Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Eribulin mesylate (Halaven®)	MP-RX-FP-35-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Eribulin mesylate (Halaven®), a microtubule inhibitor approved by the Food and Drug Administration (FDA) for the treatment of certain patients with metastatic breast cancer and unresectable or metastatic liposarcoma.

Background Information

Halaven is a non-taxane microtubule dynamics inhibitor that is a synthetic analogue of halichondrin B, a product isolated from a marine sponge. Although the exact mechanism is unknown, it is believed to work through inhibition of the growth phase of microtubule dynamics, without affecting the shortening phase, sequestering tubulin into nonproductive aggregates.

The FDA approved indications for Halaven include metastatic breast cancer or unresectable or metastatic liposarcoma. The National Comprehensive Cancer Network (NCCN) provides additional recommendations with a category 1 and 2A level of evidence for the uses in invasive breast cancer and soft tissue sarcoma.

Definitions and Measures

- Adjuvant therapy: Treatment given after the primary treatment to increase the chances of a cure; may include chemotherapy, radiation, hormone or biological therapy.
- Anthracycline: A type of antibiotic that comes from certain types of Streptomyces bacteria and are used to treat many types of cancer. Anthracyclines damage the DNA in cancer cells, causing the cells to die.
- Gleason Grading system: A prostate cancer grading system. A primary and secondary pattern, the number range of each is from 1 to 5, are assigned and then summed to yield a total score.
- Human epidermal growth factor 2 (ERBB2) status: A laboratory finding related to the presence or absence of cellular receptors for HER2/neu; also known as ErbB-2 protein family.
- Line of Therapy:
    - First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
    - Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
    - Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

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- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.
- Microtubule inhibitors (MTI): A class of drugs including taxanes, vinca alkaloids, and epothilones that stabilize or destabilize microtubules, thereby suppressing microtubule dynamics required for proper mitotic function, effectively blocking cell cycle progression and resulting in cell death.
- Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.
- One line of therapy: Single line of therapy.
- Taxane: A type of mitotic inhibitor and antimicrotubule drug used to treat cancer that blocks cell growth by stopping mitosis (cell division).

Approved Indications

Halaven is indicated by the FDA for the treatment of patients with:

- Metastatic breast cancer in patients 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.
- Unresectable or metastatic liposarcoma in patients who have received a prior anthracycline-containing regimen.

Other Uses

See Background section above

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9179	Injection, eribulin mesylate, 0.1 mg

ICD-10	Description
C48.0-C48.8	Malignant neoplasm of retroperitoneum and peritoneum
C49.0-C49.9	Malignant neoplasm of other connective and soft tissue
C50.011-C50.929	Malignant neoplasm of breast

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ICD-10	Description
C79.81	Secondary malignant neoplasm of breast
Z17.0	Estrogen receptor negative status [ER-]
Z17.1	Estrogen receptor positive status [ER+]

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Eribulin mesylate (Halaven®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of locally recurrent or metastatic breast cancer (Label, NCCN 2A); **AND**
ii. Individual is using as monotherapy; **AND**
iii. Individual is using as a single line of therapy; **AND**
iv. Individual has previously received at least two chemotherapeutic regimens for locally recurrent or metastatic disease;

OR

v. Individual has a diagnosis of locally recurrent or metastatic HER2 positive breast cancer (NCCN 2A); **AND**
vi. Individual is using in one of the following ways:
    A. Individual is using in combination with trastuzumab (or trastuzumab biosimilars); **OR**
    B. Individual is using in combination with Margenza (margetuximab-cmkb) as fourth line therapy and beyond;

AND

vii. Individual has symptomatic visceral disease; **OR**
viii. Individual has either hormone receptor-negative disease or hormone-receptor positive and endocrine refractory disease;

OR

ix. Individual has recurrent unresectable or metastatic HER2-negative breast cancer (NCCN 2A); **AND**
x. Individual has disease that is hormone receptor-positive with visceral crisis or endocrine therapy refractory; **AND**
xi. Using in one of the following ways:
    A. First line therapy if no germline BRCA 1/2 mutation (DP B IIa); **OR**

