Clinical Policy: Denileukin Diftitox-cxdl (Lymphir)

Reference Number: PA.CP.PHAR.693
Effective Date: 11/2024
Last Review Date: 10/2024

Description
Denileukin diftitox-cxdl (Lymphir™) is an interkeukin-2 (IL2) receptor directed cytotoxin.

FDA Approved Indication(s)
Lymphir is 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Lymphir is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cutaneous T-Cell Lymphoma (must meet all)**:**

1. Diagnosis of CTCL (*see Appendix E for CTCL subtypes*);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For CTCL subtypes that are not mycosis fungoides (MF) or Sezary syndrome, all of the following (a, b, and c):
   a. Disease is relapsed or refractory;
   b. Disease is stage I, III, or III;
   c. Failure of at least one prior systemic therapy;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 9 mcg/kg per day on days 1 to 5 of a 21-day cycle;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Cutaneous T-Cell Lymphoma (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):

a. New dose does not exceed 9 mcg/kg per day on days 1 to 5 of a 21-day cycle;
b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CTCL: cutaneous T-cell lymphoma
FDA: Food and Drug Administration
IL2: interleukin-2
MF: mycosis fungoides

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
Contraindication(s): Contraindication(s): none reported

- Boxed warning(s): capillary leak syndrome

Appendix D: General Information

- Lymphir is a purified and more bioactive formulation of previously FDA-approved Ontak. Ontak was marketed in the U.S. from 1999 to 2014, when it was voluntarily withdrawn from the market due to manufacturing difficulties.
- MF is the most common cutaneous T-cell lymphoma. Sezary syndrome is closely related to MF accounting for less than 5% of cutaneous lymphomas.

Appendix E: WHO-EORTC Classification of CTCL with Primary Cutaneous Manifestations*

- Sezary syndrome
- Mycosis fungoides (MF)
  - MF variants and subtypes
    - Folliculotropic MF
    - Pagetoid reticulosis
    - Granulomatous slack skin

- Primary cutaneous CD30+ lymphoproliferative disorders
  - Lymphomatoid papulosis (LyP)
  - Primary cutaneous anaplastic large cell lymphoma (C-ALCL)
- Subcutaneous panniculitis-like T-cell lymphoma
- Adult T-cell leukemia/lymphoma (ATLL)
- Primary cutaneous peripheral T-cell lymphoma, rare subtypes
  - Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (provisional)
  - Primary cutaneous gamma/delta T-cell lymphoma
  - Primary cutaneous acral CD8+ T-cell lymphoma (provisional)
  - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)
  - Primary cutaneous peripheral T-cell lymphoma, not otherwise specified

**CTCL is classified as a non-Hodgkin T-cell lymphoma. CTCL classification schemes are periodically advanced as new information becomes available; therefore, the above list is provided as general guidance. For additional information, see WHO's 2018 updated classification of hematological malignancies for a complete list of lymphoid neoplasms, including CTCL.*

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CTCL	9 mcg/kg/day IV over 60 minutes on days 1 to 5 of a 21- day treatment cycle. Administer until disease progression or unacceptable toxicity.	9 mcg/kg/day

VI. Product Availability

Single-dose vial: 300 mcg

VII. References

1. Lymphir Prescribing Information. Cranford, NJ: Citius Pharmaceuticals, Inc.; August 2024. Available at: www.lymphirhcp.com. Accessed August 20, 2024.
2. National Comprehensive Cancer Network Guidelines. Primary Cutaneous Lymphomas Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed August 22, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date
Policy created	10/2024