Clinical Policy: Bexarotene (Targretin Capsules, Gel)

Reference Number: CP.PHAR.75
Effective Date: 09.01.11
Last Review Date: 05.23
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®) 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® that Targretin is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Request is for bexarotene capsules;
2. Diagnosis of CTCL *(see Appendix D for CTCL subtypes)*;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. For Targretin capsule requests, member must use generic bexarotene capsules, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg/m^2 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 – 12 months or duration of request, whichever is less

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 ≥ 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 – 12 months or duration of request, whichever is less

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (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. For Targretin capsule requests, member must use generic bexarotene capsules, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. Bexarotene capsules: New dose does not exceed 400 mg/m^2 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 – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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	Oral 300-400 mg/m^2/day PO Topical 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	Oral 400 mg/m^2/day Topical Four times daily

VI. Product Availability

Drug Name	Availability
Bexarotene capsules (Targretin)	Capsule: 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; April 2020. Available at https://www.targretin.com/. Accessed January 4, 2023.
2. Targretin (gel 1%) Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; February 2020. Available at https://www.targretin.com/. Accessed January 4, 2023.
3. Bexarotene. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed January 23, 2023.
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Primary Cutaneous Lymphomas. Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed January 23, 2023.
5. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. May 2005; 105(10): 3768-85.
6. 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.
7. 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
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
2Q 2022 annual review: modified commercial approval duration from length of benefit to “12 months or duration of request, whichever is less”; for Section IA, clarified this applies to bexarotene capsule requests; for continuation of therapy added requirement for Targretin capsule request, member must use generic bexarotene capsules; references reviewed and updated.	01.25.22	05.22
Template changes applied to other diagnoses/indications.	10.12.22	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2023 annual review: no significant changes; removed off-label criteria related to mycosis fungoides/Sezary syndrome as those are subtypes of CTCL, an already covered FDA approved indication; references reviewed and updated.	01.23.23	05.23

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.