Folotyn (pralatrexate)

Line(s) of Business: HMO; PPO; QUEST Integration
Akamai Advantage

Original Effective Date: 10/01/2015
Current Effective Date: 01/01/2018 TBD 03/01/2017

POLICY
A. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Folotyn is indicated for the 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.

Compendial Uses
- Mycosis fungoides/Sézary syndrome (MF/SS)
  - First-line therapy for
    - Stage IB-IIA MF with histologic evidence of folliculotropic or large cell transformation
    - Stage IIB with generalized tumor lesions
    - Stage IV non-Sézary or visceral disease
    - Stage III MF or SS which has progressed or is refractory to multiple previous therapies
  - Single-agent therapy for tumors with histologic evidence of large cell transformation and aggressive growth rate for
    - Stage IB-IIA MF with histologic evidence of folliculotropic or large cell transformation
    - Stage IIB with generalized tumor lesions
    - Stage IV non-Sézary or visceral disease
- Adult T-cell leukemia/lymphoma (ATLL)
  - Second-line therapy as a single agent for nonresponders to first-line therapy for acute disease or lymphoma
  - Subsequent therapy after high dose therapy/autologous stem cell rescue (HDT/ASCR)
- Primary cutaneous CD30+ T-cell lymphoproliferative disorders (LPDs), single-agent therapy as primary treatment or therapy for relapsed or refractory disease:
  - Primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions
  - Cutaneous ALCL with regional nodes
- Peripheral T-cell lymphoma (PTCL), second-line or subsequent therapy for relapsed or refractory:
  - Angioimmunoblastic T-cell lymphoma (AITL)
  - PTCL, not otherwise specified
B. REQUIRED DOCUMENTATION
The following documentation from the medical record is necessary to initiate the prior authorization review:

- Initial therapy:
  - Current oncology notes
  - Clinical notes that include the history of previous treatments
  - Pertinent pathology reports and/or imaging studies
- Continuation of therapy: documentation (including clinical notes and objective findings such as imaging studies) that demonstrate lack of disease progression on therapy

C. INITIAL CRITERIA FOR APPROVAL

1. Adult T-cell leukemia/lymphoma (ATLL)
   Authorization of 6 months may be granted to members who are prescribed Folotyn when Folotyn is used for second-line therapy as a single agent and either ALL of the following criteria are met:
   a. The member has one of the following subtypes of ATLL:
      i. Acute
      ii. Lymphoma
   b. Folotyn will be used as subsequent therapy after high-dose therapy/autologous stem cell rescue

2. Peripheral T-cell lymphoma (PTCL)
   Authorization of 6 months may be granted to members who are prescribed Folotyn when ALL of the following criteria are met:
   a. The member has one of the following subtypes of PTCL:
      i. Angioimmunoblastic T-cell lymphoma (AITL)
      ii. PTCL, not otherwise specified
      iii. ALC
      iv. Enteropathy-associated T-cell lymphoma (EATL)
      v. Monomorphic epitheliotropic intestinal T-cell lymphoma
   b. Folotyn will be used as second-line or subsequent therapy for relapsed or refractory disease

3. Primary cutaneous CD30+ T-cell lymphoproliferative disorder (LDP)
   Authorization of 6 months may be granted to members who are prescribed Folotyn when ALL of the following criteria are met:
   a. Member has one of the following disease subtypes:
      i. Primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions
      ii. Cutaneous ALCL with regional nodes
      iii. CD30+ transformed mycosis fungoides (Refer to criteria for approval in Section 4)
   b. Folotyn will be used as primary treatment OR as therapy for relapsed or refractory disease
   c. Folotyn will be used as a single agent (as monotherapy)
4. **Mycosis fungoides (MF)/Sézary syndrome (SS)**

Authorization of 6 months may be granted to members who are prescribed Folotyn for when ALL of the criteria pertaining to the MF/SS disease stage are met (Sections 4.1 to 4.34 below)

