GIVE YOUR CUTANEOUS T-CELL LYMPHOMA PATIENTS

THE POWER OF TARGRETIN[1,2]

Targretin® (bexarotene) 1% gel

Targretin® (bexarotene) 75 mg capsules

INDICATION AND USAGE

TARGRETIN® (bexarotene) capsules and gel are indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma (only stages 1A and 1B for gel) in patients who are refractory to at least one prior systemic therapy.

IMPORTANT SAFETY INFORMATION

BIRTH DEFECTS

Because of the risk of fetal harm, Targretin capsules and gel must not be given to a woman who is pregnant or who intends to become pregnant. If a woman becomes pregnant during treatment with Targretin, treatment must be stopped immediately, and the woman provided appropriate counseling about the risks.

PLEASE SEE IMPORTANT SAFETY INFORMATION TAB AND ACCOMPANYING FULL PRESCRIBING INFORMATION FOR TARGRETIN GEL AND CAPSULES IN POCKET.

UNDERSTANDING CUTANEOUS T-CELL LYMPHOMAS

CTCL—a complicated disease

Cutaneous T-cell lymphomas (CTCL) are characterized by the presence of malignant T cells in chronically inflamed skin lesions.

Mycosis fungoides (MF) is the main manifestation of the disease, making up 54%-72% of all cases. MF presents as erythematous skin patches that are often confused for immune-related diseases like eczema, psoriasis, parapsoriasis, or pityriasis lichenoides.[3] Only proper testing can ensure an accurate diagnosis of CTCL-MF.

MF ENCOMPASSES
54%-72%
OF ALL CASES

Early MF is often diagnosed through clinical, histopathologic and immunopathologic methods including[4]:

Physical exam
With complete skin evaluation and palpation of peripheral lymph node regions

Blood testing
To check for the presence of malignant T-cells

Biopsy
Of skin and/or lymph node for pathology

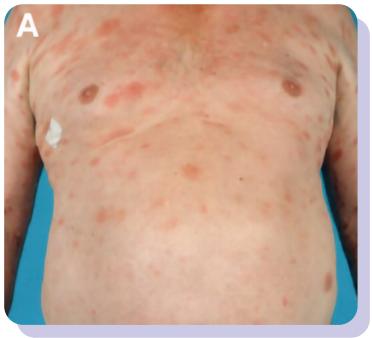
Imaging tests
Such as CT or MRI scans

Histologic evaluation of an enlarged node can also be used to confirm the type and stage of CTCL

IDENTIFYING STAGES OF CUTANEOUS T-CELL LYMPHOMAS

CTCL—a complicated disease

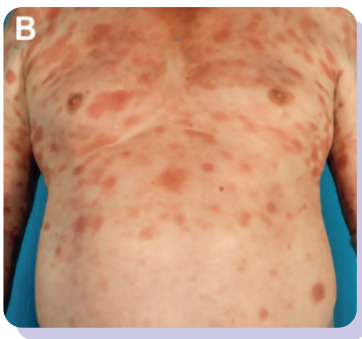
MF presents as erythematous skin patches that are often confused for immune-related diseases like eczema, psoriasis, or pityriasis lichenoides.[3]

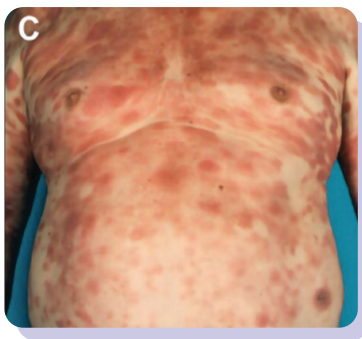


EARLY STAGES OF CTCL

Early stages of CTCL show as limited patches or plaques. If diagnosed early, prognosis is favorable with management and the disease is considered non–life-threatening. A majority of CTCL cases will not progress beyond this stage.[3]

*For early-stage CTCL, **topicals** can lead to complete remission*[5]





