# Medical Drug Clinical Criteria

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| **Subject:** | Ixempra (ixabepilone) | | |
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## Overview

This document addresses the use of Ixempra (ixabepilone). Ixempra is a microtubule inhibitor, classified as an epothilone. Similar to taxanes, epothilones bind to b-tubulin sites which polymerize and stalize microtubules, thus preventing mitosis and causing apoptosis. While this mechanism is similar to taxanes, epothilones appear to bind to different sites than taxanes and remain active in cases of Taxane resistance.

The FDA approved indications for Ixempra includes metastatic or locally advanced breast cancer resistant to treatment with an anthracycline and a taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated or as monotherapy after failure of an anthracycline, a taxane, and capecitabine.

The National Comprehensive Cancer Network (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Ixempra in the treatment of recurrent or metastatic breast cancer. NCCN recommends Ixempra in combination therapy with trastuzumab in human epidermal growth factor receptor 2 (HER2)+ positive disease that is hormone receptor- negative or hormone receptor-positive with or without endocrine therapy (Perez E, et al 2007).

Ixempra has a black box warning for toxicity in hepatic impairment. Ixempra in combination with capecitabine must not be given to patients with AST or ALT > 2.5 X ULN or bilirubin >1 X ULN due to increased risk of toxicity and neutropenia-related death.

Another NCCN recommendation with a category 2A level of evidence for the use of Ixempra as single agent therapy for recurrent or metastatic breast cancer HER2- negative disease that is hormone receptor-negative or hormone receptor-positive with visceral crisis or refractory to endocrine therapy. This recommendation was based on three phase II studies; however, these studies support the FDA indication and not the specific population of individuals within this 2A recommendation.

**Definitions and Measures**

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.

Locally advanced cancer: Cancer that has spread only to nearby tissues or lymph nodes.

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.

Taxane resistance: Progression during therapy or within 12 months in the adjuvant setting or 4 months in the metastatic setting.

## Clinical Criteria

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.

**Ixempra (ixabepilone)**

Requests for Ixempra (ixabepilone) may be approved if the following criteria are met:

I. Individual has a diagnosis of breast cancer, metastatic or locally advanced: **AND**
II. *Any* of the following indications:
   A. As monotherapy in individuals treated with two prior lines of therapy (Label, NCCN 2A); **OR**
   B. In combination with capecitabine in individuals previously treated with two lines of therapy, or whose cancer is taxane resistant and further anthracycline therapy is contraindicated (Label); **OR**
   C. In combination with trastuzumab (or trastuzumab biosimilars) in individuals with disease resistant to treatment with taxanes (NCCN 2A); **OR**
   D. As fourth-line therapy and beyond ~~i~~in combination with trastuzumab (or trastuzumab biosimilars) in the treatment of an individual with locally recurrent or metastatic HER2-positive~~+~~ breast cancer with either (NCCN 2A);
      1. Hormone receptor-negative disease; **OR**
      2. Hormone receptor-positive with or without endocrine therapy; **OR**
   E. As single agent therapy for recurrent unresectable or stage IV HER2-negative disease that is HR-positive with visceral crisis or endocrine therapy refractory used in *one* of the following lines of therapy (NCCN 2A):
      1. As first-line therapy if no germline BRCA 1/2 mutation; **OR**
      2. As second-line therapy if not a candidate for fam trastuzumab deruxetecan-nxki; **OR**
      3. As third-line therapy and beyond;

   **OR**

   F. As single agent therapy for recurrent unresectable or stage IV triple negative breast cancer (TNBC) used in one of the following lines of therapy (NCCN 2A):
      1. First-line therapy if PD-L1 CPS <10 and no germline BRCA 1/2 mutation; **OR**
      2. Second-line therapy and beyond.

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Requests for Ixempra (ixabepilone) may not be approved for any of the following:

I. If the baseline neutrophil count is <1500 cells/mm$^3$ or the platelet count is < 100,000 cells/mm$^3$; **OR**
II. If Ixempra is used in combination with capecitabine and individual has hepatic impairment defined as AST or ALT > 2.5 x ULN or bilirubin > 1 x ULN; **OR**
III. When the above criteria are not met and for all other indications.

## Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

**HCPCS**

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| J9207 | Injection, ixabepilone, 1 mg [Ixempra] |

**ICD-10 Diagnosis**

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| C50.011-C50.929 | Malignant neoplasm of breast |
| C79.81 | Secondary malignant neoplasm of breast |
| Z85.3 | Personal history of malignant neoplasm of breast |
| Z17.0 | Estrogen receptor positive status [ER+] |
| Z17.1 | Estrogen receptor positive status [ER-] |

## Document History

Revised: 02/23/2024
Document History:

- 02/23/2024 – Annual Review: Updated existing criteria from NCCN category 2A recommendation for use as fourth-line therapy and beyond (previously unstated) when used in combination with trastuzumab (or biosimilars) in locally recurrent or metastatic HER2-positive breast cancer. Add NCCN category 2A recommendations for use in recurrent unresectable or stage IV HER2-negative breast cancer that is HR-positive with visceral crisis or endocrine therapy refractive. Add NCCN category 2A recommendation for use in recurrent unresectable or stage IV TNBC. Coding Reviewed: No changes.
- 02/24/2023 – Annual Review: Update criteria for combination use with capecitabine due to FDA label update. Minor wording and formatting updates. Coding Reviewed: No changes.

- 02/25/2022 – Annual Review: Update Ixempra Kit criteria to clarify use. Add contraindications to may not be approved criteria. Coding Reviewed: No changes.
- 02/19/2021– Annual Review: Update Ixempra Kit criteria with clarification from NCCN breast cancer guideline for Ixempra's use in combination with trastuzumab (or biosimilars) in recurrent or metastatic HER2+ breast cancer. Coding Reviewed: No changes.
- 02/21/2020– Annual Review: Update Ixempra Kit criteria with clarification for use with trastuzumab or trastuzumab biosimilars. Coding Reviewed: Added ICD-10-CM C79.81
- 11/15/2019 – Annual Review: No changes.
- 05/17/2019 – Annual Review: Initial review of Ixempra (ixabepilone). Minor wording and formatting updates. Coding Review. Added ICD-10 codes Z17.0-Z17.1

## References


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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.