of patients who had neuropathy at the last treatment visit. Patients should be monitored for signs of peripheral motor and sensory neuropathy. Withhold HALAVEN in patients who experience Grade 3 or 4 peripheral neuropathy until resolution to Grade 2 or less.

Please see all Selected Safety Information throughout, full Prescribing Information, and Patient Information.

Halaven® (eribulin mesylate) Injection | 0.5 mg/mL

Grading neutropenia[1,2]*

Monitor complete blood cell counts prior to each dose, and increase the frequency of monitoring in patients who develop Grade 3 or 4 cytopenias.

ANC decreased	
Grade 1	• LLN to 1,500/mm^3; <LLN to 1.5 x 10^9/L
Grade 2	• <1,500 to 1,000/mm^3; <1.5 to 1.0 x 10^9/L
Grade 3	• <1,000 to 500/mm^3; <1.0 to 0.5 x 10^9/L
Grade 4	• <500/mm^3; <0.5 x 10^9/L

Febrile neutropenia	
Grade 3	• ANC <1,000/mm^3 with a single temperature of >38.3°C (101°F) or a sustained temperature of ≥38°C (100.4°F) for more than 1 hour
Grade 4	• Life-threatening consequences; urgent intervention indicated
Grade 5	• Death

ANC=absolute neutrophil count; LLN=lower limit of normal.
*Adapted from Common Terminology Criteria for Adverse Events version 5.

Selected Safety Information

Embryo-Fetal Toxicity: HALAVEN® can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with HALAVEN and for at least 2 weeks following the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with HALAVEN and for 3.5 months following the final dose.

QT Prolongation: Monitor for prolonged QT intervals in patients with congestive heart failure, bradyarrhythmias, drugs known to prolong the QT interval, and electrolyte abnormalities. Correct hypokalemia or hypomagnesemia prior to initiating HALAVEN and monitor these electrolytes periodically during therapy. Avoid in patients with congenital long QT syndrome.

Adverse Reactions

In patients with mBC receiving HALAVEN, the most common adverse reactions (≥25%) were neutropenia (82%), anemia (58%), asthenia/fatigue (54%), alopecia (45%), peripheral neuropathy (35%), nausea (35%), and constipation (25%). Febrile neutropenia (4%) and neutropenia (2%) were the most common serious adverse reactions. The most common adverse reaction resulting in discontinuation was peripheral neuropathy (5%).

In patients with liposarcoma and leiomyosarcoma receiving HALAVEN, the most common adverse reactions (≥25%) reported in patients receiving HALAVEN were fatigue (62%), nausea (41%), alopecia (35%), constipation (32%), peripheral neuropathy (29%), abdominal pain (29%), and pyrexia (28%). The most common (≥5%) Grade 3-4 laboratory abnormalities reported in patients receiving HALAVEN were neutropenia (32%), hypokalemia (5.4%), and hypocalcemia (5%). Neutropenia (4.9%) and pyrexia (4.5%) were the most common serious adverse reactions. The most common adverse reactions resulting in discontinuation were fatigue and thrombocytopenia (0.9% each).

Use in Specific Populations

Lactation: Because of the potential for serious adverse reactions in breastfed infants from eribulin mesylate, advise women not to breastfeed during treatment with HALAVEN and for 2 weeks after the final dose.

Hepatic and Renal Impairment: A reduction in starting dose is recommended for patients with mild or moderate hepatic impairment and/or moderate or severe renal impairment.

Please see all Selected Safety Information throughout, full Prescribing Information, and Patient Information.

References: 1. HALAVEN [package insert]. Woodcliff Lake, NJ: Eisai Inc. **2.** National Cancer Institute. Cancer Therapy Evaluation Program, Common Terminology Criteria for Adverse Events v5. Quick reference 8.5 x 11. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm#ctc_50. Published November 27, 2017. Accessed April 19, 2019.

To report suspected adverse reactions, contact Eisai Inc. at 1-888-274-2378 or the FDA at 1-800-FDA-1088 or www.FDA.gov/medwatch.

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Halaven® (eribulin mesylate) Injection | 0.5 mg/mL