Clinical Policy: Pralatrexate (Folotyn)

Reference Number: CP.PHAR.313
Effective Date: 02.01.17
Last Review Date: 11.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

Pralatrexate injection (Folotyn®) is a folate analog metabolic inhibitor.

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***For Health Insurance Marketplace (HIM) – all states EXCEPT Florida and Arizona,** if request is through pharmacy benefit, Folotyn (40 mg/2 mL vial) is non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)

Folotyn is indicated for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL).

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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 pralatrexate and Folotyn are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of PTCL (*see Appendix D for examples of PTCL subtypes*);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. Prescribed as initial palliative intent therapy;
   b. Failure of at least one prior therapy (*see Appendix B for examples*);*
   **Prior authorization may be required for prior therapies*
5. Prescribed as a single agent;
6. If request is for Folotyn, member must use pralatrexate, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 30 mg/m^2 once weekly for 6 weeks in 7-week cycles;
   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 Florida and Arizona – 12 months
HIM, all other states – 12 months for Folotyn 20 mg/1 mL *(refer to HIM.PA.103 for Folotyn 40 mg/2 mL if pharmacy benefit)*
Commercial – 6 months or to the member's renewal date, whichever is longer

B. NCCN-Recommended Off-Label Indications (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Primary cutaneous lymphomas (i, ii, or iii):
      i. Mycosis fungoides or Sézary syndrome;
      ii. Primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions, or cutaneous ALCL with regional nodes;
      iii. Subcutaneous panniculitis-like T-cell lymphoma with one of the following (1 or 2):
         1) Hemophagocytic lymphohistiocytosis, systemic disease, or high tumor burden;
         2) Inadequate response to first-line therapy (*see Appendix B for examples*);
   b. Other T-cell lymphomas (i, ii, iii, or iv):
      i. Adult T-cell leukemia/lymphoma (ATLL) after failure of first-line therapy (*see Appendix B for examples*);
      ii. Extranodal NK/T-cell lymphoma (NKTL) following asparaginase-based therapy (*see Appendix B for examples*);
      iii. Hepatosplenic T-cell lymphoma after failure of 2 prior treatment regimens (*see Appendix B for examples*);
      iv. Breast implant (BI)-associated ALCL after failure of first-line therapy (*see Appendix B for examples*);

   **Prior authorization may be required for prior line therapies*
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For diagnoses other than Mycosis fungoides or Sézary syndrome, prescribed as a single agent;
5. If request is for Folotyn, member must use pralatrexate, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose is within FDA maximum limit for any FDA-approved indication or 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 Florida and Arizona – 12 months
HIM, all other states – 12 months for Folotyn 20 mg/1 mL *(refer to HIM.PA.103 for Folotyn 40 mg/2 mL if pharmacy benefit)*
Commercial – 6 months or to the member's renewal date, whichever is longer

C. 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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Folotyn 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 Folotyn, member must use pralatrexate, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 30 mg/m^2 once weekly for 6 weeks in 7-week cycles;
   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 Florida and Arizona – 12 months
HIM, all other states – 12 months for Folotyn 20 mg/1 mL *(refer to HIM.PA.103 for Folotyn 40 mg/2 mL if pharmacy benefit)*
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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALCL: anaplastic large cell lymphoma
ATLL: adult T-cell leukemia/lymphoma
BI-ALCL: breast implant-associated anaplastic large cell lymphoma
FDA: Food and Drug Administration
HGTL: hepatosplenic gamma-delta T-cell lymphoma
NCCN: National Comprehensive Cancer Network
NKTL: extranodal NK/T-cell lymphoma
PTCL: peripheral T-cell lymphoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
PTCL - examples of first-line and subsequent therapy: • Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone) • CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone) • CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) • Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) • DHAP (dexamethasone, cisplatin, cytarabine) • ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) • Belinostat, brentuximab vedotin, romidepsin as single agents	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ATLL - examples of first-line therapy: • Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone) • CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone) • CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) • Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) • HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine	Varies	Varies
NKTL - examples of asparaginase-based therapy: • AspaMetDex (pegaspargase, methotrexate, dexamethasone) • DDGP (dexamethasone, cisplatin, gemcitabine, pegaspargase) • Modified-SMILE (steroid, methorexate, ifosfamide, pegaspargase, etoposide) • P-GEMOX (gemcitabine, pegaspargase, oxaliplatin)	Varies	Varies
Hepatosplenic T-cell lymphoma - examples of first-line therapy (for subsequent therapy examples see PTCL): • ICE (ifosfamide, carboplatin, etoposide) • CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone) • Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone)	Varies	Varies
BI-ALCL - examples of first-line therapy: • Brentuximab vedotin • Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone) • CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) • CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone) • Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)	Varies	Varies
Subcutaneous panniculitis-like T-cell lymphoma – examples of first-line therapy: • Cyclosporine • Romidepsin • CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) • ESHA (ifosfamide, carboplatin, etoposide) + platinum (cisplatin or oxaliplatin) • ICE (ifosfamide, carboplatin, etoposide)		

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

*Appendix D: PTCL Subtypes/Histologies**
- PTCL, not otherwise specified
- Anaplastic large cell lymphoma
- Angioimmunoblastic T-cell lymphoma
- Enteropathy-associated T-cell lymphoma
- Monomorphic epitheliotropic intestinal T-cell lymphoma
- Nodal peripheral T-cell lymphoma with TFH phenotype
- Follicular T-cell lymphoma

PTCL is classified as a non-Hodgkin T-cell lymphoma. PTCL 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 2016 updated classification of hematological malignancies for a complete list of lymphoid neoplasms, including PTCL.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PTCL	30 mg/m^2 IV once weekly for 6 weeks in 7-week cycles until progressive disease or unacceptable toxicity	30 mg/m^2 once weekly

VI. Product Availability
Single-dose vials: 20 mg/1 mL, 40 mg/2 mL

VII. References
1. Folotyn Prescribing Information. East Windsor, NJ: Acrotech Biopharma LLC; August 2024. Available at: https://www.folotyn.com. Accessed July 14, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed July 14, 2025.
3. National Comprehensive Cancer Network. T-Cell Lymphomas Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed July 14, 2025.

4. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed July 14, 2025.

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
J9307	Injection, pralatrexate, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2021 annual review: added option for use as initial palliation for PTCL and clarified use as a single-agent therapy per NCCN; added BI-ALCL indication to criteria per NCCN; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	07.30.21	11.21
4Q 2022 annual review: no significant changes; added Commerical line of business approval duration; removal of nasal type for NKTL per NCCN; references reviewed and updated. Template changes applied to other diagnoses/indications.	08.01.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	06.30.23	11.23
4Q 2024 annual review: updated notation regarding HIM non-formulary status for 40 mg/2 mL vials to exclude HIM FL and AZ per current formulary status; revised policy/criteria section to also include generic pralatrexate; for non-cutaneous T-cell lymphomas, added requirement that Folotyn be prescribed as a single agent per NCCN; removed "gamma delta" qualifier from hepatosplenic T-cell lymphoma as NCCN does not specify this; references reviewed and updated.	08.07.24	11.24
4Q 2025 annual review: added NCCN off-label use for subcutaneous panniculitis-like T-cell lymphoma; for brand requests, added redirection to generic; extended initial approval duration for HIM/Medicaid from 6 to 12 months; references reviewed and updated.	07.14.25	11.25

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.