
5.21.227

Section:	Prescription Drugs	Effective Date:	April 1, 2026
Subsection:	Antineoplastic Agents	Original Policy Date:	August 30, 2024
Subject:	Lymphir	Page:	1 of 4

Last Review Date: March 6, 2026

Lymphir

Description

Lymphir (denileukin diftitox-cxdl)

Background

Lymphir (denileukin diftitox-cxdl) is a fusion protein designed to direct the cytotoxic action of diphtheria toxin (DT) to cells which express the interleukin-2 (IL-2) receptor. After uptake into the cell, the DT fragment is cleaved and the free DT fragments inhibit protein synthesis, resulting in cell death. Lymphir demonstrated the ability to deplete immunosuppressive regulatory T lymphocytes and antitumor activity through a direct cytotoxic action on IL-2R-expressing tumors (1).

Regulatory Status

FDA-approved indication: Lymphir is an IL2-receptor-directed cytotoxin indicated 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 (1).

Lymphir has a boxed warning regarding capillary leak syndrome (CLS). Lymphir can cause CLS, including life-threatening or fatal reactions. CLS was defined in clinical trials as the occurrence of at least 2 of the following symptoms at any time during Lymphir therapy: hypotension, edema, serum albumin < 3 g/dL. If serum albumin is less than 3 g/dL, delay administration of Lymphir until serum albumin is greater than or equal to 3 g/dL. Monitor patients for signs and symptoms of CLS during treatment and withhold until CLS resolves or permanently discontinue based on severity (1).

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Lymphir has warnings for visual impairment, infusion-related reactions, and hepatotoxicity. Patients should be monitored and evaluated for visual impairment and infusion reactions throughout treatment. If the patient experiences visual impairment or infusion reactions, treatment should be withheld or permanently discontinued based on severity. Liver enzymes and bilirubin should be monitored at baseline and during treatment as clinically indicated (1).

Lymphir can cause fetal harm when administered to a pregnant woman. Pregnant women and females of reproductive potential should be advised of the potential risk to a fetus. Females of reproductive potential should be advised to use effective contraception during treatment with Lymphir and for 7 days after the last dose (1).

The safety and effectiveness of Lymphir in pediatric patients under the age of 18 have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Lymphir may be considered **medically necessary** if the conditions indicated below are met.

Lymphir may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Stage I-III cutaneous T-cell lymphoma (CTCL)

AND ALL of the following:

1. Disease must be relapsed or refractory after one prior systemic therapy

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2. Prescriber agrees to monitor for signs and symptoms of capillary leak syndrome (CLS)
3. If serum albumin is less than 3 g/dL, treatment with Lymphir will be delayed until serum albumin is greater than or equal to 3 g/dL
4. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Lymphir and for 7 days after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Stage I-III cutaneous T-cell lymphoma (CTCL)

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor for signs and symptoms of capillary leak syndrome (CLS)
3. If serum albumin is less than 3 g/dL, treatment with Lymphir will be delayed until serum albumin is greater than or equal to 3 g/dL
4. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Lymphir and for 7 days after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

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Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Lymphir is indicated for the treatment of relapsed or refractory stage I-III cutaneous T-cell lymphoma (CTCL) after at least one prior systemic treatment. Lymphir has a boxed warning for capillary leak syndrome, including life-threatening or fatal reactions. Lymphir also carries warnings for visual impairment, infusion-related reactions, hepatotoxicity, and embryo-fetal toxicity. The safety and effectiveness of Lymphir in pediatric patients under the age of 18 have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Lymphir while maintaining optimal therapeutic outcomes.

References

1. Lymphir [package insert]. Cranford, NJ: Citius Pharmaceuticals, Inc.; August 2024.
2. NCCN Drugs & Biologics Compendium® Denileukin diftitox-cxdl 2026. National Comprehensive Cancer Network, Inc. Accessed on January 12, 2026.

Policy History

Date	Action
August 2024	Addition to PA
March 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.