I. PURPOSE

To define and describe the accepted indications for Halaven (eribulin) usage in the treatment of cancer.

II. DEFINITIONS

**Halaven (eribulin):** is a synthetic macrocyclic ketone analog of the naturally occurring macrolide halichondrin B, which is isolated from the marine sponge *Halichondria okadai*. It is a potent antimitotic agent, with a distinct mechanism from other known antimitotic agents, such as taxanes, vinca alkaloids, and epothilones. Eribulin blocks cell cycle progression in the G2-M phase. It inhibits the growth phase of microtubules and sequesters tubulin in nonproductive aggregates, ultimately leading to disruption of mitotic spindles and apoptotic cell death after prolonged mitotic blockage. The suppression of microtubule dynamics by eribulin, and subsequent prolonged mitotic blockage, leads to apoptotic cell death.

Halaven (eribulin) is FDA approved for the treatment of members with metastatic breast cancer who have previously received at least two 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.

Halaven (eribulin) is available as Eribulin mesylate solution for Injection: 1 mg single use vials.

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable.

Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must be supported by, at minimum, two peer reviewed citations. If references are not produced, delays may occur to the processing of such request.

**Inclusion Criteria:** Halaven (eribulin) may be considered medically necessary when any of the following selection criteria is met:

1. **Breast Cancer**
   a. The member has recurrent or metastatic breast cancer, and Halaven (eribulin) is being used as a preferred single agent for members with any of the following:
      i. Hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative with visceral crisis
ii. HER2-negative and either hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory

iii. Progressive with no clinical benefit after three consecutive endocrine therapy regimens or with symptomatic visceral disease.

AND

b. The member has all the following:
   i. Previously received at least 2 prior chemotherapy regimens for metastatic breast cancer
   ii. Has failed both an anthracycline and a taxane in either the metastatic or adjuvant setting.

c. The member has recurrent or metastatic breast cancer, and Halaven (eribulin) is being used in combination with trastuzumab for members with the following:
   i. HER2-positive with symptomatic visceral disease or visceral crisis and prior trastuzumab exposure
   ii. HER2-positive and either hormone receptor-negative or hormone receptor-positive with endocrine therapy refractory and prior trastuzumab exposure.

AND

d. The member has ALL the following:
   i. Previously received at least 2 prior chemotherapy regimens for metastatic breast cancer
   ii. Has failed both an anthracycline and a taxane in either the metastatic or adjuvant setting.

2. Soft Tissue Sarcoma
   a. Angiosarcoma
      i. Halaven (eribulin) is being used as a single agent palliative therapy in the member with disease progression on an anthracycline-containing regimen.

b. Retroperitoneal/Intra-abdominal
   i. The member has unresectable or progressive disease and Halaven (eribulin) is being used as a single agent palliative therapy in the member with disease progression on an anthracycline-containing regimen.

c. Rhabdomyosarcoma
   i. Halaven (eribulin) is being used as single agent in palliative therapy for pleomorphic rhabdomyosarcoma in member with disease progression on anthracycline-containing regimen.

d. Soft tissue sarcoma of the extremity/superficial trunk, head/neck
   i. The member has synchronous stage IV or recurrent disease with disseminated metastases, and Halaven (eribulin) is being used as a single agent for palliative therapy in member with disease progression on anthracycline-containing regimen.
Exclusion Criteria: Halaven (eribulin) is not considered medically necessary when any of the following selection criteria is met:

1. The member did not received prior treatment with an anthracycline AND taxane based chemotherapy for breast cancer.
2. Member has severe hepatic (Child-Pugh C) or renal (Crcl < 30 ml/min) impairment.
3. Used concurrently with other chemotherapy.
4. Dosing exceeds single dose limit of Halaven (eribulin) 1.4 mg/m².
5. Member has disease progression while on Halaven (eribulin).
6. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Halaven (eribulin) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. Dosage and Administration: 1.4 mg/m² IV over 2 to 5 minutes on days 1 and 8, repeated every 21 days. Continue treatment until disease progression or unacceptable toxicity.

Dosage Adjustments

   a. Renal impairment, moderate (CrCl 30 to 50 mL/min): reduce dose to 1.1 mg/m² IV over 2 to 5 minutes on days 1 and 8 of a 21-day cycle.
   b. Hepatic impairment, mild (Child-Pugh Class A): reduce dose to 1.1 mg/m² over 2 to 5 minutes on days 1 and 8 of a 21-day cycle.
   c. Hepatic impairment, moderate (Child-Pugh Class B): reduce dose to 0.7 mg/m² IV over 2 to 5 minutes on days 1 and 8 of a 21-day cycle.
   d. Hematologic or grade 3 or 4 non-hematologic toxicities: do not administer on day 1 or 8 if absolute neutrophil count (ANC) is below 1000/mm³, platelet count is below 75,000/mm³, or if grade 3 or 4 non-hematologic toxicity occurs; day 8 dose may be held for a maximum of 1 week; if toxicities do not improve to grade 2 or less by day 15, omit the dose; if toxicities improve to grade 2 or less by day 15 permanently reduce dose (no sooner than 2 weeks later) to 1.1 mg/m² for ANC less than 500/mm³ for greater than 7 days or less than 1000/mm³ with fever or infection, platelet count less than 25,000/mm³ or less than 50,000/mm³ requiring transfusion, or any grade 3 or 4 non-hematologic toxicity, or if the day 8 dose was held or delayed in the previous cycle for toxicity; if events occur that would require permanent dose reduction while receiving 1.1 mg/m², then reduce dose to 0.7 mg/m²; if events occur that would require permanent dose reduction while receiving 0.7 mg/m², then discontinue therapy.

Monitoring

b. Monitor CBC prior to each dose including differential. Increase frequency in patients who develop grade 3 or 4 cytopenias.

c. Monitor for radiographic (eg, computed tomography) evidence of breast tumor response to eribulin mesylate therapy.

d. Monitor the patient prior to each dose and closely for peripheral motor or sensory neuropathy.

e. Monitor ECG in patients with risk factors for QT prolongation (ie, congestive heart failure, bradyarrhythmias, concomitant use of drugs known to prolong the QT interval, and electrolyte abnormalities).

V. APPROVAL AUTHORITY
1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS
None

VII. REFERENCES