bexarotene (Targretin®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO115

Description

Bexarotene (Targretin) is an orally and topically administered retinoid that binds to and activates retinoid X receptor subtypes to inhibit growth and induce the regression of tumor cells.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
bexarotene	75 mg capsule	Primary cutaneous T-cell lymphoma, refractory to one prior systemic therapy	Based on body surface area calculation, dose to be rounded to the nearest 75 mg
	75 mg liquid capsule		
bexarotene (Targretin)	75 mg capsule		
	1% topical gel/jelly	Primary cutaneous T-cell lymphoma, refractory to one prior therapy	60 grams/30 days

Initial Evaluation

I. Bexarotene (Targretin) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with an oncologist; **AND**
   C. Bexarotene (Targretin) will **not** be used in combination with mechlorethamine (Valchlor);; **AND**
   D. If the member is a woman of child-bearing potential, the prescriber attests the member has had a negative pregnancy test prior to starting therapy; **AND**
   E. A diagnosis of **primary cutaneous T-cell lymphoma** (e.g., mycosis fungosides, Sezary Syndrome) when the following are met:
      1. For the request of **bexarotene capsules or liquid capsules**;
         i. The member is relapsed and/or refractory to one prior systemic therapy (e.g., oral retinoids, interferon, methotrexate, cyclophosphamide, chemotherapy); **AND**
         ii. The request is for generic bexarotene capsules or liquid capsules, unless generic bexarotene has been ineffective or contraindicated; **AND**
         iii. A body surface area that has been documented utilizing weight recorded in the past three months ; **AND**

iv. The dose prescribed does not exceed 300 mg/m2/day for at least eight weeks before dose escalation to a maximum of 400 mg/m2/day; **OR**

2. For the request of **bexarotene (Targretin) topical gel/jelly**;
   i. The member has stage IA or IB disease (i.e., limited/localized skin involvement); **AND**
   ii. The member has had a relapse, refractory of, or intolerance to at least two other skin-directed therapies (e.g., mechlorethamine, corticosteroids, phototherapy, imiquimod, topical retinoids)

II. Bexarotene (Targretin) is considered investigational when used for all other conditions, including but not limited to:
   A. Breast cancer
   B. Lung cancer
   C. Gastroesophageal cancers
   D. Acute myeloid leukemia
   E. Non-Hodgkin Lymphoma
   F. Thyroid cancer
   G. Aids-related Kaposi's sarcoma
   H. Alzheimer's disease
   I. Schizophrenia

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited response to therapy as evidenced by an improvement in CAILS score **or** a decrease in affected surface area, plaque/scale elevation, or severity; **AND**
IV. For bexarotene capsules or liquid capsules:
   A. A body surface area that has been documented utilizing weight recorded in the past three months; **AND**
   B. The dose will not exceed 400 mg/m2/day; **AND**
   C. The request is for generic bexarotene capsules or liquid capsules, unless generic bexarotene has been ineffective or contraindicated

Supporting Evidence

I. Bexarotene (Targretin) gel was evaluated in an open-label, Phase I-II trial for the treatment of early stage (IA-IIA) cutaneous T-cell lymphoma in those that were refractory, intolerant to, or reached plateaued response to two prior therapies. Tumor response was assessed via the Composite Assessment of Index Lesion Disease Severity, and was based on a summation of the grades for index lesions, erythema, scaling, plaque elevation, hypo or hyperpigmentation, and area of involvement. Partial response was defined as improvement of at least 50% of the index lesions and did not require confirmation by biopsy. The primary outcome was overall response rate, which occurred in 26% (CI 15%, 40%) of subjects. There was no response seen in those that had stage II disease; thus, the FDA-approval was granted to stage IA/IB only. Additionally, due to the single-arm, open-label trial design, results should be interpreted with caution.

