Clinical Policy: Bexarotene (Targretin Capsules, Gel)

Reference Number: ERX.SPA.79
Effective Date: 03.01.14
Last Review Date: 05.20
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. 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:
Commercial – Length of Benefit
Medicaid – 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 ≥ 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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^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:
Commercial – Length of Benefit (capsules) or 12 months (gel)
Medicaid – 12 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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

Indication	Dosing Regimen
Bexarotene capsules (Targretin)	Capsule: 75 mg
Bexarotene 1% gel (Targretin)	Gel: 600 mg/600 g

VII. 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 February 13, 2020.
2. Targretin (gel 1%) Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; October 2016. Available at https://www.targretin.com/. Accessed February 28, 2020.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 13, 2020.

4. National Comprehensive Cancer Network Guidelines. T-Cell Lymphomas Version 2.2019. Available at www.nccn.org. Accessed February 7, 2019.
5. National Comprehensive Cancer Network Guidelines. Primary Cutaneous Lymphomas Version 1.2020. Available at www.nccn.org. Accessed February 13, 2020.
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
Policy converted to new template. Added NCCN compendial uses. Reduced approval period to 3 months as monitoring is required at least every two months. Added appendix B (subtypes of cutaneous T-cell lymphoma), drawing from WHO-EORTC categories presented in Willenze 2005.	08.16	09.16
Converted to new template. Age added. Maximum dose added. Dosing guidance for off-label use added. Approval periods lengthened from 3/3 to 6/12 months. References updated.	07.17	08.17
2Q 2018 annual review: NCCN and FDA approved uses summarized for improved clarity; specialist involvement in care added; continuity of care statement added; approval durations increased to length of benefit; references reviewed and updated.	02.13.18	05.18
2Q 2019 annual review: no significant changes; pregnancy contraindication removed; references reviewed and updated.	12.19.19	05.19
2Q 2020 annual review: added bexarotene gel formulation and criteria; added Medicaid line of business with 6/12 month approval durations for bexarotene gel; updated appendix D primary cutaneous lymphoma classification; references reviewed and updated.	03.04.20	05.20

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.