09-J1000-76

Original Effective Date: 12/15/12

Reviewed: 03/12/25

Revised: 04/15/25

Subject: Eribulin Mesylate (Halaven®) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Eribulin mesylate (Halaven) is a non-taxane microtubule dynamics inhibitor. Although eribulin is characterized in the group of antitubulin drugs, including vinblastine and paclitaxel, it exerts its inhibition of microtubule dynamics via a novel mechanism of action, which is thought to involve binding to a unique site on tubulin. Ultimately, eribulin causes irreversible mitotic block and apoptosis. Due to its novel mechanism of action, it has been hypothesized that eribulin may have efficacy in individuals with malignancies that are resistant to other tubulin-targeted agents as well as a more favorable tolerability profile.

Eribulin was approved by the Food and Drug administration (FDA) on November 15, 2010, for the treatment of individuals with metastatic breast cancer who have previously received an anthracycline and a taxane in either the adjuvant or metastatic setting, and at least two chemotherapeutic regimens for the treatment of metastatic disease. In 2016, eribulin was approved by the FDA for unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimenThe current indication for eribulin is based principally on the results of the EMBRACE trial, which compared eribulin monotherapy to any single-agent treatment of the physician's choice, which served as a control designed to represent actual clinical options available for the management of metastatic breast cancer. Key inclusion criteria included previous therapy with 2 to 5 chemotherapy regimens, including an anthracycline- and a taxane-based regimen for adjuvant or metastatic disease. The one-year overall survival (OS) was 53.9% in the eribulin arm and 43.7% in the control arm and the median OS was 13.12 versus 10.65 months, representing a 19% statistically significant risk reduction (p=0.041).

Eribulin is included in National Comprehensive Cancer Network (NCCN) Breast Cancer Guidelines (version 1.2024) and Soft Tissue Sarcoma Guidelines (version 3.2023).

POSITION STATEMENT:

Initiation of eribulin mesylate (Halaven) **meets the definition of medical necessity** for the following indications when **ALL** indication-specific criteria are met:

1. Breast cancer
    a. Member's disease is recurrent or metastatic **OR** member is diagnosed with inflammatory breast cancer and did not have a response to preoperative systemic therapy
    b. Member meets one of the following:
        i Eribulin is prescribed as a single agent for HER2-negative disease
        ii Eribulin is prescribed as a single agent for triple negative disease
        iii Eribulin is prescribed in combination with margetuximab-cmkb or trastuzumab AND member has HER2-positive disease defined as:
            - Immunohistochemistry (IHC) is 3+
            - Dual-probe ISH assay results:
                - HER2/CEP17 ratio ≥2.0 AND average HER2 copy number ≥ 4.0 signals/cell
            - Concurrent dual-probe ISH assay and IHC results:
                - HER2/CEP17 ratio ≥2.0 AND average HER2 copy number <4.0 signals/cell and concurrent IHC 3+
                - HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥6.0 signals/cell and concurrent IHC 2+ or 3+
                - HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥4.0 and <6.0 signals/cell and concurrent IHC 3+
    c. Dose does not exceed 2.8 mg/m2 every 21 days
2. Soft Tissue Sarcoma
    a. Eribulin is prescribed as a single agent for palliative therapy
    b. Dose does not exceed 2.8 mg/m2 every 21 days
3. Other FDA-approved or NCCN supported diagnosis (not previously listed above)
    a. Member meets one of the following:
        i Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
        ii Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
    b. Dose does not exceed 2.8 mg/m2 every 21 days

Approval duration: 1 year

Continuation of eribulin mesylate (Halaven) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of breast cancer, soft tissue sarcoma, or other FDA-approved or NCCN supported diagnosis, OR the member has previously met all indication-specific initiation criteria
2. Dose does not exceed 2.8 mg/m2 every 21 days

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved:

- Administer 1.4 mg/m2 intravenously over 2 to 5 minutes on Days 1 and 8 of a 21-day cycle

Dosage Adjustments

- Members should be assessed for peripheral neuropathy and a complete blood count (CBC) should be obtained prior to each dose.
- Once the dose is reduced, do not re-escalate.
- Refer to prescribing information for detailed dose adjustments

Drug Availability

- Injection: 1 mg per 2 mL (0.5 mg per mL)

PRECAUTIONS:

Contraindications:

- None

WARNINGS

- Neutropenia: Monitor peripheral blood counts and adjust dose as appropriate.
- Peripheral neuropathy: Monitor for signs of neuropathy; manage with dose delay and adjustment

- QT Prolongation: Monitor for prolonged QT intervals in members with congestive heart failure, bradyarrhythmias, drugs known to prolong the QT interval, and electrolyte abnormalities. Avoid in members with congenital long QT syndrome.
- Pregnancy and lactation:
    - Eribulin is classified as Pregnancy Category D. There are no adequate and well-controlled studies of eribulin in pregnant women; however, eribulin was embryotoxic, fetotoxic, and teratogenic in rats that received half of the recommended human eribulin dose.
    - There were no human or animal studies conducted to determine if eribulin is excreted into breast milk. Avoidance in nursing women is recommended.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9179	Injection, eribulin mesylate, 0.1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

C47.0-C47.9	Malignant neoplasm of peripheral nerves and autonomic nervous system
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified

C49.A0 - C49.A9	Gastrointestinal stromal tumor
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast

C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Adjuvant Treatment: Additional cancer treatment given after the primary treatment to lower the risk that the cancer will return. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy, or biologic therapy. Adjuvant therapy can be used after or in combination with another form of cancer therapy and is commonly used following removal of a cancerous tumor to further help in treatment.

RELATED GUIDELINES:

Capecitabine (Xeloda®) Tablets 09-J1000-42
Docetaxel (Taxotere®) IV 09-J0000-95
Doxorubicin HCl Liposome (Doxil®) IV 09-J0000-91

Gemcitabine (Gemzar®) IV 09-J0000-96
Paclitaxel and Nab-Paclitaxel IV 09-J1000-05
Vinorelbine tartrate (Navelbine®) IV 09-J1000-03

OTHER:

Table 3: Common Terminology Criteria for Adverse Events v4.0 (CTCAE)	
Grade	Description
1	Mild; asymptomatic or mild symptoms; clinical diagnostic observations only; intervention not indicated
2	Moderate; minimal, local or noninvasive intervention indicated; limited age-appropriate instrumental activities of daily living
3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living
4	Life-threatening consequences; urgent intervention indicated
5	Death related to adverse event

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5. NCCN Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2025 [cited 3/28/25]. Available from: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.
6. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 3/28/25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 03/12/25.

GUIDELINE UPDATE INFORMATION:

12/15/12	New Medical Coverage Guideline.
04/01/13	Revision to guideline; consisting of adding quantity limit.
10/15/13	Review and revision to guideline; consisting of reformatting the position statement; updating references, coding, and program exceptions.
04/15/14	Review and revision to guideline; consisting of reformatting position statement and updating references.

04/15/15	Review and revision to guideline; consisting of program exceptions, references.
10/01/15	Revision to guideline; consisting of coding update.
11/01/15	Revision: ICD-9 Codes deleted.
01/15/16	Revision; ICD10 codes added.
03/15/16	Revision; consisting of position statement.
04/15/16	Review and revision; description, coding, dosage/administration, precautions/warning, position statement, references.
07/15/16	Revision to guideline; consisting of updating position statement.
10/01/16	Revision to guideline; consisting of ICD10 codes
04/15/17	Review and revision; description, coding, position statement, references.
04/15/18	Review and revision; updated description, coding, position statement, references.
05/15/19	Review and revision; updated description, references.
04/15/20	Review and revision; updated description, references.
04/15/23	Review and revision; updated position statement, references.
04/15/24	Review and revision; updated position statement, references.
04/15/25	Review and revision; updated references.