

BEXAROTENE- bexarotene gel
Amneal Pharmaceuticals NY LLC

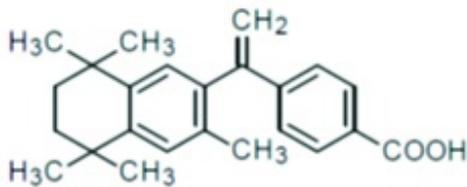
Bexarotene Gel, 1%

Rx Only

DESCRIPTION

Bexarotene gel, 1% contains bexarotene and is intended for topical application only. Bexarotene is a member of a subclass of retinoids that selectively activate retinoid X receptors (RXRs). These retinoid receptors have biologic activity distinct from that of retinoic acid receptors (RARs).

The chemical name is 4-[1-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)ethenyl] benzoic acid, and the structural formula is as follows:



Bexarotene is a white to off-white powder with a molecular weight of 348.478 and a molecular formula of C₂₄H₂₈O₂. It is practically insoluble in water, slightly soluble in methanol, sparingly soluble in acetone, soluble in dimethyl sulfoxide, slightly soluble in ethanol and very slightly soluble in vegetable oil.

Bexarotene gel, 1% is a clear gelled solution containing 1.0% (w/w) bexarotene in a base of dehydrated alcohol, polyethylene glycol 400, hydroxypropyl cellulose, and butylated hydroxytoluene.

CLINICAL PHARMACOLOGY

Mechanism of Action

Bexarotene selectively binds and activates retinoid X receptor subtypes (RXR α , RXR β , RXR γ). RXRs can form heterodimers with various receptor partners such as retinoic acid receptors (RARs), vitamin D receptor, thyroid receptor, and peroxisome proliferator activator receptors (PPARs). Once activated, these receptors function as transcription factors that regulate the expression of genes that control cellular differentiation and proliferation. Bexarotene inhibits the growth *in vitro* of some tumor cell lines of hematopoietic and squamous cell origin. It also induces tumor regression *in vivo* in some animal models. The exact mechanism of action of bexarotene in the treatment of cutaneous T-cell lymphoma (CTCL) is unknown.

Pharmacokinetics

General

Plasma concentrations of bexarotene were determined during clinical studies in patients with CTCL or following repeated single or multiple-daily dose applications of bexarotene gel, 1% for up to 132 weeks. Plasma bexarotene concentrations were generally less than 5 ng/mL and did not exceed 55 ng/mL. However, only two patients with very intense dosing regimens (> 40% BSA lesions and QID dosing) were sampled. Plasma bexarotene concentrations and the frequency of detecting quantifiable plasma bexarotene concentrations increased with increasing percent body surface area treated and increasing quantity of bexarotene gel applied. The sporadically observed and generally low plasma bexarotene concentrations indicated that, in patients receiving doses of low to moderate intensity, there is a low potential for significant plasma concentrations following repeated application of bexarotene gel. Bexarotene is highly bound (>99%) to plasma proteins. The plasma proteins to which bexarotene binds have not been elucidated, and the ability of bexarotene to displace drugs bound to plasma proteins and the ability of drugs to displace bexarotene binding have not been studied (see **PRECAUTIONS: Protein Binding**). The uptake of bexarotene by organs or tissues has not been evaluated.

Metabolism

Four bexarotene metabolites have been identified in plasma following oral administration of bexarotene: 6- and 7-hydroxy-bexarotene and 6- and 7-oxo-bexarotene. *In vitro* studies suggest that cytochrome P450 3A4 is the major cytochrome P450 responsible for formation of the oxidative metabolites and that the oxidative metabolites may be glucuronidated. The oxidative metabolites are active in *in vitro* assays of retinoid receptor activation, but the relative contribution of the parent and any metabolites to the efficacy and safety of bexarotene gel is unknown.

Elimination

The renal elimination of bexarotene and its metabolites was examined in patients with Type 2 diabetes mellitus following oral administration of bexarotene. Neither bexarotene nor its metabolites were excreted in urine in appreciable amounts.

SPECIAL POPULATIONS

Elderly, Gender, Race: Because of a large number of immeasurable plasma concentrations (< 1ng/mL), any potential pharmacokinetic differences between Special Populations could not be assessed.

