Clinical Policy: Bexarotene (Targretin Capsules, Gel)

Reference Number: PA.CP.PHAR.75
Effective Date: 01/2018
Last Review Date: 04/2025

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
It is the policy of PA Health & Wellness that bexarotene and Targretin are **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 cutaneous T-cell lymphoma (CTCL) (see Appendix D for CTCL subtypes);
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. For Targretin capsule request, 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*).

Approval duration: 6 months

B. Primary Cutaneous Lymphomas of the Skin (must meet all):
1. Request is for bexarotene 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. For Targretin gel requests, member must use generic bexarotene gel, unless contraindicated or clinically significant adverse effects are experienced;
7. 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*).

Approval duration: 6 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. For Targretin request, member must use generic bexarotene, 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*).

Approval duration: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.PHARM.01) applies;
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. 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 cutaneousmarginal 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.*

IV. 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

V. Product Availability

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

VI. References

1. Targretin (capsules) Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; April 2020. Available at https://www.targretin.com/. Accessed January 24, 2025.
2. Targretin (gel 1%) Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; February 2020. Available at https://www.targretin.com/. Accessed January 24, 2025.
3. Bexarotene. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 5, 2025.
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Primary Cutaneous Lymphomas. Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed February 5, 2025.
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
2Q 2018 annual review: added age; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; references reviewed and updated.	02/2023
2Q 2019 annual review: no significant changes; references reviewed and updated.	04/2019
2Q 2020 annual review: added bexarotene gel formulation and criteria; updated appendix D primary cutaneous lymphoma classification; references reviewed and updated.	04/2020
2Q 2021 annual review: added off-label indication for Mycosis Fungoides/Sezary Syndrome; added generic redirection language to "must use" since oral oncology product; references reviewed and updated.	04/2021
2Q 2022 annual review: 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.	04/2022
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.	04/2023

Reviews, Revisions, and Approvals	Date
2Q 2024 annual review: no significant changes; revised policy/criteria section to also include generic bexarotene; added redirection to generic bexarotene gel for Targretin gel requests; references reviewed and updated.	04/2024
2Q 2025 annual review: modified continued approval duration from 6 months to 12 months per standard oncology approach; references reviewed and updated.	04/2025