4.1 Stage IB, and IIA MF/SS:

— Members with Stage IB or IIA disease must meet **the criteria criterion a) and EITHER criterion b) or c)** below:

a. **Member has histologic evidence of folliculotropic or large cell transformation is present**

b. **Folotyn is used either in low doses as first-line therapy or in standard doses as a single agent (monotherapy) for tumors with histologic evidence of large cell transformation and aggressive growth rate**

c. **Members with histologic evidence of large cell transformation must meet either i) or ii)** below:

i. **Members with evidence of an aggressive growth rate must use Folotyn as a single agent (monotherapy)**

ii. **Members WITHOUT evidence of an aggressive growth rate must meet ALL of the following criteria:**

   1. **Folotyn must be used as first-line therapy**
   2. **Low-dose Folotyn must be prescribed (less than 30 mg/m^2 per week)**

4.2 Stage IIB MF/SS:

— Members with Stage IIB disease must meet **the criteria criterion a) and EITHER criterion b) or c)** below:

a. **Member has generalized extensive tumor lesions, transformed, and/or folliculotropic disease**

b. **Folotyn is used either in low doses as first-line therapy or in standard doses as a single agent (monotherapy) for tumors with histologic evidence of large cell transformation and aggressive growth rate**

a. b. **Members with histologic evidence of large cell transformation must meet either i) or ii)** below:

i. **Members with evidence of an aggressive growth rate must use Folotyn as a single agent (monotherapy)**

   1. **Folotyn must be used as first-line therapy**
   2. **Low-dose Folotyn must be prescribed (less than 30 mg/m^2 per week)**

ii. **Members WITHOUT evidence of an aggressive growth rate must meet ALL of the following criteria:**

   1. **Folotyn must be used as first-line therapy**
   2. **Low-dose Folotyn must be prescribed (less than 30 mg/m^2 per week)**

4.3 Stage III and Stage IV (Sézary syndrome) MF:
Members with either Stage III disease or Stage IV Sézary syndrome must meet the ALL of the following criteria below:

a. Member must have progressive disease or disease refractory to multiple previous therapies
b. Folotyn is used in low doses as first-line therapy
b. Low-dose Folotyn must be prescribed (less than 30 mg/m² per-week)

4.4 Stage IV, non-Sézary or visceral (solid organ) disease

Members with Stage IV non-Sézary or visceral (solid organ) disease must meet EITHER the following criterion:

Folotyn is used either in low doses as first-line therapy or in standard doses as a single agent (monotherapy) for tumors with histologic evidence of large cell transformation and aggressive growth rate
a). or b)

Below:

a. Members with histologic evidence of large cell transformation must meet either i) or ii) below:
   i. Members with evidence of an aggressive growth rate must use Folotyn as a single agent (monotherapy)
   ii. Members WITHOUT evidence of an aggressive growth rate must meet ALL of the following criteria:
      1. Folotyn must be used as first line therapy
      2. Low-dose Folotyn must be prescribed (less than 30 mg/m² per-week)

b. Members WITHOUT histologic evidence of large cell transformation must meet ALL of the following criteria:
   i. Folotyn must be used as first-line therapy
   ii. Low-dose Folotyn must be prescribed (less than 30 mg/m² per-week)

C.D. CONTINUATION OF THERAPY

Authorization of an additional 6 months may be granted to members who are prescribed Folotyn for continuation of therapy that were previously approved by HMSA if there is evidence of a lack of disease progression on therapy.

1. No previous authorization/precertification:
   All members (including members currently receiving treatment without prior authorization) must meet criteria for initial approval in section C.

2. Reauthorization:
   Authorization of 6 months may be granted to members requesting authorization for continuation of therapy if Folotyn was previously authorized by HMSA/CVS and there is evidence of a lack of disease progression on therapy.

E. DOSAGE AND ADMINISTRATION

Dosage and administration approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

D.F. ADMINISTRATIVE GUIDELINES

Precertification is required. Please refer to the HMSA medical policy web site for the fax form.
E-G. IMPORTANT REMINDER
The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that CVS/caremark reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

H.H. REFERENCES

Revised: May 2016.
Document History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/01/2015</td>
<td>Original effective date</td>
</tr>
<tr>
<td>05/2016</td>
<td>Annual review</td>
</tr>
<tr>
<td>03/01/2017</td>
<td>Revision effective date</td>
</tr>
<tr>
<td>05/2017</td>
<td>Annual review</td>
</tr>
<tr>
<td>TBD</td>
<td>Revision effective date</td>
</tr>
</tbody>
</table>