Pediatric: Studies to evaluate bexarotene pharmacokinetics in the pediatric population have not been conducted (see **PRECAUTIONS: Pediatric Use**).

Renal Insufficiency: No formal studies have been conducted with bexarotene gel in patients with renal insufficiency. Urinary elimination of bexarotene and its known metabolites is a minor excretory pathway (<1% of an orally administered dose), but because renal insufficiency can result in significant protein binding changes, pharmacokinetics may be altered in patients with renal insufficiency (see **PRECAUTIONS: Renal Insufficiency**).

Hepatic Insufficiency: No specific studies have been conducted with bexarotene gel in patients with hepatic insufficiency. Because less than 1% of the dose of oral bexarotene

is excreted in the urine unchanged and there is *in vitro* evidence of extensive hepatic contribution to bexarotene elimination, hepatic impairment would be expected to lead to greatly decreased clearance (see **PRECAUTIONS: Hepatic Insufficiency**).

DRUG-DRUG INTERACTIONS

No formal studies to evaluate drug interactions with bexarotene or bexarotene gel have been conducted. Bexarotene oxidative metabolites appear to be formed through cytochrome P450 3A4. Drugs that affect levels or activity of cytochrome P450 3A4 may potentially affect the disposition of bexarotene. Concomitant gemfibrozil was associated with increased bexarotene concentrations following oral administration of bexarotene.

CLINICAL STUDIES

Bexarotene gel was evaluated for the treatment of patients with early stage (Stage IA-IIA) CTCL in one multicenter, open-label, clinical trial as well as in a Phase I-II program (dose-seeking trials with different response criteria than the multicenter trial). These clinical studies enrolled a total of 117 patients.

In the multicenter, open-label clinical trial, bexarotene gel was evaluated for the treatment of patients with early stage CTCL who were refractory to, intolerant to, or reached a response plateau for at least six months on at least two prior therapies. The study was conducted in the U.S., Canada, Europe, and Australia and enrolled a total of 50 patients; 46% of these patients were male, 80% were Caucasian, and the median age was 64 years (range 13 to 85).

Bexarotene gel was also evaluated for the treatment of patients with CTCL in a U.S. Phase I-II program involving patients with early stage CTCL. This program enrolled a total of 67 patients; 55% of these patients were male, 85% were Caucasian, and the median age was 61 years (range 30 to 87).

In the multicenter, open-label clinical trial, considering prior systemic, irradiation, and topical treatments, patients had been exposed to a median of three prior therapies (range 2 to 7). All patients failed at least two treatments; the majority (68%) of patients were either refractory to two or more therapies or were refractory to one therapy and intolerant to at least one therapy.

Patients were treated with Bexarotene gel 1% for a planned 16-week period with an option to continue provided that no unacceptable toxicity was occurring.

Tumor response was assessed in the multicenter study by observation of up to five baseline-defined index lesions using a Composite Assessment of Index Lesion Disease Severity (CA). This endpoint was based on a summation of the grades, for all index lesions, of erythema, scaling, plaque elevation, hypopigmentation or hyperpigmentation, and area of involvement. New cutaneous lesions or tumors and extracutaneous disease manifestations were not considered in response or disease progression assessments.

All tumor responses required confirmation over at least two assessments separated by at least four weeks. A partial response was defined as an improvement of at least 50% in the index lesions. A complete clinical response required complete disappearance of the index lesions, but did not require confirmation by biopsy.

Bexarotene gel produced an overall response rate of 26% (13/50) with a corresponding exact 95% confidence interval from 14.6% to 40.3% by the Composite Assessment of

Index Lesion Severity. For the Stage IA and IB patients, the response rate was 28% (13/47) with a corresponding exact 95% confidence interval from 15.6% to 42.6%. For the Stage II patients the response rate was 0% (0/3). Two percent of patients (1/50) had a clinical complete response. The median time to best response on the Composite Assessment of Index Lesion Severity (n=13) was 85 days (range: 36 to 154).

The rate of relapse in responding patients by the Composite Assessment of Index Lesion Severity was 23% (3/13) over a median observation period of 149 days (range 56 to 342). Fourteen patients developed new lesions in untreated areas (14/50; 28%). Four patients developed clinically abnormal lymph nodes (≥ 1 cm diam) (4/50; 8%). One patient developed a cutaneous tumor (1/50; 2%).

