

CLINICAL POLICY

BEXAROTENE (TARGRETIN CAPSULES, GEL)

Clinical Policy: Bexarotene (Targretin Capsules, Gel)

Reference Number: PA.CP.PHAR.75

Effective Date: 01/2018

Last Review Date: 04/2022

[Revision Log](#)

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 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 D for CTCL subtypes);
2. Request is for bexarotene capsules
3. Prescribed by or in consultation with an oncologist;
4. Age \geq 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/m² 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 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 or 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*).

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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 ≥ 18 years;
4. Request meets one of the following:
 - a. For Targretin capsule request, member must use generic bexarotene capsules, 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*).

Approval duration: 6 months

D. 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.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. For Targretin capsule request, 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 or b):
 - a. Bexarotene capsules: New dose does not exceed 400 mg/m² 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: 6 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.LTSS.PHAR.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

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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.*

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CTCL	<u>Oral</u> 300-400 mg/m ² /day PO <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>Oral</u> 400 mg/m ² /day <u>Topical</u> 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; August 2020. Available at <https://www.targretin.com/>. Accessed January 25, 2022.
2. Targretin (gel 1%) Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; October 2016. Available at <https://www.targretin.com/>. Accessed January 25, 2022.
3. Bexarotene. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed January 25, 2022.
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Primary Cutaneous Lymphomas. Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed January 25, 2022.
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	Approval 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.	02.13.18	

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2019 annual review: no significant changes; references reviewed and updated.	04/19	
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	