ADVANCED STAGES OF CTCL

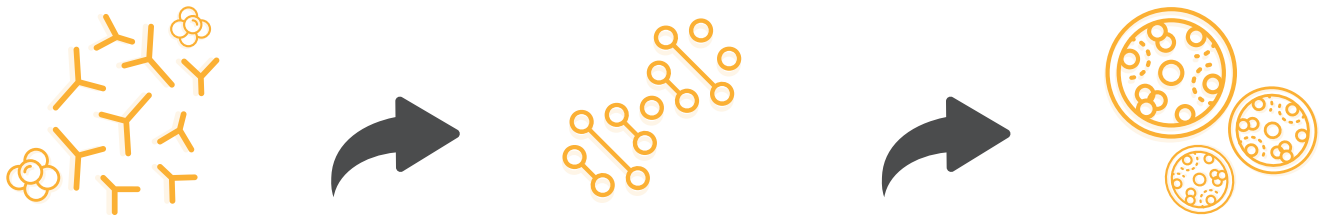
About one-third of patients progress to later stages of CTCL. The skin lesions start to spread and noticeable tumors and skin redness may develop.[3]

*For progressing cases of CTCL, **systemic therapy** may be appropriate to manage patients' disease*[4]

HOW CAN TARGRETIN HELP YOUR PATIENTS?

The active ingredient in Targretin is bexarotene

Bexarotene is in a subclass of retinoids (rexinoids) that selectively activate retinoid X receptors (RXRs). These retinoid receptors have biologic activity distinct from that of retinoic acid receptors (RARs).[1,2]



Bexarotene selectively activates retinoid X receptors

Activated receptors regulate gene expression in the cell

Tumor growth is inhibited and regression is induced

Targretin® (bexarotene) 1% gel

INDICATED FOR

the topical treatment of cutaneous lesions from CTCL (Stage IA and IB) in patients who:

Have refractory or persistent disease **OR**
Have not tolerated other therapies

<10% BSA INVOLVEMENT: **A TOPICAL TREATMENT** MAY BE APPROPRIATE[4]

Targretin® (bexarotene) 75 mg capsules

INDICATED FOR

the treatment of cutaneous manifestations of CTCL in patients who:

Are refractory to at least one prior systemic therapy

≥10% BSA INVOLVEMENT: **A SYSTEMIC TREATMENT** MAY BE APPROPRIATE[4]

IMPORTANT SAFETY INFORMATION (CONT'D)

To prevent pregnancy, effective contraception must be used for one month prior to the initiation of Targretin therapy, during therapy and for at least one month following discontinuation of therapy; it is recommended that two reliable forms of contraception be used simultaneously unless abstinence is the chosen method. Male patients with sexual partners who are pregnant, possibly pregnant or who could become pregnant must use condoms during treatment and for at least one month after the last dose of drug.

PLEASE SEE IMPORTANT SAFETY INFORMATION TAB AND ACCOMPANYING FULL PRESCRIBING INFORMATION FOR TARGRETIN GEL AND CAPSULES IN POCKET.

DEMONSTRATED EFFICACY ACROSS STAGES OF CTCL

Study Design

Targretin® (bexarotene) 1% gel

Targretin Gel was evaluated in a multicenter, open-label trial of **50 patients with early-stage CTCL** who had undergone and failed (i.e. were refractory to, intolerant to, or reached a plateau for) at least 2 prior therapies.[1]

Study Design

Targretin® (bexarotene) 75 mg capsules

Targretin Capsules were evaluated in 2 multicenter, open-label, historically-controlled clinical trials in **152 patients with advanced and early-stage CTCL**[2]:

- 102 patients had disease refractory to at least 1 prior therapy
- 90 with advanced, 12 with early stage

In these trials, a Composite Assessment of Index Lesion Severity was used to assess tumor response. This endpoint was based on summation of the grades for all of the following signs and symptoms[1,2]:

- Erythema
- Scaling
- Plaque elevation
- Hypo- and hyperpigmentation
- Area of involvement

Targretin Gel was also evaluated for the treatment of patients with CTCL in a Phase I-II program involving patients with early-stage CTCL. This program enrolled a total of 67 patients.[1]

Targretin Gel

Targretin Gel produced an **overall response rate of 26%** (13/50) by the Composite Assessment of Index Lesion Severity.[3]

- 2% (1/50) had a complete clinical response
- **For Stage IA and IB patients, the response rate was 28% (13/47)**

The results of the Phase I-II (dose-seeking trials) support these findings.

23% RELAPSE RATE IN RESPONDERS OVER MEDIAN OBSERVATION PERIOD OF 149 DAYS

Targretin Capsules

Targretin Capsules produced an **overall response rate of 32%** (20/62) by the Composite Assessment of Index Lesion Severity.[4]

- 1.6% (1/62) of patients had a complete clinical response

30% RELAPSE RATE IN RESPONDERS OVER MEDIAN OBSERVATION PERIOD OF 147 DAYS

4 WEEKS

Responses may be seen with Targretin Gel or Targretin Capsules as early as 4 weeks after starting treatment. ***The median time to best response was 85 days for both*** *Targretin Gel and Targretin Capsules.*[3,4]

IMPORTANT SAFETY INFORMATION (CONT'D)

No more than a one month supply of Targretin should be given to the patient so that the results of pregnancy testing can be assessed and counseling regarding avoidance of pregnancy and birth defects can be reinforced.

PLEASE SEE IMPORTANT SAFETY INFORMATION TAB AND ACCOMPANYING FULL PRESCRIBING INFORMATION FOR TARGRETIN GEL AND CAPSULES IN POCKET.

SAFETY WITH TARGRETIN[1,2]

Targretin® (bexarotene) 1% gel

Targretin® (bexarotene) 75 mg capsules

Pregnancy and Lactation Considerations

Effective contraception

Effective contraception must be used for one month prior to initiation of therapy, during therapy, and for at least one month following discontinuation of therapy. Male patients with sexual partners who are pregnant, possibly pregnant, or who could become pregnant must use condoms during sexual intercourse while using Targretin for at least one month after the last dose of drug.

May cause fetal harm

TARGRETIN is a member of the retinoid class of drugs that is associated with birth defects in humans and in rats.

If pregnant, discontinue use

Stop treatment with Targretin immediately if a patient becomes pregnant.

Nursing

Due to potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Adverse Reactions — Targretin Gel

The most common adverse events reported with **Targretin Gel** in clinical trials, with an incidence at the application site of at least 10%, were:

- Rash
- Pruritus
- Skin disorder
- Pain

Overdosage

Systemic toxicity following acute overdosage with topical application of Targretin Gel is unlikely because of low systemic plasma levels observed with normal therapeutic doses. Doses up to 1000 mg/m^2/day of Targretin Capsules, 30 times the recommended dose, have been administered in short-term trials in patients with advanced CTCL without acute toxic effects.

Adverse Reactions — Targretin Capsules

The most common adverse events reported with **Targretin Capsules** in clinical trials, with an incidence of at least 10%, were:

- Hyperlipidemia
- Hypercholesteremia
- Headache
- Hypothyroidism
- Asthenia
- Rash
- Dry skin
- Leukopenia
- Nausea
- Infection
- Peripheral edema
- Abdominal pain
- Chills
- Exfoliative dermatitis

General Precautions

- Because of the relationship of bexarotene to vitamin A, patients should be advised to limit vitamin A supplements to avoid potential additive toxic effects.
- Retinoids as a class have been associated with photosensitivity. Patients should be advised to minimize exposure to sunlight and artificial ultraviolet light while using Targretin.
- Patients who are applying Targretin Gel should not concurrently use products that contain DEET, a common component of insect repellent products.

