TAZAROTENE - tazarotene gel
Solaris Pharma Corporation

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TAZAROTENE GEL safely and effectively. See full prescribing information for TAZAROTENE GEL.
TAZAROTENE gel, 0.05% and 0.1%, for topical use
Initial U.S. Approval: 1997

INDICATIONS AND USAGE

- Tazarotene gel, 0.05% and 0.1% is a retinoid indicated for the topical treatment of plaque psoriasis of up to 20% body surface area involvement. (1.1)
- Tazarotene gel, 0.1% is indicated for the topical treatment of mild to moderate facial acne vulgaris. (1.2)

Limitations of Use

- The safety of tazarotene gel use on more than 20% body surface area has not been established. (1.3)

DOSAGE AND ADMINISTRATION

- Apply a thin layer of tazarotene gel only to the affected area once daily in the evening. (2.1, 2.2)
- Not for ophthalmic, oral, or intravaginal use. (2.2)
- If contact with eyes occurs, rinse thoroughly with water. (2.2)

DOSAGE FORMS AND STRENGTHS

- Gel, 0.05% and 0.1% (3)

CONTRAINDICATIONS

- Pregnancy (4, 8.1)
- Hypersensitivity (4)

WARNINGS AND PRECAUTIONS

- Embryofetal Toxicity: Tazarotene gel contains tazarotene, which is a teratogen. Tazarotene gel is contraindicated in pregnancy. Females of child-bearing potential should have a negative pregnancy test within 2 weeks prior to initiating treatment and use an effective method of contraception during treatment. (5.1)
- Local Irritation: Excessive pruritus, burning, skin redness or peeling can occur. If these reactions occur, discontinue until the integrity of the skin has been restored, or consider reducing dosing frequency or in the case of psoriasis, consider switching to the lower concentration. Tazarotene gel should not be used on eczematous skin, as it may cause severe irritation. (5.2)
- Photosensitivity and Risk for Sunburn: Avoid exposure to sunlight, sunlamps, and weather extremes. Wear sunscreen daily. Tazarotene gel should be administered with caution if the patient is also taking drugs known to be photosensitizers. (5.3)

ADVERSE REACTIONS

- Plaque Psoriasis: Most common adverse reactions occurring in 10 to 30% of patients are pruritus, burning/stinging, erythema, worsening of psoriasis, irritation, and skin pain. (6.1)
- Acne Vulgaris: Most common adverse reactions occurring in 10 to 30% of patients are desquamation, burning/stinging, dry skin, erythema and pruritus. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Solaris Pharma Corporation at 1-833-919-0527 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch
See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.
Revised: 1/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Plaque Psoriasis

Tazarotene gel, 0.05% and 0.1% are indicated for the topical treatment of patients with plaque psoriasis of up to 20% body surface area involvement.

1.2 Acne Vulgaris

Tazarotene gel, 0.1% is also indicated for the topical treatment of patients with facial acne vulgaris of mild to moderate severity.

The efficacy of tazarotene gel in the treatment of acne previously treated with other retinoids or resistant to oral antibiotics has not been established.

1.3 Limitations of Use

The safety of tazarotene gel use on more than 20% body surface area has not been established in psoriasis or acne *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1)]*.

2 DOSAGE AND ADMINISTRATION

Tazarotene gel is for topical use only. Tazarotene gel is not for ophthalmic, oral, or intravaginal use. Avoid accidental transfer of tazarotene gel into eyes, mouth, or other mucous membranes. If contact with mucous membranes occurs, rinse thoroughly with water *[see Warnings and Precautions (5.2)]*.

Wash hands thoroughly after application.

2.1 Psoriasis

It is recommended that treatment starts with tazarotene gel, 0.05%, with strength increased to 0.1% if tolerated and medically indicated. Apply a thin film (2 mg/cm^2) of tazarotene gel once per day, in the evening, to cover only the psoriatic lesions on no more than 20% of body surface area. If a bath or shower is taken prior to application, the skin should be dry before applying the gel. If emollients are used, they should be applied at least an hour before application of tazarotene gel. Because unaffected skin may be more susceptible to irritation, application of tazarotene to these areas should be carefully avoided. Tazarotene gel was investigated for up to 12 months during clinical trials for psoriasis.

