

**Clinical Policy: Bexarotene (Targretin Capsules, Gel)**

Reference Number: CP.PHAR.75

Effective Date: 09.01.11

Last Review Date: 05.21

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Bexarotene (Targretin<sup>®</sup>) is a retinoid X receptor activator.

**FDA Approved Indication(s)**

Targretin capsules are indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma (CTCL) in patients who are refractory to at least one prior systemic therapy.

Targretin gel is indicated for the topical treatment of cutaneous lesions in patients with CTCL (Stage IA and IB) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.

**Policy/Criteria**

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

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> 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 CTCL (*see Appendix D for CTCL subtypes*);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member must use generic bexarotene, unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 400 mg/m<sup>2</sup> per day;
  - 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:****Medicaid/HIM** – 6 months**Commercial** – Length of Benefit**B. Primary Cutaneous Lymphomas of the Skin** (must meet all):

1. Request is for Targretin gel;

2. Diagnosis of CTCL or cutaneous B-cell lymphoma (CBCL) (*see Appendix D for CTCL and CBCL subtypes*);
3. Prescribed by or in consultation with an oncologist;
4. Age  $\geq$  18 years;
5. Disease manifestation is localized to skin only;
6. Request meets one of the following (a of b):\*
  - a. Dose does not exceed application of four times per day;
  - 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:**

**Medicaid/HIM** – 6 months

**Commercial** – Length of Benefit

**C. Off-Label Indications** (must meet all):

1. Diagnosis of Mycosis Fungoides/Sezary Syndrome;
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;
4. Request meets one of the following:
  - a. For Targretin capsule request, member must use generic bexarotene, unless contraindicated or clinically significant adverse effects are experienced;
  - b. For Targretin gel request, disease is limited and localized to skin involvement only;
5. 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:**

**Medicaid/HIM** – 6 months

**Commercial** – Length of Benefit

**D. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Primary Cutaneous Lymphoma** (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Targretin for a covered indication, 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. Bexarotene capsules: New dose does not exceed 400 mg/m<sup>2</sup> per day;
  - b. Bexarotene gel: New dose does not exceed application of four times per day;

- c. 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:**

**Medicaid/HIM** – 6 months

**Commercial** – Length of Benefit

**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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

ALCL: anaplastic large cell lymphoma  
ATLL: adult T-cell leukemia/lymphoma  
C-ALCL: primary cutaneous anaplastic large cell lymphoma  
CBCL: cutaneous B-cell lymphoma  
CTCL: cutaneous T-cell lymphoma  
EBV: Epstein-Barr virus

FDA: Food and Drug Administration  
LyP: lymphomatoid papulosis  
MF: mycosis fungoides  
NK cells: natural killer cells  
RAR: retinoid acid receptor  
RXR: retinoic X receptors

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): Pregnancy; known hypersensitivity to bexarotene
- Boxed warning(s): Birth defects

*Appendix D: WHO-EORTC Classification of primary cutaneous lymphomas*

- CTCL
  - 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 (C-ALCL)
  - Lymphomatoid papulosis (LyP)
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK\*/T-cell lymphoma, nasal type
- Chronic active EBV infection
- Primary cutaneous peripheral T-cell lymphoma, not otherwise specified
- Primary cutaneous peripheral T-cell lymphoma, rare subtypes
  - Primary cutaneous gamma/delta T-cell lymphoma
  - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)
  - Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (provisional)
  - Primary cutaneous acral CD8+ T-cell lymphoma (provisional)
- CBCL
  - primary cutaneous marginal zone lymphoma
  - primary cutaneous follicle center lymphoma
  - primary cutaneous large B-cell lymphoma, leg type
  - Epstein-Barr virus mucocutaneous ulcer (provisional)
  - Intravascular large B-cell lymphoma

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

## V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CTCL	<u>Oral</u> 300-400 mg/m <sup>2</sup> /day PO	<u>Oral</u> 400 mg/m <sup>2</sup> /day
	<u>Topical</u> Initially applied once every other day for the first week. The application frequency should be increased at weekly intervals to once daily, then twice daily, then three times daily and finally four times daily according to individual lesion tolerance	<u>Topical</u> Four times daily

## VI. Product Availability

Drug Name	Availability
Bexarotene capsules (Targretin)	Capsules: 75 mg
Bexarotene 1% gel (Targretin)	Gel: 600 mg active bexarotene per 600 g

## VII. References

1. Targretin (capsules) Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; July 2015. Available at <https://www.targretin.com/>. Accessed February 21, 2021..
2. Targretin (gel 1%) Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; October 2016. Available at <https://www.targretin.com/>. Accessed February 21, 2021.
3. Bexarotene. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at [www.nccn.org](http://www.nccn.org). Accessed February 21, 2021.
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.
6. Willemze R, Cerroni L, Kempf W, et al. The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas. *Blood*. 2019; 133(16): 1703-1714.

Reviews, Revisions, and Approvals	Date	P&T 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
2Q 2018 annual review: Commercial and HIM lines of business added; added age; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; added continuity of care statement; references reviewed and updated.	02.13.18	05.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	12.19.19	05.19
2Q 2020 annual review: added bexarotene gel formulation and criteria; updated appendix D primary cutaneous lymphoma classification; references reviewed and updated.	03.04.20	05.20
2Q 2021 annual review: added off-label indication for Mycosis Fungoides/Sezary Syndrome; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); added generic redirection language to “must use” since oral oncology product; references reviewed and updated.	02.21.21	05.21

### **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.

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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.

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