The Phase I-II program (dose-seeking trials with different response criteria than the multicenter trial) was supportive of the multicenter study results.

INDICATIONS AND USAGE

Bexarotene gel, 1% 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.

CONTRAINDICATIONS

Bexarotene gel, 1% is contraindicated in patients with a known hypersensitivity to bexarotene or other components of the product.

PREGNANCY

Bexarotene gel, 1% may cause fetal harm when administered to a pregnant woman.

Bexarotene gel must not be given to a pregnant woman or a woman who intends to become pregnant. If a woman becomes pregnant while taking bexarotene gel, bexarotene gel must be stopped immediately and the woman given appropriate counseling.

Bexarotene caused malformations when administered orally to pregnant rats during days 7 to 17 of gestation. Developmental abnormalities included incomplete ossification at 4 mg/kg/day and cleft palate, depressed eye bulge/microphthalmia, and small ears at 16 mg/kg/day. At doses greater than 10 mg/kg/day, bexarotene caused developmental mortality. The no-effect oral dose in rats was 1 mg/kg/day. Plasma bexarotene concentrations in patients with CTCL applying bexarotene gel, 1% were generally less than one hundredth the C_{max} associated with dysmorphogenesis in rats, although some patients had C_{max} levels that were approximately one eighth the concentration associated with dysmorphogenesis in rats.

Women of child-bearing potential should be advised to avoid becoming pregnant when bexarotene gel is used. The possibility that a woman of child-bearing potential is pregnant at the time therapy is instituted should be considered. A negative pregnancy test (e.g., serum beta-human chorionic gonadotropin, beta-HCG) with a sensitivity of at least 50 mIU/L should be obtained within one week prior to bexarotene gel therapy, and the pregnancy test must be repeated at monthly intervals while the patient remains on bexarotene gel. Effective contraception must be used for one month prior to the

initiation of 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 sexual intercourse while applying bexarotene gel and for at least one month after the last dose of drug. Bexarotene gel therapy should be initiated on the second or third day of a normal menstrual period. No more than a one month supply of bexarotene gel 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.

PRECAUTIONS

Pregnancy. See **CONTRAINDICATIONS**

General:

Bexarotene gel should be used with caution in patients with a known hypersensitivity to other retinoids. No clinical instances of cross-reactivity have been noted.

Vitamin A Supplementation: In clinical studies, patients were advised to limit vitamin A intake to $\leq 15,000$ IU/day. Because of the relationship of bexarotene to vitamin A, patients should be advised to limit vitamin A supplements to avoid potential additive toxic effects.

Photosensitivity: Retinoids as a class have been associated with photosensitivity. *In vitro* assays indicate that bexarotene is a potential photosensitizing agent. There were no reports of photosensitivity in patients in the clinical studies. Patients should be advised to minimize exposure to sunlight and artificial ultraviolet light during the use of bexarotene gel.

Information for Patients

Please see accompanying “**Patient’s Instructions for Use**”

DRUG-DRUG INTERACTIONS

Patients who are applying bexarotene gel should not concurrently use products that contain DEET (*N,N*-diethyl-*m*-toluamide), a common component of insect repellent products. An animal toxicology study showed increased DEET toxicity when DEET was included as part of the formulation.

No formal studies to evaluate drug interactions with bexarotene have been conducted. Bexarotene oxidative metabolites appear to be formed through cytochrome P450 3A4.

On the basis of the metabolism of bexarotene by cytochrome P450 3A4, concomitant ketoconazole, itraconazole, erythromycin and grapefruit juice could increase bexarotene plasma concentrations. Similarly, based on data that gemfibrozil increases bexarotene concentrations following oral bexarotene administration, concomitant gemfibrozil could increase bexarotene plasma concentrations. However, due to the low systemic exposure to bexarotene after low to moderately intense gel regimens (see **CLINICAL PHARMACOLOGY**), increases that occur are unlikely to be of sufficient magnitude to result in adverse effects.

No drug interaction data are available on concomitant administration of bexarotene gel and other CTCL therapies.