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B. Second-line therapy if not a candidate for fam trastuzumab deruxtecan-nxki (DP B IIa); **OR**
C. Third-line therapy and beyond;

OR

xii. Individual has recurrent unresectable or metastatic triple negative breast cancer (TNBC) (NCCN 2A); **AND**
xiii. Using in one of the following ways:
A. First-line therapy if PD-L1 CPS <10 and no germline BRCA 1/2 mutation; **OR**
B. Second-line therapy and beyond;

OR

xiv. Individual has a diagnosis of locally recurrent or metastatic soft tissue sarcoma (Label, NCCN 1, 2A); **AND**
xv. Individual is using as a monotherapy; **AND**
xvi. Individual is using as a single line of therapy; **AND**
xvii. Individual has previously received at least two chemotherapeutic regimens for locally recurrent or metastatic disease.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Eribulin mesylate (Halaven®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of an unacceptable toxicity or disease progression while on the current regimen. The following information should be submitted for reauthorization:
A. A current oncology note documenting the patient's response to treatment showing no progression of disease.
B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Individual has a diagnosis of head and neck cancer; **OR**
ii. Individual has a diagnosis of non-small cell lung cancer; **OR**
iii. When the above criteria (Section A: Criteria or Initial Approval) are not met and for all other indications.

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Limits or Restrictions

A. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Eribulin mesylate (Halaven®)	1.4 mg/m^2 administered intravenously over 2 to 5 minutes on Days 1 and 8 of a 21-day cycle.
Exceptions	

• Dose calculated based on Body Surface Area (BSA).
• Dose should be adjusted in patients with hepatic impairment:
  ○ The recommended dose of Halaven in patients with mild hepatic impairment (Child-Pugh A) is 1.1 mg/m^2 i.v. on Days 1 and 8 of a 21-day cycle.
  ○ The recommended dose of Halaven in patients with moderate hepatic impairment (Child-Pugh B) is 0.7 mg/m^2 i.v. on Days 1 and 8 of a 21-day cycle.
• Dose should be adjusted in patients with renal impairment:
  ○ The recommended dose in patients with moderate or severe renal impairment (CrCl 15-49 mL/min) is 1.1 mg/m^2 i.v. on Days 1 and 8 of a 21-day cycle.	

Reference Information

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. Cortes J, O'Shaughnessy J, Loesch D, et al. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. Lancet. 2011;377(9769):914-923. doi:10.1016/S0140-6736(11)60070-6 Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60070- 6/fulltext. Accessed January 17, 2023
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Kaufman PA, Awada A, Twelves C, et al. Phase III open-label randomized study of eribulin mesylate versus capecitabine in patients with locally advanced or metastatic breast cancer previously treated with an anthracycline and a taxane. J Clin Oncol. 2015;33(6):594-601. doi:10.1200/JCO.2013.52.4892. Available at: https://ascopubs.org/doi/full/10.1200/JCO.2013.52.4892. Accessed January 17, 2023

6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
7. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 17, 2023.
    a. Breast Cancer. V4.2022. Revised June 21, 2022.
    b. Soft Tissue Sarcoma. V2.2022. Revised May 17, 2022.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Annual Review 06/09/2024	Update existing criteria for use in recurrent unresectable or metastatic breast cancer when used in combination with margetuximab-cmkb as fourth line therapy vs. third line according to NCCN guidelines. Add NCCN 2A recommendation for use in HER2-negative breast cancer in recurrent unresectable or metastatic disease that is hormone receptor-positive with visceral crisis or endocrine therapy refractory. Add NCCN 2A recommendations for use in triple negative breast cancer. Coding Reviewed: No changes.	2/18/2025	3/6/2025
Select Review 02/15/2024	Update statement for criteria for initial approval: Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.	3/25/2024	5/9/2024
Policy Inception 06/16/2023	Elevance Health's Medical Policy adoption.	N/A	11/30/2023