



PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Targretin® (bexarotene gel 1% – Valeant)

TAC APPROVAL DATE: 09/20/2017

OVERVIEW

Targetin gel is indicated for the topical treatment of cutaneous lesions in patients with cutaneous T-cell lymphoma (CTCL) [Stage 1A and 1B] who have refractory or persistent disease after other therapies or who have not tolerated other therapies.¹ Targretin gel is contraindicated in pregnant patients and it should not be given to a pregnant patient or a patient who intends to become pregnant. If a patient becomes pregnant while using Targetin gel, it must be discontinued immediately.

Targretin contains bexarotene, a member of the retinoid class of drugs that selectively binds and activates retinoid X receptor subtypes (RXR α , RXR β , RXR γ).¹ Retinoid X receptors, once activated, function as transcription factors that regulate the expression of genes that control cellular differentiation and proliferation. Targretin inhibits the growth (*in vitro*) of some tumor cell lines of hematopoietic and squamous cell origin and it also induces tumor regression (*in vivo*) in some animal models. The exact mechanism of action in the treatment of CTCL is unknown.

DISEASE OVERVIEW

T-cell lymphoma accounts for approximately 15% of all non-Hodgkin lymphoma (NHL) in the US.² CTCL is one of the most common forms of T-cell lymphoma.²⁻³ The World Health Organization (WHO) and the European Organization for Research and Treatment of Cancer (EORTC) published the classification of primary CTCL in 2007.⁴ The CTCLs are grouped according to clinical behavior: indolent: mycosis fungoides, folliculotropic mycosis fungoides, pagetoid reticulosis, granulomatous slack skin, primary cutaneous anaplastic large cell lymphoma, lymphomatoid papulosis, subcutaneous panniculitis-like-T-cell lymphoma, and primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma (provisional entity); or aggressive: Sézary syndrome, primary cutaneous natural killer/T-cell lymphoma - nasal type, primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma (provisional entity), cutaneous gamma/delta-positive T-cell lymphoma (provisional entity), and primary cutaneous peripheral T-cell lymphoma-undefined.

The most common type of CTCL is mycosis fungoides and its variants, which accounts for approximately 50% to 70% of all CTCLs.⁴ Skin symptoms associated with mycosis fungoides include patches, plaques, or tumors and treatment is directed at the skin or the entire body (systemic).²⁻³ Sézary syndrome is an advanced, variant form of mycosis fungoides and is characterized by the presence of lymphoma cells in the blood. Patients with Sézary syndrome will have extensive thin, red, itchy rashes usually covering over 80% of the body and treatment will generally include systemic therapies since the use of skin-directed therapies alone is typically inadequate. Skin-directed therapies are useful for patch and limited plaque disease. Systemic therapies are reserved for more advanced disease and initiation of systemic therapy is usually deferred until patients have not responded well to topical therapies.

The American Cancer Society characterizes both CTCL Stage 1A and Stage 1B diseases as diseases that involve skin lesions (that cover < 10% of the skin surface) but no tumors, no enlarged lymph nodes,

lymphoma cells have not spread to other organs or tissues, and the number of Sézary cells in the blood is not high.⁵