RENAL INSUFFICIENCY

No formal studies have been conducted with bexarotene gel in patients with renal insufficiency. Urinary elimination of bexarotene and its known metabolites is a minor excretory pathway for bexarotene (<1% of an orally administered dose), but because renal insufficiency can result in significant protein binding changes, and bexarotene is >99% protein bound, pharmacokinetics may be altered in patients with renal insufficiency.

HEPATIC INSUFFICIENCY

No specific studies have been conducted with bexarotene gel in patients with hepatic insufficiency. Because less than 1% of the dose of oral bexarotene is excreted in the urine unchanged and there is *in vitro* evidence of extensive hepatic contribution to bexarotene elimination, hepatic impairment would be expected to lead to greatly decreased clearance.

PROTEIN BINDING

Bexarotene is highly bound (>99%) to plasma proteins. The plasma proteins to which bexarotene binds have not been elucidated, and the ability of bexarotene to displace drugs bound to plasma proteins and the ability of drugs to displace bexarotene binding have not been studied.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

Long-term studies in animals to assess the carcinogenic potential of bexarotene have not been conducted. Bexarotene was not mutagenic to bacteria (Ames assay) or mammalian cells (mouse lymphoma assay). Bexarotene was not clastogenic *in vivo* (micronucleus test in mice). No formal fertility studies were conducted with bexarotene. Bexarotene caused testicular degeneration when oral doses of 1.5 mg/kg/day were given to dogs for 91 days.

Use in Nursing Mothers

It is not known whether bexarotene is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from bexarotene, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Of the total patients with CTCL in clinical studies of bexarotene gel, 62% were under 65 years and 38% were 65 years or older. No overall differences in safety were observed between patients 65 years of age or older and younger patients, but greater sensitivity

of some older individuals to bexarotene gel cannot be ruled out. Responses to bexarotene gel were observed across all age group decades, without preference for any individual age group decade.

ADVERSE REACTIONS

The safety of bexarotene gel has been assessed in clinical studies of 117 patients with CTCL who received bexarotene gel for up to 172 weeks. In the multicenter open-label study, 50 patients with CTCL received bexarotene gel for up to 98 weeks. The mean duration of therapy for these 50 patients was 199 days. The most common adverse events reported with an incidence at the application site of at least 10% in patients with CTCL were rash, pruritus, skin disorder, and pain.

Adverse events leading to dose reduction or study drug discontinuation in at least two patients were rash, contact dermatitis, and pruritus.

Of the 49 patients (98%) who experienced any adverse event, most experienced events categorized as mild (9 patients, 18%) or moderate (27 patients, 54%). There were 12 patients (24%) who experienced at least one moderately severe adverse event. The most common moderately severe events were rash (7 patients, 14%) and pruritus (3 patients, 6%). Only one patient (2%) experienced a severe adverse event (rash).

In the patients with CTCL receiving bexarotene gel, adverse events reported regardless of relationship to study drug at an incidence of $\geq 5\%$ are presented in Table 1.

A similar safety profile for bexarotene gel was demonstrated in the Phase I-II program. For the 67 patients enrolled in the Phase I-II program, the mean duration of treatment was 436 days (range 12 to 1,203 days). As in the multicenter study, the most common adverse events regardless of relationship to study drug in the Phase I-II program were rash (78%), pain (40%), and pruritus (40%).

Table 1. Incidence of All Adverse Events* and Application Site Adverse Events with Incidence $\geq 5\%$ for All Application Frequencies of Bexarotene Gel in the Multicenter CTCL Study

	All Adverse Events	Application Site Adverse Events
COSTART 5	N = 50	N = 50
Body System/Preferred Term	n (%)	n (%)
Skin and Appendages		
Contact Dermatitis ¹	7 (14)	4 (8)
Exfoliative Dermatitis	3 (6)	0
Pruritus ²	18 (36)	9 (18)
Rash ³	36 (72)	28 (56)
Maculopapular Rash	3 (6)	0
Skin Disorder (NOS) ⁴	13 (26)	9 (18)
Sweating	3 (6)	0
Body as a Whole		
Asthenia	3 (6)	0

