**09-J4000-97**

**Original Effective Date: 11/15/24**

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**Revised: 04/01/25**

# Subject: Denileukin diftitox-cxdl (Lymphir) injection

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## DESCRIPTION:

Cutaneous T-cell lymphomas (CTCLs) are a group of Non-Hodgkin's lymphomas of mature T cells that present in the skin and may involve lymph nodes and visceral organs. Mycosis Fungoides (MF) is the most common subtype with primary cutaneous involvement and accounts for 50 to 70% of CTCLs. In 2016, approximately 1620 people in the US were diagnosed with MF. Sézary Syndrome (SS) accounts for approximately 1 to 3% of CTCLs and involves blood and lymph nodes. Treatment varies by disease stage and blood involvement and may include topical therapy, phototherapy, radiation, or systemic therapy.

Denileukin diftitox-cxdl (Lymphir™) is a fusion protein containing diptheria toxin fragments A and B and human interleukin-2 amino acid sequences. The diphtheria toxin directs toward cells expressing interleukin-2 receptor and inhibits protein synthesis causing cell death. This results in anti-tumor activity of interleukin-2-receptor expressing tumors. Denileukin diftitox-cxdl (Lymphir™) was approved by the US Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or refractory stage I-III cutaneous T-cell lymphoma (CTCL) after at least one prior systemic therapy.

In an open-label, single-arm trial, 302 patients with relapsed or refractory stage I to IV CTCL received denileukin diftitox infusion. Patients received 9 mcg/kg of denileukin diftitox as an intravenous infusion from Day 1 to 5 of each 21 day cycle. Patients had a median of 4 prior therapies including skin-directed and systemic therapies. Patients were excluded with cardiac disease or uncontrolled infection. Efficacy was established based on objective response rate (ORR), according to ISCL/EORTC Global Response Score (GRS) according to an independent review committee. The ORR was 36% (95% CI 25%,49%) with complete response in 9% and partial response in 27% of patients. The duration of response was greater than 6 months in 52% of patients and greater than 12 months in 20% of patients.

The most common adverse reactions occurring in greater than or equal to 20% of patients included lab abnormalities (increased transaminases, decreased albumin), nausea, edema, decreased hemoglobin,

fatigue, musculoskeletal pain, rash, chills, constipation, pyrexia and capillary leak syndrome. There is a black box warning for capillary leak syndrome including life-threatening or fatal reactions.

National Comprehensive Cancer Network (NCCN) Guidelines for Primary cutaneous lymphomas include denileukin diftitox-cxdl as a systemic therapy option for mycosis fungoides and Sezary syndrome.

## POSITION STATEMENT:

Initiation of denileukin diftitox-cxdl (Lymphir™) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. The member's dosage does not exceed 9 mg/kg/day based on actual body weight administered intravenously on day 1 through 5 of a 21 day cycle
2. The member has a serum albumin greater than 3 g/L prior to treatment
3. The member has an indication listed in Table 1 and **ALL** indication-specific criteria are met

### Table 1

| Disease | Criteria for Use |
|---|---|
| Cutaneous T-cell lymphoma (Mycosis fungoides [MF]/ Sézary syndrome [SS]) | When used as a single systemic agent (may be used with or without skin-directed therapy or local radiation therapy) for disease classified as **ONE** of the following:<br>1. Stage IB-IIA disease with higher disease burden (e.g., extensive skin involvement, predominately plaque disease, blood involvement)<br>2. Stage IIB disease with tumor lesions<br>3. Stage III disease |
| **Other FDA-approved or NCCN supported diagnosis** (not previously listed above) | **ONE** of the following is met:<br>1. 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)<br>2. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation |

**Approval duration**: 6 months

Continuation of denileukin diftitox-cxdl (Lymphir™) **meets the definition of medical necessity** for the indications in Table 1 when **ALL** of the following criteria are met:

1. An authorization or reauthorization for Denileukin diftitox-cxdl (Lymphir™) has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of indications in Table 1, **OR** the member has previously met **ALL** indication-specific criteria.
2. The member's disease has not progressed during treatment with denileukin diftitox-cxdl
3. The member has a serum albumin greater than 3 g/L prior to treatment
4. The dose does not exceed 9 mg/kg/day based on actual body weight on days 1 through 5 of each 21 day cycle

**Approval duration**: 1 year

## DOSAGE/ADMINISTRATION:

Relapsed or refractory Stage I-III cutaneous T-cell lymphoma (CTCL) after at least one prior systemic therapy: 9 mcg/kg/day actual body weight administered as an intravenous infusion of days 1 through 5 of a 21 day cycle. Administer premedications including an antipyretic, antihistamine, antiemetic, and hydration for cycles 1 through 3. If a grade 2 or higher infusion reaction occurs, premedicate with a systemic steroid for at least 3 cycles. Prior to each treatment cycle, assess hepatic and renal function. If serum albumin is less than 3 g/dL, delay administration. See prescribing information for dose adjustments due to adverse reactions and delays due to toxicity.

**Drug availability:** 300 mcg single-dose vial

## PRECAUTIONS:

**Contraindications:** none

**Boxed warning:**

Capillary leak syndrome (CLS), including life-threatening or fatal reactions, can occur in patients receiving denileukin diftitox-cxdl. Monitor for signs and symptoms of CLS during treatment. Withhold until CLS resolves or permanently discontinue based on severity.

**Precautions/Warnings:**

Visual impairment: Monitor and evaluate for visual impairment throughout treatment. Withhold until visual impairment resolves or permanently discontinue based on severity.

Infusion-related reactions: Monitor patients closely during infusions. Interrupt or discontinue for infusion-related reactions based on severity.

Hepatotoxicity: Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated.

Embryo-fetal toxicity: Can cause fetal harm. Advise females of reproductive potential of risk to fetus and use effective contraception.

## BILLING/CODING INFORMATION:

### HCPCS Coding

| | |
|---|---|
| J9161 | Injection, denileukin diftitox-cxdl, 1 mcg |

### ICD-10 Diagnosis Codes That Support Medical Necessity

| | |
|---|---|
| C84.00 – C84.09 | Mycosis fungoides |
| C84.10 – C84.19 | Sézary disease |

## 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:

**Brentuximab (Adcetris) Injection, 09-J1000-53**

**Mogamulizumab-kpkc (Poteligeo) Injection, 09-J3000-05**

## OTHER:

### Table 2: Common Terminology Criteria for Adverse Events v4.0 (CTCAE)

| Grade | Description |
|---|---|
| 1 | Mild; asymptomatic or mild symptoms; clinical diagnostic observations only; intervention not indicated |
| 2 | Moderate; minimal, local or noninvasive intervention indicated; limited age-appropriate instrumental activities of daily living |

| | |
|---|---|
| 3 | Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living |
| 4 | Life-threatening consequences; urgent intervention indicated |
| 5 | Death related to adverse event |

## REFERENCES:


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4. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed September 26, 2024.
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7. Lymphir (Denileukin dititox-cxdl) [package insert]. Citius Pharmaceuticals, Inc. Cranford, NJ. August 2024.


## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 10/09/24.

## GUIDELINE UPDATE INFORMATION:

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|---|---|
| 11/15/24 | New Medical Coverage Guideline. |
| 04/01/25 | Revision: Added HCPCS code J9161 and deleted code J9999. |