Clinical Policy: Pralatrexate (Folotyn)

Reference Number: PA.CP.PHAR.313
Effective Date: 01/2018
Last Review Date: 10/2023

Coding Implications
Revision Log

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
It is the policy of PA Health & Wellness ® that Folotyn is **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*).

Approval duration: 6 months

B. NCCN-Recommended Off-Label Indications (must meet all)**:**
1. Diagnosis of one of the following conditions (a, b, or c):
   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), nasal type 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-associated anaplastic large cell lymphoma (BI-ALCL) after failure of first-line therapy (*see Appendix B for examples*);

c. Other NCCN category 1, 2A, or 2B recommendations;

**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. 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*).

Approval duration: 6 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. 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*).

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.LTSS.PHAR.01) applies; or
2. Refer to 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

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
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
HGTL - 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

**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: 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.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed July 10, 2023..
3. National Comprehensive Cancer Network. T-Cell Lymphomas Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed July 10, 2023..

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	Approval Date
4Q 2018 annual review: no significant changes; summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; added COC; references reviewed and updated.	10/2018	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019	
4Q 2020 annual review: FDA/NCCN dosing requirement added; failed prior therapy added for PTCL; off-label uses added with prior therapy (HGTL, NKTL); prior therapy added for ATLL; added additional PTCL subtypes per NCCN; added Appendix D; updated HGTL use after 2 prior therapy regimens per NCCN; references reviewed and updated.	10/2020	
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; references reviewed and updated.	10/2021	
4Q 2022 annual review: no significant changes;; removal of nasal type for NKTL per NCCN; references reviewed and updated.	10/2022	
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023	