2.2 Acne

Cleanse the face gently. After the skin is dry, apply a thin layer (2 mg/cm^2) of tazarotene gel 0.1% once per day, in the evening, to the skin where acne lesions appear. Use enough to cover the entire affected area. Tazarotene gel was investigated for up to 12 weeks during clinical trials for acne. Use effective sunscreens and wear protective clothing while using tazarotene gel *[see Warnings and Precautions (5.3)]*.

3 DOSAGE FORMS AND STRENGTHS

Gel, 0.05% and 0.1%, in 30 g and 100 g tubes. Each gram of tazarotene gel, 0.05% and 0.1% contains 0.5 mg and 1 mg of tazarotene, respectively in a translucent, aqueous gel.

4 CONTRAINDICATIONS

Tazarotene gel is contraindicated in:

- Pregnancy. Retinoids may cause fetal harm when administered to a pregnant female *[see Warnings and Precautions (5.1), Use in Specific Populations (8.1, 8.3)]*.
- Individuals who have known hypersensitivity to any of its components *[see Warnings and Precautions (5.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Embryofetal Toxicity

Based on data from animal reproduction studies, retinoid pharmacology and the potential for systemic absorption, tazarotene gel may cause fetal harm when administered to a pregnant female and is contraindicated during pregnancy. Tazarotene elicits malformations and developmental effects associated with retinoids after topical and oral administration to pregnant rats and rabbits during organogenesis.

Systemic exposure to tazarotenic acid is dependent upon the extent of the body surface area treated. In patients treated topically over sufficient body surface area,

exposure could be in the same order of magnitude as in orally treated animals.

Although there may be less systemic exposure in the treatment of acne of the face alone due to less surface area for application, tazarotene is a teratogenic substance and causes fetal malformations in animals, and it is not known what level of exposure is required for teratogenicity in humans *[see Clinical Pharmacology (12.3)]*.

There were thirteen reported pregnancies in subjects who participated in the clinical trials for topical tazarotene. Nine of the subjects had been treated with topical tazarotene, and the other four had been treated with vehicle. One of the subjects who was treated with tazarotene cream elected to terminate the pregnancy for non-medical reasons unrelated to treatment. The other eight pregnant women who were inadvertently exposed to topical tazarotene during the clinical trials subsequently delivered apparently healthy babies. As the exact timing and extent of exposure in relation to the gestation times are not certain, the significance of these findings is unknown.

Females of Child-bearing Potential
Females of child-bearing potential should be warned of the potential risk and use adequate birth-control measures when tazarotene gel is used. The possibility that a female of child-bearing potential is pregnant at the time of institution of therapy should be considered.

A negative result for pregnancy test should be obtained within 2 weeks prior to tazarotene gel therapy. Tazarotene gel therapy should begin during a normal menstrual period *[see Use in Specific Populations (8.1)]*.

5.2 Local Irritation and Hypersensitivity Reactions

Application of tazarotene gel may cause excessive irritation in the skin of certain sensitive individuals. Local reactions (including blistering and skin desquamation, pruritus, burning, erythema) and hypersensitivity adverse reactions (including urticaria) have been observed with topical tazarotene.

If these adverse reactions occur, consider discontinuing the medication or reducing the dosing frequency, as appropriate, until the integrity of the skin is restored. Alternatively, patients with psoriasis who are being treated with the 0.1% concentration can be switched to the lower concentration. Frequency of application should be closely monitored by careful observation of the clinical therapeutic response and skin tolerance. Therapy can be resumed, or the drug concentration or frequency of application can be increased as the patient becomes able to tolerate treatment.

Concomitant topical medications and cosmetics that have a strong drying effect should be avoided. It is also advisable to "rest" a patient's skin until the effects of such preparations subside before treatment with tazarotene gel is initiated.

Tazarotene gel, should not be used on eczematous skin, as it may cause severe irritation.

Weather extremes, such as wind or cold, may be more irritating to patients using tazarotene gel.

5.3 Photosensitivity and Risk for Sunburn

Because of heightened burning susceptibility, exposure to sunlight (including sunlamps) should be avoided unless deemed medically necessary, and in such cases, exposure should be minimized during the use of tazarotene gel. Patients must be warned to use sunscreens and protective clothing when using tazarotene gel. Patients with sunburn should be advised not to use tazarotene gel until fully recovered. Patients who may have considerable sun exposure due to their occupation and those patients with inherent sensitivity to sunlight should exercise particular caution when using tazarotene gel.

