

Ixempra® (ixabepilone) (Intravenous)

Document Number: IC-0072

Last Review Date: 09/04/2025

Date of Origin: 01/01/2012

Dates Reviewed: 12/2011, 02/2013, 11/2013, 06/2014, 05/2015, 04/2016, 04/2017, 04/2018, 05/2019, 05/2020, 05/2021, 05/2022, 05/2023, 09/2024, 09/2025

I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months.
- Renewal: Prior authorization validity may be renewed every 6 months thereafter.

II. Dosing Limits

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

- 90 billable units every 21 days

III. Initial Approval Criteria ¹

Prior authorization validity is provided in the following conditions:

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

Universal Criteria ¹

- 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 † ‡ ¹⁻⁴

- Used for recurrent unresectable (local or regional) or metastatic (stage IV [M1]) disease OR inflammatory breast cancer with no response to preoperative systemic therapy ‡; **AND**
 - Patient has human epidermal growth factor receptor 2 (HER2)-negative* disease as confirmed by an FDA-approved or CLIA-compliant test ❖; **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 and/or HER2 IHC 0+, 1+, or 2+/ISH negative; **OR**
 - Used as second-line therapy if not a candidate for fam-trastuzumab deruxtecan; **OR**
 - Used as third-line therapy and beyond; **OR**

- Patient has triple-negative breast cancer (TNBC) Ψ ; **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 in combination with trastuzumab as fourth-line therapy and beyond \ddagger ; **OR**
- Used for locally advanced or metastatic disease \dagger ; **AND**
 - Patient has failed or is resistant*** to treatment with an anthracycline and a taxane OR patient is 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.

***HER2-negative expression criteria: ^{5,6}**

- 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 \geq 4.0 and <6.0 signals/cell and concurrent IHC 0-1+ or 2+

Ψ ER/PR-negative expression criteria: ⁷

- 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)

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

**Note: Invasive cancers with between 1%–10% ER positivity are considered ER-low–positive. However, this group is noted to be heterogeneous and the biologic behavior of ER-low–positive cancers may be more similar to ER-negative cancers. This should be considered in decision making for other adjuvant therapy and overall treatment pathway.*

****HER2-positive overexpression criteria:** ^{5,6}

- 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); Ⓞ Orphan Drug

IV. Renewal Criteria ¹

Prior authorization validity 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 ^{1-4,8,9}

Indication	Dose
Breast Cancer	Administer 40 mg/m ² intravenously (IV) over 3 hours every 21 days until disease progression or unacceptable toxicity. (Doses for patients with a BSA > 2.2 m ² should be calculated based on 2.2 m ²)

VI. Billing Code/Availability Information

HCPCS Code:

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

NDC(s):

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

VII. References

1. Ixempra [package insert]. Princeton, NJ; R-Pharm US LLC; January 2023. Accessed July 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for ixabepilone. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® 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 July 2025.
3. Thomas ES, Gomez HL, Li RK, et al. Ixabepilone plus capecitabine for metastatic breast cancer progressing after anthracycline and taxane treatment. J Clin Oncol. 2007 Nov 20;25(33):5210-7. doi: 10.1200/JCO.2007.12.6557.
4. Perez EA, Lerzo G, Pivot X, et al. Efficacy and safety of ixabepilone (BMS-247550) in a phase II study of patients with advanced breast cancer resistant to an anthracycline, a taxane, and capecitabine. J Clin Oncol. 2007 Aug 10;25(23):3407-14. doi: 10.1200/JCO.2006.09.3849.
5. Wolff AC, Hammond MEH, Allison KH, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. Arch Pathol Lab Med. 2018 Nov;142(11):1364-1382. doi: 10.5858/arpa.2018-0902-SA. Epub 2018 May 30. Arch Pathol Lab Med. 2018. PMID: 29846104.
6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer, Version 4.2025. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® 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 July 2025.
7. Allison KH, Hammond EH, Dowsett M, et al. Estrogen and Progesterone Receptor Testing in Breast Cancer: ASCO/CAP Guideline Update. J Clin Oncol 38:1346-1366(2020).
8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ixabepilone: Breast Cancer Chemotherapy Order Template, BRS64. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® 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 July 2025.
9. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ixabepilone + Trastuzumab: Breast Cancer Chemotherapy Order Template,

BRS152. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® 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 July 2025.

Appendix A – Non-Quantitative Treatment Limitations (NQL) Factor Checklist

Non-quantitative treatment limitations (NQLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime’s assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	Yes: Consider for PA
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

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

ICD-10	ICD-10 Description
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

ICD-10	ICD-10 Description
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
Z85.3	Personal history of malignant neoplasm of breast

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents:

<https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied 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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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