

# Ixempra® (ixabepilone) (Intravenous)

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## I. Length of Authorization

Coverage is provided for 6 months and may be renewed.

## II. Dosing Limits

### A. Quantity Limit (max daily dose) [NDC Unit]:

- Ixempra 15 mg single-dose vial powder for injection: 2 vials per 21 days
- Ixempra 45 mg single-dose vial powder for injection: 2 vials per 21 days

### B. Max Units (per dose and over time) [HCPCS Unit]:

- 90 billable units every 21 days

## III. Initial Approval Criteria <sup>1</sup>

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

### Universal Criteria <sup>1</sup>

- Patient does not have a history of a severe hypersensitivity to agents containing Cremophor® EL or its derivatives (e.g., polyoxyethylated castor oil); **AND**
- If used in combination with capecitabine, the patient must not have an AST or ALT > 2.5 x ULN or bilirubin > 1 x ULN; **AND**

### Breast Cancer † ‡ <sup>1-4,1e,2e,4e,6e,8e,14e,15e,17e,21e</sup>

- Used for recurrent unresectable or metastatic disease ‡; **AND**
  - Patient has human epidermal growth factor receptor 2 (HER2)-negative\* disease as confirmed by an FDA-approved or CLIA-compliant test †; **AND**
    - Patient was previously treated with an anthracycline; **AND**
    - Used as a single agent; **AND**
      - Patient has hormone-receptor positive disease with visceral crisis or refractory to endocrine therapy; **AND**

- Used as first-line therapy if no germline BRCA 1/2 mutation; **OR**
- Used as second-line therapy if not a candidate for fam-trastuzumab deruxtecan-nxki; **OR**
- Used as third-line therapy and beyond; **OR**
- Patient has triple-negative breast cancer (TNBC)  $\Psi$ ; **AND**
  - Used as first-line therapy if PD-L1 CPS <10 and no germline BRCA 1/2 mutation; **OR**
  - Used as subsequent therapy; **OR**
- Patient has HER2-positive\*\* disease as confirmed by an FDA-approved or CLIA-compliant test $\diamond$ ; **AND**
  - Used as fourth-line therapy and beyond in combination with trastuzumab  $\ddagger$ ; **OR**
- Patient has locally advanced or metastatic disease  $\dagger$ ; **AND**
  - Patient has failed on an anthracycline\* and a taxane\*\* (or taxane resistant and further anthracycline therapy is contraindicated); **AND**
    - Used in combination with capecitabine; **OR**
    - Used as a single agent after failure on capecitabine

\*\*\*Note: Anthracycline resistance is defined as progression while on therapy or within 6 months in the adjuvant setting or 3 months in the metastatic setting. Taxane resistance is defined as progression while on therapy or within 12 months in the adjuvant setting or 4 months in the metastatic setting.

**Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.**

**\*HER2-negative expression criteria: <sup>5,6</sup>**

- Immunohistochemistry (IHC) assay is 0 or 1+; **OR**
- Dual-probe in situ hybridization (ISH) assay indicating (Group 5) HER2/CEP17 ratio <2.0 AND average HER2 copy number <4.0 signals/cell; **OR**
- Concurrent dual-probe ISH and IHC assay results indicating one of the following:
  - (Group 2) HER2/CEP17 ratio  $\geq$ 2.0 AND average HER2 copy number <4.0 signals/cell and concurrent IHC 0-1+ or 2+; **OR**
  - (Group 3) HER2/CEP17 ratio <2.0 AND average HER2 copy number  $\geq$ 6.0 signals/cell and concurrent IHC 0-1+; **OR**

- (Group 4) HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥4.0 and <6.0 signals/cell and concurrent IHC 0-1+ or 2+

**Ψ ER/PR-negative expression criteria: <sup>7</sup>**

- Immunohistochemistry (IHC) assay: Sample is considered ER/PR negative if the percentage of cancer cells staining on evaluation is <1% OR 0% of tumor cell nuclei are immunoreactive  
*Note: A sample may be deemed uninterpretable for ER or PR if the sample is inadequate (insufficient cancer or severe artifacts present, as determined at the discretion of the pathologist), if external and internal controls (if present) do not stain appropriately, or if pre-analytic variables have interfered with the assay's accuracy.*

**Ψ ER Scoring Interpretation (following ER testing by validated IHC assay)**

<b>Results</b>	<b>Interpretation</b>
– 0% – <1% of nuclei stain	– ER-negative
– 1%–10% of nuclei stain	– ER-low–positive*
– >10% of nuclei stain	– ER-positive

*\*Note: Patients with cancers with ER-low–positive (1%–10%) results are a heterogeneous group with reported biologic behavior often similar to ER-negative cancers; thus, as such these cancers inherently behave aggressively and may be treated similar to triple-negative disease. Individualized consideration of risks versus benefits should be incorporated into decision-making.*

**\*\*HER2-positive overexpression criteria: <sup>5,6</sup>**

- Immunohistochemistry (IHC) assay 3+; **OR**
- Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number ≥ 4.0 signals/cell; **OR**
- Dual-probe in situ hybridization (ISH) assay AND concurrent IHC indicating one of the following:
  - HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; **OR**
  - HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; **OR**
  - HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell AND concurrent IHC 3+

❖ *If confirmed using an FDA approved assay – <http://www.fda.gov/companiondiagnostics>*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

## IV. Renewal Criteria <sup>1</sup>

Coverage may be renewed based on the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in Section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: peripheral neuropathy (sensory and motor neuropathy), myelosuppression (e.g., neutropenia, leukopenia, anemia, thrombocytopenia, etc.), toxicity in patients with hepatic impairment, hypersensitivity reactions (including anaphylaxis), cardiac adverse reactions (e.g., myocardial ischemia and ventricular dysfunction), etc.

## V. Dosage/Administration <sup>1-4</sup>

Indication	Dose
Breast Cancer	Administer 40 mg/m <sup>2</sup> intravenously (IV) over 3 hours every 21 days. <i>(Doses for patients with a BSA &gt; 2.2 m<sup>2</sup> should be calculated based on 2.2 m<sup>2</sup>)</i>

## VI. Billing Code/Availability Information

HCPCS Code:

- J9207 – Injection, ixabepilone, 1mg: 1mg = 1 billable unit

NDC(s):

- Ixempra 15 mg single-dose powder for injection: 70020-1910-xx
- Ixempra 45 mg single-dose powder for injection: 70020-1911-xx

## VII. References (STANDARD)

1. Ixempra [package insert]. Princeton, NJ; R-Pharm US LLC; January 2023. Accessed May 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium<sup>®</sup>) for ixabepilone. National Comprehensive Cancer Network, 2023. The NCCN Compendium<sup>®</sup> is a derivative work of the NCCN Guidelines<sup>®</sup>. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>, NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed May 2023.

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6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Breast Cancer, Version 4.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>, NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2023.
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## VIII. References (ENHANCED)

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- 31e. Rugo HS, Bardia A, Marme F, et al. Sacituzumab Govitecan in Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer. *J Clin Oncol*. 2022 Oct 10;40(29):3365-3376. doi: 10.1200/JCO.22.01002. Epub 2022 Aug 26.
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## Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
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



ICD-10	ICD-10 Description
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

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC