Clinical Policy: Bexarotene (Targretin)
Reference Number: ERX.SPMN.120
Effective Date: 03/14
Last Review Date: 09/16

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that bexarotene (Targretin®) capsules are medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Cutaneous T-Cell Lymphoma (must meet all):
      1. Diagnosis of cutaneous T-cell lymphoma (CTCL) (see Appendix B for CTCL subtypes);
      2. Member meets a or b:
         a. FDA approved use:
            i. Treatment of CTCL cutaneous manifestations refractory to at least one prior systemic therapy (e.g., interferons, histone deacetylase inhibitors [vorinostat, romidepsin], extracorporeal photopheresis, methotrexate);
         b. Off-label NCCN recommended use (i or ii):
            (not limited to cutaneous manifestations, refractory disease or prior systemic therapy):
               i. Primary or adjuvant treatment of mycosis fungoides (MF) or Sezary syndrome (SS), or for refractory or progressive MF or SS;
               ii. Primary treatment of primary cutaneous CD30+ lymphoproliferative disorders, or for relapsed or refractory primary cutaneous CD30+ lymphoproliferative disorders (a or b):
                  a) Primary cutaneous anaplastic large cell lymphoma (ALCL);
                  b) Lymphomatoid papulosis (LyP).

      Approval duration: 3 months

   B. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy.

II. Continued Approval
   A. All Indications (must meet all):
      1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria.

      Approval duration: 3 months

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
2. Refer to ERX.SPMN.16 - Global Biopharm Policy.

Background
Description/Mechanism of Action:
Targretin (bexarotene) is a member of a subclass of retinoids that selectively activate retinoid X receptors (RXRs). These retinoid receptors have biologic activity distinct from that of retinoic acid receptors (RARs). RXRs can form heterodimers with various receptor partners such as retinoic acid receptors (RARs), vitamin D receptor, thyroid receptor, and peroxisome proliferator activator receptors (PPARs). Once activated, these receptors function as transcription factors that regulate the expression of genes that control cellular differentiation and proliferation. Bexarotene inhibits the growth in vitro of some tumor cell lines of hematopoietic and squamous cell origin. It also induces tumor regression in vivo in some animal models. The exact mechanism of action of bexarotene in the treatment of CTCL is unknown.

Formulations:
Capsule, Oral:
  Targretin: 75 mg
  Generic: 75 mg

FDA Approved Indications:
Targretin (bexarotene), oral capsule formulation, is a retinoid indicated for:
- Treatment of cutaneous manifestations of cutaneous T-cell lymphoma in patients who are refractory to at least one prior systemic therapy.

Appendices
Appendix A: Abbreviation Key
ALCL: anaplastic large cell lymphoma
ATLL: adult T-cell leukemia/lymphoma
CTCL: cutaneous T-cell lymphoma
LyP: lymphomatoid papulosis
MF: mycosis fungoides
PTCL-NOS: primary cutaneous peripheral T-cell lymphoma, unspecified

NK cells: natural killer cells
RAR: retinoid acid receptor
RXR: retinoic X receptors
SS: Sezary syndrome

Appendix B: WHO-EORTC classification of cutaneous T-cell lymphomas with primary cutaneous manifestations:
- Mycosis fungoides (MF)
- MF variants and subtypes
  - Folliculotropic MF
  - Pagetoid reticulosis
  - Granulomatous slack skin
- Sezary syndrome (SS)
- Adult T-cell leukemia/lymphoma (ATLL)
- Primary cutaneous CD30+ lymphoproliferative disorders
  - Primary cutaneous anaplastic large cell lymphoma (ALCL)
Lymphomatoid papulosis
Subcutaneous panniculitis-like T-cell lymphoma
Extranodal NK*/T-cell lymphoma, nasal type
Primary cutaneous peripheral T-cell lymphoma, unspecified (PTCL-NOS)
  Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma
Cutaneous gamma/delta T-cell lymphoma
Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma

*Extranodal NK-cell lymphoma is considered a CTCL subtype under the policy criteria.

Reviews, Revisions, and Approvals

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<tr>
<th>Event Description</th>
<th>Date</th>
<th>Approval Date</th>
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<tbody>
<tr>
<td>Policy created.</td>
<td>02/14</td>
<td>03/14</td>
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<tr>
<td>Policy converted to new template. Added NCCN compendial uses. Reduced approval period to 3 months as monitoring is required at least every two months. Added appendix B (subtypes of cutaneous T-cell lymphoma), drawing from WHO-EORTC categories presented in Willenze 2005.</td>
<td>08/16</td>
<td>09/16</td>
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References

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.

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