Headache	7 (14)	0
Infection	9 (18)	0
Pain	15 (30)	9 (18)
Cardiovascular		
Edema	5 (10)	0
Peripheral Edema	3 (6)	0
Hemic and Lymphatic		
Leukopenia	3 (6)	0
Lymphadenopathy	3 (6)	0
WBC Abnormal	3 (6)	0
Metabolic and Nutritional		
Hyperlipemia	5 (10)	0
Nervous		
Paresthesia	3 (6)	3 (6)
Respiratory		
Cough Increased	3 (6)	0
Pharyngitis	3 (6)	0
* Regardless of association with treatment		
Includes Investigator terms such as:		
¹ Contact dermatitis, irritant contact dermatitis, irritant dermatitis		
² Pruritus, itching, itching of lesion		
³ Erythema, scaling, irritation, redness, rash, dermatitis		
⁴ Skin inflammation, excoriation, sticky or tacky sensation of skin; NOS = Not Otherwise Specified		

To report SUSPECTED ADVERSE REACTIONS, contact Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.com

OVERDOSAGE

Systemic toxicity following acute overdosage with topical application of bexarotene gel is unlikely because of low systemic plasma levels observed with normal therapeutic doses. There is no specific antidote for overdosage.

There has been no experience with acute overdose of bexarotene gel in humans. Any overdose with bexarotene gel should be treated with supportive care for the signs and symptoms exhibited by the patient.

DOSAGE AND ADMINISTRATION

Bexarotene gel, 1% should be 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. Generally, patients were able to maintain a dosing frequency of two to four times per day. Most responses were seen at dosing frequencies of two times per day and higher. If application site toxicity occurs, the application frequency can be reduced. Should severe irritation occur, application of drug can be temporarily discontinued for a

few days until the symptoms subside. See **CONTRAINDICATIONS: Pregnancy.**

Sufficient gel should be applied to cover the lesion with a generous coating. The gel should be allowed to dry before covering with clothing. Because unaffected skin may become irritated, application of the gel to normal skin surrounding the lesions should be avoided. In addition, do not apply the gel near mucosal surfaces of the body.

A response may be seen as soon as four weeks after initiation of therapy but most patients require longer application. With continued application, further benefit may be attained. The longest onset time for the first response among the responders was 392 days based on the Composite Assessment of Index Lesion Severity in the multicenter study. In clinical trials, bexarotene gel, 1% was applied for up to 172 weeks.

Bexarotene gel, 1% should be continued as long as the patient is deriving benefit.

Occlusive dressings should not be used with bexarotene gel, 1%.

BEXAROTENE GEL, 1% IS A TOPICAL THERAPY AND IS NOT INTENDED FOR SYSTEMIC USE. BEXAROTENE GEL, 1% HAS NOT BEEN STUDIED IN COMBINATION WITH OTHER CTCL THERAPIES.

HOW SUPPLIED

Bexarotene gel, 1% is supplied as a clear, colorless gelled solution free from lumps and foreign matter with homogeneous consistency packaged in white aluminum tubes with a white pointed cap fitted on it containing 60 g (600 mg active bexarotene).

60 g tubeNDC 69238-2088-6

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Avoid exposing to high temperatures and humidity after the tube is opened. Protect from light.

Distributed by:

Amneal Pharmaceuticals, LLC
Bridgewater, NJ 08807

Rev. 11-2021-00

Bexarotene (bex ar' oh teen) Gel, 1%

Patient's Instructions for Use

(For Topical Use Only)

To help you get the full benefits from this medicine, you should read this leaflet carefully and ask your doctor to explain anything you do not understand.

What are the most important things I should know about bexarotene gel?

Do not use bexarotene gel if you are pregnant or if you plan to become pregnant.

- Bexarotene gel may harm your fetus (unborn baby). You should contact your doctor

immediately if you believe or suspect you are pregnant while you are using bexarotene gel and until one month after you stop using bexarotene gel.

- If you are capable of becoming pregnant, you must have a pregnancy test, within one week before you start bexarotene gel therapy and monthly while you are using bexarotene gel, confirming you are not pregnant.
- You must use effective contraception (birth control) continuously starting one month before beginning treatment with bexarotene gel until one month after you stop using bexarotene gel. It is recommended that two reliable forms of contraception be used together.
- If you are male and your partner is pregnant or capable of becoming pregnant, you should discuss with your doctor the precautions you should take.