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on T-cell lymphomas (version 2.2017) provide treatment recommendations for the different types of CTCLs.³ Initial treatment options for patients with mycosis fungoides or Sézary Syndrome consist of skin-directed therapies with the addition of milder systemic therapies (Category A drugs) for refractory, persistent, or progressive disease with skin-directed therapies. Skin-directed therapy options are grouped into two categories: options for limited/localized skin involvement and options for widespread skin involvement. Topical corticosteroids, topical chemotherapy (Valchlor[®] [mechlorethamine gel]), local radiation, topical retinoids (Targretin[®] gel, Tazorac[®] [tazarotene cream/gel]), phototherapy (ultraviolet B [UVB], narrow band UVB [NB-UVB] for patch/thin plaques and psoralen and ultraviolet A [PUVA] for thicker plaques), and topical imiquimod cream (Aldara[®], generics; Zyclara[®]) are recommended for limited/localized skin involvement. Options for widespread skin involvement are topical corticosteroids, topical chemotherapy (Valchlor[®]), phototherapy (UVB, NB-UVB, or PUVA), and total skin electron beam therapy (TSEBT). Topical retinoids and topical imiquimod are not recommended for widespread disease due to skin irritation toxicity. Systemic Category A therapies are: retinoids (bexarotene capsules [Targretin[®]/generics], tretinoin capsules, isotretinoin capsules [Absorica[®], Amnesteem[®], Claravis[™], Myorisan[™], Zenatane[™]], acitretin capsules [Soriatane[®], generics]), interferons (Intron-A[®]/Pegasys[®] [interferon-alpha injection], Actimmune[®] [interferon-gamma injection]), histone deacetylase (HDAC) inhibitors (Zolinza[®] [vorinostat capsules], Istodax[®] [romidepsin injection]), extracorporeal photopheresis, and methotrexate tablets or injection. Systemic Category B and C drugs, consisting of chemotherapeutic drugs (e.g., gemcitabine injection [Gemzar[®], generics], liposomal doxorubicin injection [Doxil[®], generics], Leukeran[®] [chlorambucil tablets], cyclophosphamide tablets or injection, Velcade[®] [bortezomib injection]), are recommended for advanced, refractory, or progressive disease. The NCCN also recommends combination therapies (skin-directed plus systemic therapies or two systemic therapies) in some situations. Many of these drug therapies are also recommended for other forms of T-cell lymphoma (e.g., primary cutaneous CD30+ T-cell lymphoproliferative disorders, adult T-cell leukemia/lymphoma). [Please refer to the NCCN guidelines for details].

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Targretin gel. Because of the specialized skills required for evaluation and diagnosis of patients treated with Targretin gel as well as the monitoring required for adverse events and long-term efficacy, approval requires Targretin gel to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 3 years in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Targretin gel is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Cutaneous manifestations of cutaneous T-cell lymphoma (CTCL).

- A) Initial therapy. Approve Targretin gel for 3 years if the patient meets all of the following criteria (i and ii):
- i. Targretin gel is prescribed by, or in consultation with, an oncologist or a dermatologist; AND
 - ii. The patient has tried a topical corticosteroid and topical imiquimod cream (Aldara[®], generics; Zyclara[®]).
- (NOTE: An exception to the requirement for a trial of a topical corticosteroid and topical imiquimod cream can be made if the patient has already used one of the following: a skin-directed therapy, e.g., topical chemotherapy, topical retinoids, local radiation, phototherapy [UVB, NB-UVB, PUVA], TSEBT; or a systemic therapy, e.g., oral retinoids, interferons, histone deacetylase [HDAC] inhibitors, extracorporeal photopheresis, methotrexate, systemic chemotherapeutic agents. These patients are not required to “step back” and try a topical corticosteroid and topical imiquimod cream).
- B) Patient is currently receiving Targretin gel or has received Targretin gel in the past. Approve for 3 years if Targretin gel is prescribed by, or in consultation with, an oncologist or dermatologist.

Targretin gel is indicated for the topical treatment of cutaneous lesions in patients with CTCL (Stage 1A and 1B) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.¹

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Targretin gel has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for conditions not included in the Recommended Authorization Criteria.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Targretin[®] gel [prescribing information]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; October 2016.
2. Cutaneous T-cell lymphoma. Available at: <http://www.lymphoma.org/site/pp.asp?c=bkLTKaOQLmK8E&b=6300151>. Accessed on August 1, 2017.
3. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 2.2017 – February 21, 2017). © 2017 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 1, 2017.
4. Kinney MC, Jones D. Cutaneous T-cell and natural killer (NK)-cell lymphomas. The World Health Organization (WHO) and European Organization for Research and Treatment of Cancer (EORTC) classification and the increasing recognition of specialized tumor types.
5. American Cancer Society – How is lymphoma of the skin staged? Available at: <https://www.cancer.org/cancer/skin-lymphoma/detection-diagnosis-staging/staging.html>. Accessed on August 1, 2017.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New Policy	---	09/20/2017

TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.

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