# Clinical Policy: Bexarotene (Targretin) Capsules

Reference Number: CP.PHAR.75
Effective Date: 09/11 Revision Log
Last Review Date: 07/17

**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 bexarotene (Targretin®) capsules

**Policy/Criteria**
It is the policy of health plans affiliated with Centene Corporation® that Targretin is **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):
      i. Primary or adjuvant treatment or treatment for refractory or progressive disease (a or b):
         a) Mycosis fungoides (MF);
         b) Sezary syndrome;
      ii. Primary treatment or treatment for relapsed or refractory disease (a or b):
         a) Primary cutaneous anaplastic large cell lymphoma (ALCL);
         b) Lymphomatoid papulosis (LyP);
3. If female and of childbearing age, negative pregnancy test within the last 30 days;
4. Request meets one of the following (a or b):
   a. Dose does not 400mg/m2 daily;
   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. Other diagnoses/indications:** Refer to CP.PHAR.57 - Global Biopharm Policy.

**II. Continued Approval**

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. No disease progression or unacceptable toxicity;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. Does does not exceed 400mg/m2 daily;
   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 Centene benefit and documentation supports positive response to therapy;
   **Approval duration: Duration of request or 6 months (whichever is less);** or
2. Refer to CP.PHAR.57 - 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 administration
Targretin: 75 mg
Generic: 75 mg

*FDA Approved Indications:*

Targretin (bexarotene) is a retinoid/oral capsule formulation 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
NK cells: natural killer cells
RAR: retinoid acid receptor
RXR: retinoic X receptors

*Appendix B: WHO-EORTC Classification of Cutaneous T-Cell Lymphomas (CTCLs) with Primary Cutaneous Manifestations*

- Mycosis fungoides (MF)
- MF variants and subtypes
  - Folliculotropic MF
  - Pagetoid reticulosis
  - Granulomatous slack skin
- Sezary syndrome
- Adult T-cell leukemia/lymphoma (ATLL)
- Primary cutaneous CD30+ lymphoproliferative disorders
  - Primary cutaneous anaplastic large cell lymphoma (ALCL)
  - Lymphomatoid papulosis (LyP)
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK*/T-cell lymphoma, nasal type
- Primary cutaneous peripheral T-cell lymphoma, unspecified
  - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma
  - Cutaneous gamma/delta T-cell lymphoma
  - Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma

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

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| No changes | 07/12 | |
| Removed questions related to pregnancy and contraception<br>Changed the re-auth question about continuing benefits to inquire about disease progression and unacceptable toxicity<br>Updated the clinical background information. | 08/13 | 08/13 |
| Updated clinical background information to include efficacy<br>Added adverse effect leukopenia and monitoring in background<br>Added Appendix A<br>Algorithm: added appendix A | 07/14 | 08/14 |
| Added subheadings and safety information to narrative; added questions regarding age, labs, pregnancy, LFTs, TGLs, and gemfibrozil to algorithm. Reduced approval period to three months as monitoring is required at least every two months. | 07/15 | 07/15 |
| Policy converted to new template. Removed criteria regarding TGL levels, pancreatic risk factors, liver enzymes, bilirubin and concurrent gemfibrozil administration as they are not contraindications or absolute reason to discontinue per PI. Approval periods, initial/continued, are retained at 3 months/3 months. Subtypes of cutaneous T-cell lymphoma are added at Appendix B, drawing from WHO-EORTC categories presented in Willenze 2005. NCCN compendial uses are added. | 06/16 | 07/16 |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| Hypersensitivity precaution and reasons to discontinue removed. Added dosing information. Efficacy statement added to continuation criteria. Approval periods lengthened from 3/3 to 6/12 months. | 06/17 | 07/17 |

**References**

1. Targretin (capsules) Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; July 2015. Available at http://www.valeant.com/Portals/25/PDF/TargretinCapsules-PI.pdf?ver=2016-05-11-044521-020. Accessed June 15, 2017.
2. Bexarotene. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed June 15, 2017.
3. T-cell lymphomas (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed June 15, 2017.
4. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. May 2005; 105(10): 3768-85.
5. Olsen EA. Evaluation, diagnosis and staging of cutaneous lymphoma. *Dermato Clin.* October 2015; 33(4): 643-54. doi: 10.1016/j.det.2015.06.001.

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.

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**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 and 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.