II. Bexarotene (Targretin) capsules were evaluated as systemic therapy in 152 subjects, with advanced and early stage cutaneous T-cell lymphoma in two, open-label trials. Those with advanced disease had been treated with at least one prior systemic therapy, but with a median of two, and up to six therapies. Early disease subjects were intolerant to, were refractory to, or reached plateaued response to two prior therapies. Therapy was initiated at a starting dose of 650 mg/m2/day, with a dose reduction to 500 mg/m2/day; however, neither was tolerated in the study population. The dose was further reduced to 300 mg/m2/day with a dose increase to 400 mg/m2/day if no response was see after eight weeks of therapy. Tumor response was assessed by observation using Composite Assessment of Index Lesion Disease Severity. The endpoint was based on a summation of the grades, erythema, scaling, plaque elevation, hypo or hyperpigmentation and area of involvement. Presence or absence of cutaneous tumors and extra cutaneous manifestations was considered in the response assessment. Tumor responses required confirmation over at least two assessments separated by at least four weeks and partial response was defined as improvement of at least 50% in the index lesions without worsening or development of new cutaneous tumors or non-cutaneous manifestations. At the initial dose of 300 mg/m2/day, one subject had complete clinical tumor response, and 30% (19/62) had partial response. Median duration of tumor response had not been reached by the end of the study. Reponses may be seen as early as four weeks. Due to the single-arm, open-label trial design, results should be interpreted with caution.

III. Commonly utilized skin-directed therapies for cutaneous T-cell lymphoma (e.g., mycosis fungosides, Sezary Syndrome) include the following: topical corticosteroids, topical mechlorethamine (nitrogen mustard), local radiation, topical retinoids (tazarotene, bexarotene), phototherapy, imiquimod, and topical carmustine.

IV. Commonly utilized systemic therapies for cutaneous T-cell lymphoma include the following: brentuximab vedotin, bexarotene, interferons, methotrexate, mogamulizumab, romidepsin, vorinostat, gemcitabine, doxorubicin, and pralatrexate.

V. The cost of one 60-gram tube of topical bexarotene (Targretin) is approximately $30,500; therefore, a quantity limit of one tube per 30-day supply is in place to ensure appropriate use without waste. Should a quantity exception be requested, clinical consideration will be taken to the amount of body surface area the medication is being applied, rate of application, and amount utilized with administration.

Investigational or Not Medically Necessary Uses

I. Bexarotene (Targretin) has not been sufficiently evaluated and/or is currently in clinical trials for the following indications:
   A. Breast cancer
   B. Lung cancer
   C. Gastroesophageal cancer
   D. Acute myeloid leukemia
   E. Non-Hodgkin Lymphoma
   F. Thyroid cancer
   G. Aids-related Kaposi's sarcoma
   H. Alzheimer's disease
   I. Schizophrenia

References

1. Brenaman D., Duvic M., Kuzel T., et al. Phase 1 and 2 trial of bexarotene gel for skin directed treatment of patients with cutaneous T cell lymphoma. Arch Dermatol 2002; 138:325-332.
2. Heald P., Mehlmauer M., Martin AG., et al. Topical bexarotene therapy for patients with refractory or persistent early stage cutaneous T cell lymphoma: results of the phase III clinical trial. J Am Acad Dermatol 2003; 49:801-815.
3. Duvic M., Martin AG., Kim Y., et al, Phase 2 and 3 clinical trial of oral bexarotene (Targretin capsules) for the treatment of refractory or persistent early-stage cutaneous T-cell lymphoma. Arch Dermatol. 2001; 137:581-593.

Policy Implementation/Update:

Date Created	August 2008
Date Effective	October 2008
Last Updated	November 2019
Last Reviewed	07/2012, 09/2012, 12/2012, 11/2019

Action and Summary of Changes	**Date**
Prior authorization criteria transitioned to policy format, age edit added, updated specialist prescriber requirement to new format, removal of liver function test monitoring requirements. Addition of topical bexarotene (Targretin) to the policy. Initial approval criteria increased from six to 12 months.	11/2019