Clinical Policy: Pralatrexate (Folotyn)

Reference Number: LA.PHAR.313
Effective Date: 11.04.23
Last Review Date: ~~04.22.24~~12.10.24 Coding Implications
Line of Business: Medicaid Revision Log

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

Please note: This policy is for medical benefit

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

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 Louisiana Healthcare Connections that pralatrexate and Folotyn ~~is~~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 ~~therapy~~;
6. 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: 6 months

B. NCCN-Recommended Off-Label Indications (must meet all)**:**
1. Diagnosis of one of the following ~~conditions~~ (a or b):
   a. Primary cutaneous T-cell lymphomas (i or ii):
      i. Mycosis fungoides or Sézary syndrome;
      ii. Primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions, or cutaneous ALCL with regional nodes;
   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 ~~gamma-delta~~ T-cell lymphoma ~~(HGTL)~~ after failure of 2 prior treatment regimens (*see Appendix B for examples*);
      iv. Breast implant~~-~~ (BI)~~-~~associated ~~anaplastic large cell lymphoma (BI-~~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;

~~4.~~5. 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: 6 months

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 LA.PMN.255
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: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections 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 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: 12 months

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 LA.PMN.255
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: LA.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 policy – LA.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 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
~~HGTL~~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

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

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**PTLC 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 ~~vial~~vials: 20 mg/1 mL, 40 mg/2 mL

VII. References

1. Folotyn Prescribing Information. East Windsor, NJ: Acrotech Biopharma LLC; September 2020. Available at: https://www.folotyn.com~~/hcp/wp-content/uploads/2019/11/Folotyn-PI-09-2020-REF-0255.pdf. Accessed June 30, 2023.~~. Accessed July 17, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed ~~July 10, 2023~~August 7, 2024.
3. National Comprehensive Cancer Network. T-Cell Lymphomas Version ~~1.2023~~4.2024. Available at: ~~https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf.~~ https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed ~~July 10, 2023~~August 7, 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
J9307	Injection, pralatrexate, 1 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy.	06.15.23	10.05.23
Annual review: no significant changes; references reviewed and updated.	04.22.24	07.10.24
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.	12.10.24	

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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.