PRESCRIBING INFORMATION

Halaven® (eribulin)

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: 2 ml vial containing eribulin mesilate equivalent to 0.88 mg eribulin.

Indication: The treatment of adult patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless not suitable.

The treatment of adult patients with unresectable liposarcoma who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease.

Dose and administration: For intravenous use. Should only be administered under the supervision of a qualified physician. ***Recommended dose in adults and elderly:*** 1.23 mg/m^2 eribulin as the ready to use solution administered intravenously over 2-5 minutes on Days 1 and 8 of a 21-day cycle. The dose may be diluted in up to 100 ml of sodium chloride 9 mg/ml (0.9%) solution for injection. See SmPC for full information regarding dilution. Patients may experience nausea or vomiting. Antiemetic prophylaxis including corticosteroids should be considered. See SmPC for guidelines on dose delay and reduction due to toxicity. ***Renal impairment:*** Some patients with moderately or severely impaired renal function (creatinine clearance <50 ml/min) may have increased eribulin exposure and may need a reduction of the dose. For all patients with renal impairment, caution and close safety monitoring is advised. ***Hepatic impairment due to metastases*****:** Reduce dose for mild or moderate impairment – see SmPC for guidelines; severe impairment not studied. ***Hepatic impairment due to cirrhosis:*** Not studied; close monitoring recommended. ***Paediatrics:*** There is no relevant use in children and adolescents for the indication of breast cancer. The safety and efficacy in children from birth to 18 years of age have not yet been established in soft tissue sarcoma. No data are available.***Contra-Indications:*** Hypersensitivity to eribulin or any excipients. Breast-feeding.***Special warnings and precautions:*** Myelosuppression is dose dependent and primarily manifested as neutropenia. Monitoring of complete blood counts should be performed prior to each dose of eribulin. Treatment should only be initiated in patients with ANC values ≥1.5 x 10^9/l and platelets >100 x 10^9/l. Febrile neutropenia reported in <5% of patients. Febrile neutropenia, severe neutropenia or thrombocytopenia requires dose delay or reduction. Patients with ALT or AST >3 x ULN or bilirubin >1.5 x ULN have a higher incidence of Grade 4 neutropenia and febrile neutropenia. Fatal cases of febrile neutropenia, neutropenic sepsis, sepsis and septic shock have been reported. Severe neutropenia may be managed with granulocyte colony-stimulating factor (G-CSF) or equivalent at the physician's discretion in accordance with relevant guidelines. Monitor closely for signs of peripheral motor and sensory neuropathy. Severe peripheral neurotoxicity requires dose delay or reduction. QT prolongation on Day 8 has been observed. ECG monitoring recommended in patients with congestive heart failure, bradyarrhythmias, if also receiving medicinal products known to prolong the QT interval, including Class Ia and III antiarrhythmics, and electrolyte abnormalities. Correct hypokalaemia, hypocalcaemia or hypomagnesaemia prior to initiating eribulin and monitor during therapy. Eribulin should be avoided in patients with congenital long QT syndrome. Medicinal product contains small amounts of ethanol (<100 mg per dose).

Drug Interactions: Eribulin is mainly (up to 70%) eliminated through biliary excretion. No drug-drug interactions are expected with CYP3A4 inhibitors and inducers. Eribulin exposure (AUC and C_{max}) was unaffected by ketoconazole, a CYP3A4 and P glycoprotein (Pgp) inhibitor, and rifampicin, a CYP3A4 inducer. *In vitro* data indicate that eribulin is a mild inhibitor of CYP3A4. Exercise caution and monitor for adverse events when using concomitantly with substances that are eliminated mainly via CYP3A4 and have a narrow therapeutic window.

Pregnancy and lactation: Do not use during pregnancy unless clearly necessary. Contraception advised during and up to 3 months after treatment (either for women of childbearing potential or their male partners when receiving Halaven). Do not use during breast-feeding.

Effects on ability to drive and use machines: Do not drive or use machines if experiencing tiredness or dizziness.

Undesirable effects: **Refer to SmPC for information on all side effects.** The incidence rates of adverse reactions observed in breast cancer and soft tissue sarcoma patients who received the recommended eribulin dose in Phase 2 and Phase 3 studies: *Very common (≥1/10)*: Neutropenia, leukopenia, anaemia; Decreased appetite; Peripheral neuropathy, headache; Dyspnoea, cough; Nausea, constipation, diarrhoea, vomiting; Alopecia; Arthralgia and myalgia, back pain, pain in extremity; Fatigue/asthenia, pyrexia; Weight decreased. *Common (≥1/100 to <1/10)*: Urinary tract infection, pneumonia, oral candidiasis, oral herpes, upper respiratory tract infection, nasopharyngitis, rhinitis; herpes zoster; Lymphopenia, febrile neutropenia, thrombocytopenia; Hypokalaemia, hypomagnesaemia, dehydration, hyperglycaemia, hypophosphataemia, hypocalcaemia; Insomnia, depression; Dysgeusia, dizziness, hypoaesthesia, lethargy, neurotoxicity; Lacrimation increased, conjunctivitis; Vertigo, tinnitus; Tachycardia; Hot flush, pulmonary embolism; Oropharyngeal pain, epistaxis, rhinorrhoea; Abdominal pain, stomatitis, dry mouth, dyspepsia, gastrooesophageal reflux disease, abdominal distention; Alanine aminotransferase increased, aspartate aminotransferase increased, gamma glutamyl transferase increased, hyperbilirubinaemia; Rash, pruritus, nail disorder, night sweats, dry skin, erythema, hyperhidrosis, palmar plantar erythrodysaesthesia; Bone pain, muscle spasms, musculoskeletal pain, musculoskeletal chest pain, muscular weakness; Dysuria; Mucosal inflammation, peripheral oedema, pain, chills, chest pain, influenza like illness. *Serious but uncommon (≥1/1,000 to <1/100)*: Sepsis, neutropenic sepsis, septic shock; Deep vein thrombosis; Interstitial lung disease; Mouth ulceration, pancreatitis; Hepatotoxicity; Angioedema; Haematuria, proteinuria, renal failure. *Serious but rare (≥ 1/10,000 to < 1/1,000)*: Disseminated intravascular coagulation. *Serious but frequency not known*: Stevens-Johnson syndrome / Toxic epidermal necrolysis.

Overdose: No known antidote. Closely monitor and manage with supportive medical interventions.

Legal Category: POM

Basic UK NHS Cost: Eribulin 0.44mg/ml 2ml vial: £361 per vial

Marketing authorisation number: Eribulin 0.44mg/ml 2ml vial x 1: EU/1/11/678/001

Marketing authorisation holder: Eisai GmbH.

Further information from: Eisai Ltd., Mosquito Way, Hatfield, Hertfordshire, AL10 9SN, United Kingdom

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Adverse events should be reported. Reporting forms and Information can be found at www.mhra.gov.uk/yellowcard **or search for the MHRA Yellow Card in the Google Play or Apple App Store, or Ireland:** www.hpra.ie. **Adverse events should also be reported to Eisai Ltd on +44 (0)845 676 1400/ +44 (0)208 600 1400 or** Eumedinfo@eisai.net