Medical Drug Clinical Criteria

Subject:	Datroway (datopotamab deruxtecan-dlnk)		
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Overview

This document addresses the use of Datroway (datopotamab deruxtecan-dlnk). Datroway is a Trop-2-directed antibody and topoisomerase inhibitor conjugate. Datroway is indicated for the treatment of adult patients with unresectable or metastatic, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

Breast cancer is a type of tumor comprised of malignant (cancerous) cells that start to grow in the breast and may spread (metastasize) to surrounding tissues and other areas of the body (American Cancer Society, 2016). Breast cancer is commonly treated by various modalities which include combinations of surgery, radiation therapy, chemotherapy and hormone therapy (National Cancer Institute, 2019). The prognosis and selection of therapies can be affected by clinical and pathologic features of the tumor. One of these includes the human epidermal growth factor receptor 2 gene ERBB2 which is commonly referred to as HER2. Other names for this gene include NEU, Her-2, HER-2/neu and c-erb B2. Initially the HER2 gene was detected in frozen breast tumor samples. Amplification of the HER2 gene was later correlated to overexpression of protein levels in samples of breast cancer.

Approximately 255,000 patients are diagnosed with invasive breast cancer each year, with approximately one in five cases being classified as HER-2 positive. Antibody-drug conjugates containing trastuzumab and a second non-specific cytotoxic drug have the ability to more specifically target HER-2 cancer cells and exert their anti-tumor effects. Kadcyla and Enhertu are currently the only two HER2-directed antibody-drug conjugates on the market. Kadcyla is linked to emtansine, a tubulin inhibitor, whereas Enhertu is linked to DXd, a topoisomerase inhibitor.

Enhertu has a black box warning for interstitial lung disease and embryo-fetal toxicity. Interstitial lung disease (ILD) and pneumonitis, including fata cases, have been reported with Enhertu. Patients should be monitored for signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Enhertu should be discontinued in all patients with Grade 2 or higher ILD/pneumonitis.

The National Comprehensive Cancer Network® (NCCN) clinical practice guideline for breast cancer has not added Datroway to its guidelines.

Definitions and Measures

HER2 testing (adapted from American Society of Clinical Oncology/College of American Pathologists):

Positive HER2:

- IHC 3+ based on circumferential membrane staining that is complete, intense. (Observed in a homogeneous and contiguous population and within > 10% of the invasive tumor cells).
- ISH positive based on:
    - Single-probe average HER2 copy number ≥ 6.0 signals/cell*
    - Dual-probe HER2/CEP 17 ratio ≥ 2.0* with an average HER2 copy number ≥ 4.0 signals/cell
    - Dual-probe HER2/CEP17 ratio ≥ 2.0* with an average HER2 copy number < 4.0 signals/cell
    - Dual-probe HER2/CEP17 ratio < 2.0* with an average HER2 copy number ≥ 6.0 signals/cell

*(Observed in a homogeneous and contiguous population and within >10% of the invasive tumor cells. By counting

at least 20 cells within the area)

Equivocal HER2:

- IHC 2+ based on circumferential membrane staining that is incomplete and/or weak/moderate and within >10% of the invasive tumor cells or complete and circumferential membrane staining that is intense and within ≤10% of the invasive tumor cells.
- ISH equivocal based on:
    - Single-probe average HER2 copy number ≥ 4.0 and < 6.0 signals/cell
    - Dual-probe HER2/CEP17 ratio < 2.0 with an average HER2 copy number ≥ 4.0 signals/cell

Negative HER2 if a single test (or both tests) performed show:

- IHC 1+ as defined by incomplete membrane staining that is faint/barely perceptible and within > 10% of the invasive tumor cells
- IHC 0 as defined by no staining observed or membrane staining that is incomplete and is faint/barely perceptible and within ≤ 10% of the invasive tumor cells
- ISH negative based on:
    - Single-probe average HER2 copy number < 4.0 signals/cell
    - Dual-probe HER2/CEP17 ratio < 2.0 with an average HER2 copy number < 4.0 signals/cell

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.

Monoclonal antibody: A protein developed in the laboratory that can locate and bind to specific substances in the body and on the surface of cancer cells.

Progressive Disease (PD): Cancer that is growing, spreading, or getting worse.

Refractory Disease: Illness or disease that does not respond to treatment.

Targeted biologic agent: A newer type of drug developed specifically to target genetic changes in cells that cause cancer. It works differently than standard chemotherapy drugs, often with different side effects.

Unresectable: Unable to be removed with surgery.

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.

Datroway (datopotamab deruxtecan-dlnk)

Requests for Datroway (datopotamab deruxtecan-dlnk) may be approved if the following criteria are met:

I. Individual has a diagnosis of unresectable or metastatic HER2-negative (HER2-) breast cancer, and meets one of the following:
    A. Immunohistochemistry (IHC) is 0; **OR**
    B. IHC 1+; **OR**
    C. IHC 2+/ In situ hybridization (ISH) negative;

AND

II. Individual has hormone-receptor positive (HR+) disease; **AND**

III. Individual has received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

Requests for Datroway (datopotamab deruxtecan-dlnk) may not be approved for the following:

I. Individual has a history of Interstitial Lung Disease (ILD)/pneumonitis requiring treatment with steroids or ongoing ILD/pneumonitis; **OR**

II. Individual has clinical active brain metastases; **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

C9399	Unclassified drugs or biologicals [when specified as Datroway (datopotamab deruxtecan-dlnk)]
J9999	Not otherwise classified, antineoplastic drugs [when specified as Datroway (datopotamab deruxtecan-dlnk)]

ICD-10 Diagnosis

	All diagnosis pend

Document History

New: 02/21/2025
Document History:

- 02/21/2025 – Select Review: Add new clinical criteria document for Datroway. Coding Reviewed: Added HCPCS NOC C9399, J9999, and all diagnosis pend for Datroway.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2025; Updated periodically.
4. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 27, 2025.
    a. Breast Cancer. V6.2024. Revised November 11, 2024.

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.