Tazarotene gel should be administered with caution if the patient is also taking drugs known to be photosensitizers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides) because of the increased possibility of augmented

photosensitivity.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in more detail in other sections of the labeling:

- Embryofetal toxicity *[see Warnings and Precautions (5.1)]*
- Photosensitivity and Risk of Sunburn *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Psoriasis
A total of 439 subjects 14 to 87 years of age were treated with tazarotene gel, 0.05% and 0.1% in two controlled clinical trials. The most frequent adverse events reported with tazarotene gel, 0.05% and 0.1% occurring in 10 to 30% of subjects, in descending order, included pruritus, burning/stinging, erythema, worsening of psoriasis, irritation, and skin pain. Reactions occurring in 1 to 10% of subjects included rash, desquamation, irritant contact dermatitis, skin inflammation, fissuring, bleeding, and dry skin. Increases in "psoriasis worsening" and "sun-induced erythema" were noted in some subjects over the 4th to 12th months of treatment as compared to the first three months of a 1 year study. In general, the incidence of adverse events with tazarotene gel 0.05% was 2 to 5% lower than that seen with tazarotene gel 0.1%.

Acne
A total of 596 subjects 12 to 44 years of age were treated with tazarotene gel, 0.05% and 0.1% in two controlled clinical trials. The most frequent adverse events reported during clinical trials with tazarotene gel, 0.1% in the treatment of acne occurring in 10 to 30% of subjects, in descending order, included desquamation, burning/stinging, dry skin, erythema and pruritus. Reactions occurring in 1 to 10% of subjects included irritation, skin pain, fissuring, localized edema and skin discoloration.

6.2 Postmarketing Experience

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The following adverse reactions have been identified during postapproval use of tazarotene.

Skin and subcutaneous tissue disorders: blister, dermatitis, urticaria, skin exfoliation, skin discoloration (including skin hyperpigmentation or skin hypopigmentation), swelling at or near application sites, and pain.

7 DRUG INTERACTIONS

No formal drug-drug interaction studies were conducted with tazarotene gel.

In a trial of 27 healthy female subjects between the ages of 20-55 years receiving a combination oral contraceptive tablet containing 1 mg norethindrone and 35 mcg ethinyl estradiol, concomitant use of tazarotene administered as 1.1 mg orally (mean ± SD C_{max} and AUC_{0-24} of tazarotenic acid were 28.9 ± 9.4 ng/mL and 120.6 ± 28.5 ng·hr/mL, respectively) did not affect the pharmacokinetics of norethindrone and ethinyl estradiol over a complete cycle.

The impact of tazarotene on the pharmacokinetics of progestin only oral contraceptives (i.e., minipills) has not been evaluated.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on data from animal reproduction studies, retinoid pharmacology, and the potential for systemic absorption, tazarotene gel may cause fetal harm when administered to a pregnant female and is contraindicated during pregnancy. Safety in pregnant females has not been established. The potential risk to the fetus outweighs the potential benefit to the mother from tazarotene gel during pregnancy; therefore, tazarotene gel should be discontinued as soon as pregnancy is recognized *[see Contraindications (4), Warnings and Precautions (5.1), Clinical Pharmacology (12.3)]*. Limited case reports of pregnancy in females enrolled in clinical trials for tazarotene gel have not established a clear association with tazarotene and major birth defects or miscarriage risk. Because the exact timing and extent of exposure in relation to the gestational age are not certain, the significance of these findings is unknown.

In animal reproduction studies with pregnant rats, tazarotene dosed topically during organogenesis at 0.5 times the maximum systemic exposure in subjects treated with the maximum recommended human dose (MRHD) of tazarotene gel, 0.1% resulted in reduced fetal body weights and reduced skeletal ossification. In animal reproduction studies with pregnant rabbits dosed topically with tazarotene gel at 7 times the maximum systemic exposure in subjects treated with the MRHD of tazarotene gel, 0.1%, there were single incidences of known retinoid malformations, including spina bifida, hydrocephaly, and heart anomalies.