What is bexarotene gel?

Bexarotene gel contains bexarotene. Bexarotene gel belongs to a class of medicines known as retinoids.

What are the uses for bexarotene gel?

This medicine is used to treat the skin problems arising from a disease called cutaneous T-cell lymphoma, or CTCL. Your health care provider has prescribed bexarotene for the topical treatment of the cutaneous T-cell lymphoma (CTCL), or mycosis fungoides (MF), lesions (sometimes referred to as patches or plaques) on your skin. Your doctor must instruct you on the proper use of bexarotene gel. The following instructions will help you successfully begin and continue your treatment.

Do not use bexarotene gel if you are allergic to this medicine.

Do not use bexarotene gel if you are pregnant or believe you may be pregnant.

If you have any of the following conditions, make sure you have discussed them with your doctor before you start to take this medicine.

- If you are breast feeding.
- If you are allergic to retinoid medications (for example: Accutane[®] [isotretinoin], Soriatane[®] [acitretin], Tegison[®] [etretinate], Vesinoid[®] [tretinoin]).

When should you be extra careful while using bexarotene gel?

- Because vitamin A in large doses may cause some side effects which are similar to those seen in patients applying bexarotene gel, do not take more than the recommended daily dietary allowance of vitamin A (4,000 to 5,000 International Units). If you take vitamins, check the label to see how much vitamin A they contain. If you are not sure, ask your doctor or pharmacist.
- Your skin may become more sensitive to sunlight while using this medicine. Minimize exposure to sunlight and do not use a sunlamp.

WARNINGS

For external use only.

DO NOT apply the gel on or near mucosal surfaces of the body such as eyes, nostrils, mouth, lips, vagina, tip of the penis, rectum, or anus.

DO NOT use insect repellents containing DEET (*N,N*-diethyl-*m*-toluamide) or other products containing DEET while using bexarotene gel.

Keep out of reach of children.

Product contains alcohol and should be kept away from open flame.

DO NOT use bexarotene gel if you are pregnant or breastfeeding. Speak to your health care provider if you have any questions or need more information.

HOW TO APPLY

Apply bexarotene gel to your CTCL lesions using a clean washed finger. Place a **generous coating** of gel over the entire surface of each lesion. You should not apply gel to the healthy skin around the lesion. The extra effort you take in carefully applying the gel only to the area of the CTCL lesion will help to lessen any irritation or redness that may occur. Proper application should leave some gel visible on the surface of the lesion when you are finished with the application.

Immediately following application, wipe the finger(s) you have used to apply the gel with a disposable tissue and wash your hands using soap and water.

Allow five (5) to ten (10) minutes for the gel to dry before covering a treated area with clothing.

A mild non-deodorant soap is recommended when bathing or showering. If you apply bexarotene gel after your shower or bath, you should wait 20 minutes before application.

WHEN TO APPLY

Bexarotene gel should be applied at an initial frequency of once every other day for the first week. The frequency of application should then be increased as tolerated at weekly intervals to once daily, then twice daily, then three times daily, and finally four times daily. Your health care provider may instruct you to apply bexarotene gel at a different frequency.

YOU SHOULD AVOID...

You should avoid applying bexarotene gel to areas of healthy skin around a CTCL lesion. Exposure of healthy skin to bexarotene gel may cause unnecessary irritation or redness.

You should avoid showering, bathing, or swimming until at least three (3) hours after any application, if possible.

You should avoid covering the CTCL lesions treated with bexarotene gel with any bandage or material other than loose clothing.

You should avoid prolonged exposure of the treated area to sunlight or other ultraviolet (UV) light (such as tanning lamps).

You should avoid the use of other topical products on your treated CTCL lesions.

You should avoid scratching the treated areas.

WHAT SIDE EFFECTS DOES BEXAROTENE GEL HAVE?

While using bexarotene gel, you may experience some local effects such as redness,

itching, burning, irritation, and scaling at the area of application. In clinical trials, the majority of these effects were mild or moderate, but some patients did experience more severe rash, itching, irritation, and inflammation. A few patients discontinued treatment due to these types of effects. Should these or other effects become troublesome to you, consult your health care provider. He or she can provide information on how to manage these effects.

