Clinical Policy: Pralatrexate (Folotyn)

Reference Number: CP.PHAR.313
Effective Date: 02/17
Last Review Date: 02/17

Coding Implications
Revision Log

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for pralatrexate injection (Folotyn®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® 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 relapsed or refractory peripheral T-cell lymphoma (PTCL) (see Appendix B for examples of PTCL subtypes).

Approval duration: 3 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

1. The following NCCN recommended uses for Folotyn, meeting NCCN categories 1, 2a, or 2b, are approved per the CP.PHAR.57 Global Biopharm Policy:
   a. Non-Hodgkin lymphoma:
      i. Adult T-cell leukemia/lymphoma;
      ii. Mycosis fungoides (MF)/Sezary syndrome (SS);
      iii. Primary cutaneous CD30+ T-cell lymphoproliferative disorders.

II. Continued Approval

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member has none of the following reasons to discontinue:
   a. Disease progression or unacceptable toxicity;
   b. Mucositis: On day of treatment, Grade 4* (life-threatening);
   c. Hematologic toxicities: On day of treatment, any of the following:
      i. Platelet < 50,000/mcL lasting 3 weeks;
      ii. Absolute neutrophil count (ANC) characterized as any of the following:
         a) ANC 500-1,000/mcL with fever;
         b) ANC < 500/mcL lasting 3 weeks;
         c) ANC < 500/mcL if a second occurrence;
   d. Non-hematologic toxicities: Recurrence of CTCAE Grade 3* (severe) or 4* (life-threatening) toxicities after two dosage reductions;
   e. Any treatment-related toxicity: Grade 4* (life-threatening);

**Grading is based on the Common Terminology Criteria for Adverse Events (CTCAE).*

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

Background

Description/Mechanism of Action:

Pralatrexate is a folate analog metabolic inhibitor that competitively inhibits dihydrofolate reductase. It is also a competitive inhibitor for polyglutamylation by the enzyme folylpolyglutamyl synthetase. This inhibition results in the depletion of thymidine and other biological molecules the synthesis of which depends on single carbon transfer.

Formulations:

Folotyn is available in single-dose clear glass vials containing pralatrexate at a concentration of 20 mg/mL as a preservative-free, sterile, clear yellow solution individually packaged for intravenous use in the following presentations:

- 20 mg of pralatrexate in 1 mL solution in a vial (20 mg / 1 mL)
- 40 mg of pralatrexate in 2 mL solution in a vial (40 mg / 2 mL)

FDA Approved Indications:

Folotyn is a folate analog metabolic inhibitor/intravenous formulation indicated for:

- Treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL).
  - This indication is based on overall response rate. Clinical benefit such as improvement in progression-free survival or overall survival has not been demonstrated.

Appendices

Appendix A: Abbreviation Key

AITL: Angioimmunoblastic T-cell lymphoma
ALCL: Anaplastic large cell lymphoma
ANC: Absolute neutrophil count
CTCAE: Common Terminology Criteria for Adverse Events
EATL: Enteropathy-associated T-cell lymphoma
MEITL: Monomorphic epitheliotropic intestinal T-cell lymphoma
MF: Mycosis fungoides
PTCL-NOS: Peripheral T-cell lymphoma, not otherwise specified
SS: Sezary syndrome

Appendix B: Peripheral T-cell lymphomas* (PTCL) subtypes[3]

- Peripheral T-cell lymphoma (PTCL), not otherwise specified (NOS)
- Angioimmunoblastic T-cell lymphoma (AITL)
- Anaplastic large cell lymphoma (ALCL), ALK positive or negative

- Enteropathy-associated T-cell lymphoma (EATL)
- Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)

**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.*[4]

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
Policy split from CP.PHAR.182.Excellus Oncology.	01/17	02/17

References
1. Folotyn prescribing information. Westminster, CO: Spectrum Pharmaceuticals Inc.; May 2016. Available at http://www.folotyn.com/downloads/2016_05_folotyn_FPI.pdf. Accessed January 17, 2017.
2. Pralatrexate. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed January 17, 2017.
3. T-cell lymphomas (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 17, 2017.
4. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood.* 2016; 127: 2375-2390.

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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.