09-J5000-19

Original Effective Date: 06/15/25

Reviewed: 05/14/25

Revised: 07/01/25

Subject: Datopotamab Deruxtecan (Datroway) IV Infusion

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:

Datopotamab deruxtecan (Datroway) was approved by the U.S. Food and Drug Administration in January 2025 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.

Datopotamab deruxtecan is a TROP2-directed antibody-drug conjugate (ADC) composed of a humanized anti-TROP2 immunoglobulin G1 (IgG1) with deruxtecan (Dxd), a topoisomerase I inhibitor, attached via cleavable linker. Following binding to TROP2 on cells, including tumor cells, datopotamab deruxtecan undergoes internalization and intracellular linker cleavage by lysosomal enzymes. Upon release, the membrane-permeable DXd causes DNA damage and apoptotic cell death.

The safety and efficacy of datopotamab deruxtecan were evaluated in a phase III, randomized, multicenter, open-label clinical trial (TROPION-Breast01, NCT05104866) in in adults with HR+/HER2− (IHC 0, IHC 1+ or IHC 2+/ISH−) breast cancer who have progressed on, and are not suitable for, endocrine therapy and have received ≥1 prior line of therapy. Patients were randomized to receive datopotamab deruxtecan 6 mg/kg once every 3 weeks (n=365) or single-agent chemotherapy of the investigator's choice (n=367). The primary endpoint was progression free survival (PFS) and overall survival (OS).

Datopotamab deruxtecan significantly reduced the risk of disease progression or death by 37% compared to investigator's choice chemotherapy (ICC) (6.9 vs 4.9 months; HR, 0.63 [95% CI, 0.52 to 0.76]) at a median follow-up of 10.8 months. Median PFS was 6.9 months in patients treated with datopotamab deruxtecan versus 4.9 months with chemotherapy. The median overall survival (OS) was

18.6 months (95% CI, 17.3–20.1) in the datopotamab deruxtecan arm compared with 18.3 months (95% CI, 17.3–20.5) in the chemotherapy arm (hazard ratio [HR], 1.01; 95% CI, 0.83–1.22). Datopotamab deruxtecan did not achieve statistical significance in the final OS analysis.

The most common adverse reactions (≥20%), including laboratory abnormalities, were stomatitis, nausea, fatigue, decreased leukocytes, decreased calcium, alopecia, decreased lymphocytes, decreased hemoglobin, constipation, decreased neutrophils, dry eye, vomiting, increased alanine transaminase (ALT), keratitis, increased aspartate aminotransferase (AST), and increased alkaline phosphatase (ALP).

Datopotamab deruxtecan is included in NCCN guidelines for treatment of Breast Cancer (Version 4.2025). The safety and efficacy of datopotamab deruxtecan is currently being evaluated in multiple cancers.

POSITION STATEMENT:

Initiation of datopotamab deruxtecan (Datroway) meets the definition of medical necessity for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Breast Cancer
    a. Member has recurrent unresectable (local or regional) or stage IV (M1) breast cancer
    b. Member has hormone receptor positive disease
    c. Member has HER2-negative disease (IHC 0, 1+, or 2+/ISH-)
    d. Member has received prior endocrine-based therapy and chemotherapy for their current disease
    e. Use will be as second- or subsequent-line therapy
    f. Member is not a candidate for treatment with fam-trastuzumab deruxtecan-nxki (Enhertu)
    g. Dose does not exceed 6 mg/kg once every 3 weeks (21-day cycle)
2. 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 FDA label

Approval Duration: 6 months

Continuation of datopotamab deruxtecan (Datroway) 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 or other FDA-approved or NCCN supported diagnosis, OR the member has previously met all indication-specific initiation criteria

2. Member's disease has not progressed during treatment with datopotamab deruxtecan

3. Dose does not exceed FDA label

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

- For injection: 100 mg lyophilized powder in a single-dose vial
- For intravenous infusion only
- Premedicate for prevention of infusion reactions and nausea and vomiting
- The recommended dosage is 6 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity

PRECAUTIONS:

- Interstitial Lung Disease (ILD) and Pneumonitis: DATROWAY can cause severe and fatal cases of ILD/pneumonitis. Monitor for new or worsening signs and symptoms of ILD/pneumonitis. If ILD/pneumonitis is suspected, withhold DATROWAY and initiate corticosteroids. Permanently discontinue DATROWAY in patients with confirmed Grade 2 or higher ILD/pneumonitis.
- Ocular Adverse Reactions: DATROWAY can cause ocular adverse reactions including dry eye, keratitis, blepharitis and meibomian gland dysfunction, increased lacrimation, conjunctivitis, and blurred vision. Monitor patients for ocular adverse reactions during treatment with DATROWAY. Advise patients to use preservative-free lubricating eye drops and to avoid using contact lenses during treatment with DATROWAY. Dose delay, dose reduce, or permanently discontinue DATROWAY based on the severity of ocular adverse reactions. Refer patients to an eye care professional for any new or worsening ocular signs and symptoms.
- Stomatitis/Oral Mucositis: DATROWAY can cause stomatitis, including mouth ulcers and oral mucositis. Advise patients to use a steroid-containing mouthwash when starting treatment and to hold ice chips or ice water in mouth during the infusion of DATROWAY. Based on the seerity of the adverse reaction, withhold, dose reduce, or permanently discontinue DATROWAY.
- Embryo-Fetal Toxicity: DATROWAY can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

BILLING/CODING INFORMATION:

HCPCS Coding

C9174	Injection, datopotamab deruxtecan-dlnk, 1 mg [hospital outpatient use only]
J9999	Not otherwise classified, antineoplastic drugs

ICD-10 Diagnosis Codes That Support Medical Necessity

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: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review 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:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2025 [cited 5/6/25]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 5/6/25]. Available from: http://clinicaltrials.gov/.
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4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 5/6/25].
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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

GUIDELINE UPDATE INFORMATION:

06/15/25	New Medical Coverage Guideline
07/01/25	Revision: Added HCPCS code C9174.