PLEASE SEE IMPORTANT SAFETY INFORMATION TAB AND ACCOMPANYING FULL PRESCRIBING INFORMATION FOR TARGRETIN GEL AND CAPSULES IN POCKET.

DOSING FREQUENCY FOR TARGRETIN GEL[3]

Targretin® (bexarotene) 1% gel

Week 1

Targretin Gel should be applied **once daily, every other day, for the first week**.

Week 2 and Onward

The application frequency should be **increased at weekly intervals to once daily, then twice daily, three times daily, and four times daily** according to individual lesion tolerance.

No application hazards[3,4]

Noncytotoxic*
*Common adverse events include leukopenia

No refrigeration required

No gloves required to apply Targretin Gel

DOSING TARGRETIN CAPSULES[2]

Targretin® (bexarotene) 75 mg capsules

The initial recommended dose of Targretin is 300 mg/m²/day, taken as **a single oral daily dose with a meal**.

Initial Dose Based on Body Surface Area		
BODY SURFACE AREA (m²)	TOTAL DAILY DOSE (mg/DAY)	NUMBER OF 75 mg TARGRETIN CAPSULES
0.88 - 1.12	300	4
1.13 - 1.37	375	5
1.38 - 1.62	450	6
1.63 - 1.87	525	7
1.88 - 2.12	600	8
2.13 - 2.37	675	9
2.38 - 2.62	750	10

If Targretin Capsules are not tolerated, the 300 mg/m²/day dose level may be adjusted to 200 mg/m²/day then 100 mg/m²/day, or temporarily suspended.

If initial dose is well tolerated with no tumor response after 8 weeks of treatment, the dose may be increased to 400 mg/m²/day with careful monitoring.

Targretin therapies are a
STANDARD OF CARE
for managing CTCL, with proven efficacy across stages of CTCL[2-4]

CONTRAINDICATION
TARGRETIN capsules and gel are contraindicated in patients with a known serious hypersensitivity to bexarotene or other components of the product.

PLEASE SEE IMPORTANT SAFETY INFORMATION TAB AND ACCOMPANYING FULL PRESCRIBING INFORMATION FOR TARGRETIN GEL AND CAPSULES IN POCKET.

IMPORTANT SAFETY INFORMATION FOR TARGRETIN® (BEXAROTENE) GEL AND CAPSULES

INDICATION AND USAGE

TARGRETIN® (bexarotene) capsules and gel are indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma (only stages 1A and 1B for gel) in patients who are refractory to at least one prior systemic therapy.

IMPORTANT SAFETY INFORMATION

BIRTH DEFECTS

Because of the risk of fetal harm, Targretin capsules and gel must not be given to a woman who is pregnant or who intends to become pregnant. If a woman becomes pregnant during treatment with Targretin, treatment must be stopped immediately, and the woman provided appropriate counseling about the risks.

To prevent pregnancy, effective contraception must be used for one month prior to the initiation of Targretin therapy, during therapy and for at least one month following discontinuation of therapy; it is recommended that two reliable forms of contraception be used simultaneously unless abstinence is the chosen method. Male patients with sexual partners who are pregnant, possibly pregnant or who could become pregnant must use condoms during treatment and for at least one month after the last dose of drug.

No more than a one month supply of Targretin should be given to the patient so that the results of pregnancy testing can be assessed and counseling regarding avoidance of pregnancy and birth defects can be reinforced.

CONTRAINDICATION

TARGRETIN capsules and gel are contraindicated in patients with a known serious hypersensitivity to bexarotene or other components of the product.

WARNINGS AND PRECAUTIONS

CAPSULES

Hyperlipidemia is present in most patients treated with TARGRETIN capsules. Obtain baseline values, monitor during treatment, and manage elevations during therapy.

Acute pancreatitis, including a fatal case, has been reported in patients treated with TARGRETIN capsules. Interrupt treatment and evaluate if suspected.