In animal reproduction studies with pregnant rats and rabbits, tazarotene dosed orally during organogenesis at 0.5 and 13 times, respectively, the maximum systemic exposure in subjects treated with the MRHD of tazarotene gel, 0.1% resulted in malformations, fetal toxicity, developmental delays, and/or behavioral delays. In pregnant rats, tazarotene dosed orally prior to mating through early gestation resulted in decreased litter size, decreased numbers of live fetuses, decreased fetal body weights, and increased malformations at doses approximately 2 times higher than the maximum systemic exposure in subjects treated with the MRHD of tazarotene gel, 0.1% *[see Data]*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. Adverse outcomes in pregnancy occur regardless of the health of the mother or the use of medications. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In rats, a tazarotene gel, 0.05% formulation dosed topically during gestation days 6 through 17 at 0.25 mg/kg/day, which represented 0.5 times the maximum systemic exposure in subjects treated with the MRHD of tazarotene gel, 0.1% (i.e., 2 mg/cm^2 over a 20% body surface area), resulted in reduced fetal body weights and reduced skeletal ossification. Rabbits dosed topically with 0.25 mg/kg/day tazarotene gel, which represented 7 times the maximum systemic exposure in subjects treated with the MRHD of tazarotene gel, 0.1%, during gestation days 6 through 18 were noted with single incidences of known retinoid malformations, including spina bifida, hydrocephaly, and heart anomalies.

When tazarotene was given orally to animals, developmental delays were seen in rats, and malformations and post-implantation loss were observed in rats and rabbits at doses producing 0.5 and 13 times, respectively, the maximum systemic exposure in subjects treated with the MRHD of tazarotene gel, 0.1%.

In female rats orally administered 2 mg/kg/day of tazarotene from 15 days before mating through gestation day 7, which represented 2 times the maximum systemic

exposure in subjects treated with the MRHD of tazarotene gel, 0.1%, classic developmental effects of retinoids were observed including decreased number of implantation sites, decreased litter size, decreased numbers of live fetuses, and decreased fetal body weights. A low incidence of retinoid-related malformations was observed at that dose.

In a pre- and postnatal development toxicity study, topical administration of tazarotene gel (0.125 mg/kg/day) to pregnant female rats from gestation day 16 through lactation day 20 reduced pup survival, but did not affect the reproductive capacity of the offspring. Based on data from another study, the maximum systemic exposure in the rat would be 0.3 times the maximum systemic exposure in subjects treated with the MRHD of tazarotene gel, 0.1%.

8.2 Lactation

Risk Summary
There is no information regarding the presence of tazarotene in human milk, the effects on the breastfed infant, or the effects on milk production. After single topical doses of ^{14}C-tazarotene gel to the skin of lactating rats, radioactivity was detected in rat milk. The lack of clinical data during lactation precludes a clear determination of the risk of tazarotene gel to an infant during lactation; therefore, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for tazarotene gel and any potential adverse effects on the breastfed child from tazarotene gel or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing
Pregnancy testing is recommended for females of reproductive potential within 2 weeks prior to initiating tazarotene gel therapy which should begin during a menstrual period.

Contraception
Females
Based on animal studies, tazarotene gel may cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective contraception during treatment with tazarotene gel.

8.4 Pediatric Use

The safety and efficacy of tazarotene gel have not been established in pediatric patients with psoriasis or acne under the age of 12 years.

8.5 Geriatric Use

Of the total number of subjects in clinical trials of tazarotene gel for plaque psoriasis, 163 were over the age of 65. Subjects over 65 years of age experienced more adverse events and lower treatment success rates after 12 weeks of use of tazarotene gel compared with those 65 years of age and younger. Currently there is no other clinical experience on the differences in responses between the elderly and younger subjects, but greater sensitivity of some older individuals cannot be ruled out. Tazarotene gel for the treatment of acne has not been clinically evaluated in persons over the age of 65.

10 OVERDOSAGE

Excessive topical use of tazarotene gel, 0.05% and 0.1% may lead to marked redness, peeling, or discomfort *[see Warnings and Precautions (5.2)]*.

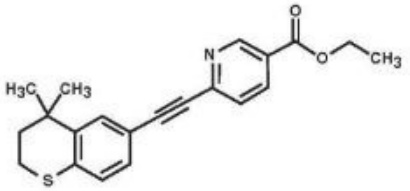
Tazarotene gel, 0.05% and 0.1% are not for oral use. Oral ingestion of the drug may lead to the same adverse effects as those associated with excessive oral intake of

Vitamin A (hypervitaminosis A) or other retinoids. If oral ingestion occurs, the patient should be monitored, and appropriate supportive measures should be administered as necessary.

