Clinical Policy Title:	pralatrexate
Policy Number:	RxA.121
Drug(s) Applied:	Folotyn®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Pralatrexate injection (Folotyn®) is a folate analog metabolic inhibitor. It is indicated for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Pralatrexate (Folotyn®)	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

Dosage Forms

- Single-dose vial: 20 mg/1 mL, 40 mg/2 mL

Clinical Policy

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

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. Failed prior therapy (see Appendix B for examples);
   *Prior authorization may be required for prior therapies
5. 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

Commercial: 6 months

Medicaid: 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 CD30+ T-cell lymphoproliferative disorders;
   b. Other T-cell lymphomas (i, ii, or iii):
      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 prior 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 of age and older;
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).*

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

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications 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:
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

ALCL: anaplastic large cell lymphoma
ATLL: adult T-cell leukemia/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

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.*Please refer to the NCCN guidelines for the most up to date recommendations.*

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)	Varies	Varies
ATLL - examples of first-line therapy: • Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) • Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone) for CD30+ cases • Zidovudine and interferon (acute and chronic/smoldering subtypes) • CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone) • HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine • Useful in certain circumstances: ○ CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) (unable to tolerate intensive regimen or non-CD30 expressing ATLL)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
NKTL - examples of asparaginase-based therapy: • Modified-SMILE (steroid [dexamethasone], methotrexate, ifosfamide, pegaspargase, and etoposide) • P-GEMOX (gemcitabine, pegaspargase, oxaliplatin) • DDGP (dexamethasone, cisplatin, gemcitabine, pegaspargase) • Useful in certain circumstances: AspaMetDex (pegaspargase, methotrexate, dexamethasone)	Varies	Varies
HGTL - examples of first-line therapy (for subsequent therapy examples see PTCL): • ICE (ifosfamide, carboplatin, etoposide) • Alemtuzumab + pentostatin • CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone) • Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) • HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine • IVAC (ifosfamide, etoposide, cytarabine) • Useful in certain circumstances: ○ Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone) for CD30+ cases ○ DHAP (dexamethasone, cisplatin, cytarabine)	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

- Contraindication(s):
  - None

- Boxed Warning(s):
  - None

APPENDIX D: General Information

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.*

References

1. Folotyn Prescribing Information. Westminster, CO: Spectrum Pharmaceuticals, Inc.;September 2020. Available ahttp://www.folotyn.com/wp-content/uploads/2019/11/PI-FOLOTYN-092019.pdf. Accessed January 29, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed January 30. 2021
3. National Comprehensive Cancer Network. T-Cell Lymphomas Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed January 30. 2021.
4. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 1.2021. Available a https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf . Accessed January 30. 2021

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Policy was reviewed: 1. Clinical policy was updated. 2. Line of business was updated to all line of business. 3. HIM was removed from Initial and continued therapy criteria approval duration. 4. Continued therapy II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..". 5. General information was updated. 6. References were reviewed and updated.	01/30/2021	03/09/2021