All medications have side effects. You should call your physician regarding any questions or concerns you may have when using bexarotene gel.

HOW QUICKLY CAN I EXPECT BEXAROTENE GEL TO WORK?

Be patient. Bexarotene gel takes time to work. In clinical trials, some patients began to respond as early as 4 weeks, but most patients did not experience their best response until 48 to 62 weeks of treatment. Do not stop treatment at the first sign of improvement. Continue to use bexarotene gel as instructed by your health care provider.

OTHER INFORMATION

The opening of the bexarotene gel tube is covered by a metal safety seal. If this seal has been punctured or is not visible when you first open the package, **DO NOT USE** this tube and promptly return the product to your pharmacy or place of purchase.

To open, use the pointed portion of the cap to puncture the metal safety seal.

Always use the cap to close the tube tightly after each use.

Store at room temperature. Keep away from heat or flame.

The gel should not be used after the expiration date printed on the tube.

Keep this medicine out of the reach and sight of children.

IF YOU HAVE QUESTIONS....

If you have questions about your treatment, talk with your health care provider.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088

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Bridgewater, NJ 08807

Rev. 11-2021-00

PRINCIPAL DISPLAY PANEL



Each gram of gel contains: 10 mg of bexarotene. Also contains dehydrated alcohol, polyethylene glycol 400, hydroxypropyl cellulose, and butylated hydroxytoluene.

Note: The opening of the bexarotene gel tube is covered by a metal safety seal. **DO NOT USE** if this seal has been punctured or is not visible when you open the package. Promptly return the product to your pharmacy or place of purchase.

To Open: Use the pointed portion of the cap to puncture the metal safety seal. Always use cap to close the tube tightly when not in use.

Note to Pharmacist: Please direct the patient to the Information for Patient section included at the end of the enclosed Prescribing Information. Please provide the enclosed Prescribing Information when you dispense this medication.

1.875" x 1.1875"
Non-Varnish Area for
Lot No. and Exp Date
and Serialization

See end flap for Lot Number and Expiration Date.

Usual Dosage: See Package Insert for prescribing information.

Keep out of reach of children.

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Avoid exposing to high temperatures and humidity after the tube is opened. Protect from light.



NDC 69238-2088-6

Bexarotene Gel, 1%

**Not For Ophthalmic Use
For Topical Use Only**

Rx only

Net Wt. 60 grams

1.875" x 1.1875"
Non-Varnish Area for
Lot No. and Exp Date
and Serialization

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Bexarotene Gel, 1%

**Not For Ophthalmic Use
For Topical Use Only**

Rx only

Net Wt. 60 grams

Each gram of gel contains: 10 mg of bexarotene. Also contains dehydrated alcohol, polyethylene glycol 400, hydroxypropyl cellulose, and butylated hydroxytoluene.

See tube crimp end for Lot Number and Expiration Date.

Use cap to puncture seal.

Usual Dosage: See Package Insert for prescribing information.

Keep out of reach of children.

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Avoid exposing to high temperatures and humidity after the tube is opened. Protect from light.

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Lot and Exp to be printed on crimped end of tube

BEXAROTENE

bexarotene gel

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:69238-2088
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
BEXAROTENE (UNII: A61RXM4375) (BEXAROTENE - UNII:A61RXM4375)	BEXAROTENE	10 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
ALCOHOL (UNII: 3K9958V90M)	
POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)	
HYDROXYPROPYL CELLULOSE, UNSPECIFIED (UNII: 9XZ8H6N6OH)	
BUTYLATED HYDROXYTOLUENE (UNII: 1P9D0Z171K)	

Product Characteristics

Color	white (clear)	Score	
Shape		Size	
Flavor		Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:69238-2088-6	1 in 1 CARTON	05/04/2022	
1		60 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA215398	05/04/2022	

Labeler - Amneal Pharmaceuticals NY LLC (123797875)

Establishment

Name	Address	ID/FEI	Business Operations
Amneal Pharmaceuticals, LLC		079389286	analysis(69238-2088) , label(69238-2088) , manufacture(69238-2088) , pack(69238-2088)

Revised: 12/2023

Amneal Pharmaceuticals NY LLC