11 DESCRIPTION

Tazarotene gel, 0.05% and 0.1% is for topical use and contains the active ingredient, tazarotene. Each gram of tazarotene gel, 0.05% and 0.1% contains 0.5 and 1 mg of tazarotene, respectively in a translucent, aqueous gel.

Tazarotene is a member of the acetylenic class of retinoids. Chemically, tazarotene is ethyl 6-[(4,4-dimethylthiochroman-6-yl)ethynyl]nicotinate. The compound has an empirical formula of $C_{21}H_{21}NO_2S$ and molecular weight of 351.46. The structural formula is shown below:



TAZAROTENE

Tazarotene gel, 0.05% and 0.1% contains the following inactive ingredients: benzyl alcohol 1%; ascorbic acid; butylated hydroxyanisole; butylated hydroxytoluene; carbomer homopolymer type B; edetate disodium; hexylene glycol; poloxamer 407; polyethylene glycol 400; polysorbate 40; purified water; and tromethamine.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Tazarotene is a retinoid prodrug which is converted to its active form, the carboxylic acid of tazarotene, by deesterification. Tazarotenic acid binds to all three members of the retinoic acid receptor (RAR) family: RARα, RARβ, and RARγ, but shows relative selectivity for RARβ, and RARγ and may modify gene expression. The clinical significance of these findings for the treatment of plaque psoriasis and facial acne vulgaris is unknown.

12.2 Pharmacodynamics

The pharmacodynamics of tazarotene gel in the treatment of plaque psoriasis and facial acne vulgaris are unknown.

12.3 Pharmacokinetics

Following topical application, tazarotene undergoes esterase hydrolysis to form its active metabolite, tazarotenic acid. Little parent compound could be detected in the plasma. Tazarotenic acid was highly bound to plasma proteins (greater than 99%).

Tazarotene and tazarotenic acid were metabolized to sulfoxides, sulfones and other polar metabolites which were eliminated through urinary and fecal pathways. The half-life of tazarotenic acid was approximately 18 hours, following topical application of tazarotene to normal, acne or psoriatic skin.

The human *in vivo* studies described below were conducted with tazarotene gel applied topically at approximately 2 mg/cm^2 and left on the skin for 10 to 12 hours. Both the peak plasma concentration (C_{max}) and area under the plasma concentration time curve

(AUC) refer to the active metabolite only.

Two single, topical dose studies were conducted using ^{14}C-tazarotene gel. Systemic absorption, as determined from radioactivity in the excreta, was less than 1% of the applied dose (without occlusion) in six subjects with psoriasis and approximately 5% of the applied dose (under occlusion) in six healthy subjects. One non-radiolabeled single-dose study comparing the 0.05% gel to the 0.1% gel in healthy subjects indicated that the C_{max} and AUC were 40% higher for the 0.1% gel.

After 7 days of topical dosing with measured doses of tazarotene 0.1% gel on 20% of the total body surface without occlusion in 24 healthy subjects, the C_{max} for tazarotenic acid was 0.72 ± 0.58 ng/mL (mean ± SD) occurring 9 hours after the last dose, and the $AUC_{0\text{-}24hr}$ for tazarotenic acid was 10.1 ± 7.2 ng·hr/mL. Systemic absorption was 0.91 ± 0.67% of the applied dose.

In a 14-day study in five subjects with psoriasis, measured doses of tazarotene 0.1% gel were applied daily by nursing staff to involved skin without occlusion (8 to 18% of total body surface area; mean ± SD: 13 ± 5%). The C_{max} for tazarotenic acid was 12.0 ± 7.6 ng/mL occurring 6 hours after the final dose, and the $AUC_{0\text{-}24hr}$ for tazarotenic acid was 105 ± 55 ng·hr/mL. Systemic absorption was 14.8 ± 7.6% of the applied dose. Extrapolation of these results to represent dosing on 20% of total body surface yielded estimates for tazarotenic acid with C_{max} of 18.9 ± 10.6 ng/mL and $AUC_{0\text{-}24hr}$ of 172 ± 88 ng·hr/mL.