Hepatotoxicity, cholestasis, and hepatic failure TARGRETIN capsules had a dose-related effect on liver chemistry tests in clinical trials, including incidence of cholestasis and liver failure.

Hypothyroidism TARGRETIN capsules induce hypothyroidism in about half of all patients; obtain baseline thyroid function tests and monitor patients during treatment.

Neutropenia Leukopenia and neutropenia occurred in clinical trials with TARGRETIN capsules; obtain complete blood counts at baseline and periodically during treatment.

Cataracts Although a causal relationship has not been established, cataracts have been observed in animal and clinical studies with TARGRETIN capsules. Refer patients who experience visual difficulties for ophthalmologic evaluation.

Hypoglycemia in Diabetes TARGRETIN capsules may cause hypoglycemia in patients using insulin, agents enhancing insulin secretions, or insulin-sensitizers.

Nursing: Discontinue nursing during treatment with TARGRETIN.

Laboratory tests including CBC, fasting lipid profile, liver function tests, and thyroid profile should be obtained prior to treatment.

CA125 assay values in ovarian cancer patients may be elevated by treatment.

CAPSULES AND GEL

Vitamin A Patients should be advised to limit Vitamin A intake to avoid potential additive toxicity.

Photosensitivity Advise patients to minimize exposure to the sun and artificial sunlight during treatment.

GEL

Patients who are applying Targretin gel should not concurrently use products that contain DEET, a common component of insect repellent products.

For nursing women, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

ADVERSE REACTIONS

CAPSULES

The most common adverse reactions (>10%) include hyperlipidemia, hypercholesteremia, headache, hypothyroidism, asthenia, leukopenia, rash, nausea, infection, peripheral edema, abdominal pain, and dry skin.

GEL

The most common adverse events reported in Targretin gel clinical trials with an incidence at the application site of at least 10% were: rash, pruritus, skin disorder, and pain.

To report SUSPECTED ADVERSE REACTIONS contact customer service at 1-800-321-4576 or FDA at 1-800-FDA-1088 or visit fda.gov/medwatch.

Targretin® (bexarotene) 1% gel

Targretin® (bexarotene) 75 mg capsules

PLEASE SEE ACCOMPANYING FULL PRESCRIBING INFORMATION FOR TARGRETIN GEL AND CAPSULES IN POCKET.

PLEASE SEE IMPORTANT SAFETY INFORMATION TAB AND ACCOMPANYING FULL PRESCRIBING INFORMATION FOR TARGRETIN GEL AND CAPSULES IN POCKET.

Targretin® (bexarotene) 1% gel

Targretin® (bexarotene) 75 mg capsules

MAKE THE MOST OF YOUR PATIENTS' CTCL TREATMENT

WITH TARGRETIN

- **DUAL FORMULATIONS TO HANDLE ANY STAGE OF CTCL**
- **EFFICACY SEEN IN AS LITTLE AS 4 WEEKS**
- **NO GLOVES REQUIRED TO APPLY TARGRETIN GEL**

*Eligible commercially insured patients may pay as little as $0 on their Targretin prescription.**
Visit **www.targretin.com** *to get started.*

*Terms, conditions, and limitations apply. Visit www.targretin.com for eligibility criteria and terms and conditions.

Ortho Dermatologics

References: 1. Targretin gel 1% [prescribing information]. Bridgewater, NJ: Bausch Health US, LLC. **2.** Targretin 75 mg capsules [prescribing information]. Bridgewater, NJ: Bausch Health US, LLC. **3.** Krejsgaard T, Lindahl LM, Mongan NP, et al. Malignant inflammation in cutaneous T-cell lymphoma—a hostile takeover. *Semin Immunopathol*. 2017;39(3):269-282. **4.** National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): T-Cell Lymphomas. Version 5.2018. Published August 13, 2018. **5.** Galper SL, Smith BD, Wilson LD. Diagnosis and management of mycosis fungoides. *Oncology* (Williston Park). 2010;24(6):491-501.