Clinical Policy: Denileukin Diftitox-cxdl (Lymphir)

Reference Number: CP.PHAR.693
Effective Date: 12.01.24
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Lymphir for a covered indication and has received this medication for at least 30 days;
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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

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): 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)
  - 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 July 10, 2026.
2. National Comprehensive Cancer Network Guidelines. Primary Cutaneous Lymphomas Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed August 30, 2026.

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
J9161	Injection, denileukin diftitox-cxdl, 1 mcg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.20.24	11.24
HCPCS code added [J9161], removed codes [J3590, C9399].	02.13.25	
4Q 2025 annual review: no significant changes; extended initial approval duration from 6 months to 12; references reviewed and updated.	07.10.25	11.25
4Q 2026 annual review: no significant changes; for Commercial approval duration, added injectable standard language of "6 months or to the member's renewal date, whichever is longer"; added ICHRA line of business; references reviewed and updated.	07.10.26	11.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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