An *in vitro* percutaneous absorption study, using radiolabeled drug and freshly excised human skin or human cadaver skin, indicated that approximately 4 to 5% of the applied dose was in the stratum corneum (tazarotene: tazarotenic acid = 5:1) and 2 to 4% was in the viable epidermis-dermis layer (tazarotene: tazarotenic acid = 2:1) 24 hours after topical application of the gel.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

A long-term study of tazarotene following oral administration of 0.025, 0.050, and 0.125 mg/kg/day to rats showed no indications of increased carcinogenic risks. Based on pharmacokinetic data from a shorter-term study in rats, the highest dose of 0.125 mg/kg/day was anticipated to give systemic exposure in the rat 0.3 times that seen in subjects treated with the MRHD of tazarotene gel, 0.1%.

A long-term study with topical administration of up to 0.1% tazarotene in a gel formulation in mice terminated at 88 weeks showed that dose levels of 0.05, 0.125, 0.25, and 1 mg/kg/day (reduced to 0.5 mg/kg/day for males after 41 weeks due to severe dermal irritation) revealed no apparent carcinogenic effects when compared to vehicle control animals. Systemic exposure at the highest dose was 2 times that seen in subjects treated with the MRHD of tazarotene gel, 0.1%.

Tazarotene was non-mutagenic in the Ames assay and did not produce structural chromosomal aberrations in a human lymphocyte assay. Tazarotene was non-mutagenic in the CHO/HGPRT mammalian cell forward gene mutation assay and was non-clastogenic in the in vivo mouse micronucleus test.

No impairment of fertility occurred in rats when male animals were treated for 70 days prior to mating and female animals were treated for 14 days prior to mating and continuing through gestation and lactation with topical doses of tazarotene gel up to 0.125 mg/kg/day. Based on data from another study, the systemic drug exposure in the rat at the highest dose was 0.3 times that observed in subjects treated with the MRHD of tazarotene gel, 0.1%.

No impairment of mating performance or fertility was observed in male rats treated for 70 days prior to mating with oral doses of up to 1 mg/kg/day tazarotene, which produced systemic exposure that was approximately equivalent to that observed in

subjects treated with the MRHD of tazarotene gel, 0.1%.

No impairment of mating performance or fertility was observed in female rats treated for 15 days prior to mating and continuing through gestation day 7 with oral doses of tazarotene up to 2 mg/kg/day. However, there was a significant decrease in the number of estrous stages and an increase in developmental effects at that dose, which produced systemic exposure 2 times that observed in subjects treated with the MRHD of tazarotene gel, 0.1% *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Psoriasis: In two large vehicle-controlled clinical trials, tazarotene gel, 0.05% and 0.1% applied once daily for 12 weeks was significantly more effective than vehicle in reducing the severity of the clinical signs of plaque psoriasis covering up to 20% of body surface area. In one of the studies, subjects were followed up for an additional 12 weeks following cessation of therapy with tazarotene gel. Mean baseline scores and changes from baseline (reductions) after treatment in these two trials are shown in Table 1.

Table 1. Plaque Elevation, Scaling, and Erythema in Two Controlled Clinical Trials for Psoriasis

		Tazarotene Gel, 0.05%				**Tazarotene Gel, 0.1%**				**Vehicle Gel**			
		Trunk/Arm/Leg Lesions		Knee/Elbow Lesions		Trunk/Arm/Leg Lesions		Knee/Elbow Lesions		Trunk/Arm/Leg Lesions		Knee/Elbow Lesions	
		N=108	N=111	N=108	N=111	N=108	N=112	N=108	N=112	N=108	N=113	N=108	N=113
Plaque Elevation	B* C-12* C-24*	2.5 -1.4 -1.2	2.6 -1.3	2.6 -1.3 -1.1	2.6 -1.1	2.5 -1.4 -1.1	2.6 -1.4	2.6 -1.5 -1.0	2.6 -1.3	2.4 -0.8 -0.9	2.6 -0.7	2.6 -0.7 -0.7	2.6 -0.6
Scaling	B* C-12* C-24*	2.4 -1.1 -0.9	2.5 -1.1	2.5 -1.1 -0.8	2.6 -0.9	2.4 -1.3 -1.0	2.6 -1.3	2.5 -1.2 -0.8	2.7 -1.2	2.4 -0.7 -0.8	2.6 -0.7	2.5 -0.6 -0.7	2.7 -0.6
Erythema	B* C-12* C-24*	2.4 -1.0 -1.1	2.7 -0.8	2.2 -0.9 -0.7	2.5 -0.8	2.4 -1.0 -0.9	2.8 -1.1	2.3 -1.0 -0.8	2.5 -0.8	2.3 -0.6 -0.7	2.7 -0.5	2.2 -0.5 -0.6	2.5 -0.5

Plaque elevation, scaling, and erythema scored on a 0-4 scale with 0=none, 1=mild, 2=moderate, 3=severe and 4=very severe.
B*=Mean Baseline Severity: C-12*=Mean Change from Baseline at end of 12 weeks of therapy: C-24*=Mean Change from Baseline at week 24 (12 weeks after the end of therapy).

Global improvement over baseline at the end of 12 weeks of treatment in these two trials is shown in Table 2.

Table 2. Global Improvement over Baseline after Twelve Weeks of Treatment in Two Controlled Clinical Trials for Psoriasis

	Tazarotene Gel, 0.05%	**Tazarotene Gel, 0.1%**	**Vehicle Gel**

	N=81	N=93	N=79	N=69	N=84	N=91
100% improvement	2 (2%)	1 (1%)	0	0	1 (1%)	0
≥75% improvement	23 (28%)	17 (18%)	30 (38%)	17 (25%)	10 (12%)	9 (10%)
≥50% improvement	42 (52%)	39 (42%)	51 (65%)	36 (52%)	28 (33%)	21 (23%)
1-49% improvement	21 (26%)	32 (34%)	18 (23%)	23 (33%)	27 (32%)	32 (35%)
No change or worse	18 (22%)	22 (24%)	10 (13%)	10 (14%)	29 (35%)	38 (42%)

The 0.1% gel was more effective than the 0.05% gel, but the 0.05% gel was associated with less local irritation than the 0.1% gel *[see Adverse Reactions (6.1)]*.

Acne: In two large vehicle-controlled trials, tazarotene gel, 0.1% applied once daily was significantly more effective than vehicle in the treatment of facial acne vulgaris of mild to moderate severity. Percent reductions in lesion counts after treatment for 12 weeks in these two trials are shown in Table 3.

Table 3. Reduction in Lesion Counts after Twelve Weeks of Treatment in Two Controlled Clinical Trials for Acne

	Tazarotene Gel, 0.1%		**Vehicle Gel**	
	N=150	N=149	N=148	N=149
Noninflammatory lesions	55%	43%	35%	27%
Inflammatory lesions	42%	47%	30%	28%
Total lesions	52%	45%	33%	27%

Global improvement over baseline at the end of 12 weeks of treatment in these two trials is shown in Table 4.

Table 4. Global Improvement over Baseline after Twelve Weeks of Treatment in Two Controlled Clinical Trials for Acne

	Tazarotene Gel, 0.1%		**Vehicle Gel**	
	N=105	N=117	N=117	N=110
100% improvement	1 (1%)	0	0	0
≥75% improvement	40 (38%)	21 (18%)	23 (20%)	11 (10%)

≥50% improvement	71 (68%)	56 (48%)	47 (40%)	32 (29%)
1-49% improvement	23 (22%)	49 (42%)	48 (41%)	46 (42%)
No change or worse	11 (10%)	12 (10%)	22 (19%)	32 (29%)

16 HOW SUPPLIED/STORAGE AND HANDLING

Tazarotene gel is a translucent, aqueous gel, available in concentrations of 0.05% and 0.1%. It is available in a collapsible aluminum tube with a tamper-evident aluminum membrane over the opening and a white propylene screw cap, in 30 g and 100 g sizes.

Tazarotene gel, 0.05% 30 g NDC 73473-309-30
Tazarotene gel, 0.05% 100 g NDC 73473-309-10
Tazarotene gel, 0.1% 30 g NDC 73473-310-30
Tazarotene gel, 0.1% 100 g NDC 73473-310-10

Storage: Store at 20℃ to 25℃ (68℉ to 77℉). Excursions permitted from 15℃ to 30℃ (59℉ to 86℉).

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Embryofetal Toxicity
Inform females of reproductive potential of the potential risk to a fetus. Advise these patients to use effective contraception during treatment with tazarotene gel. Advise patients to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1, 8.3)]*.

Photosensitivity and Risk of Sunburn
Advise patients to avoid excessive sun exposure and to use of sunscreens and protective measures (hat, visor). Advise patients to avoid using tazarotene gel if also taking other medicines may increase sensitivity to sunlight.

Important Administration Instructions
Advise the patient of the following:
1. For the patient with psoriasis, apply tazarotene gel only to psoriasis skin lesions, avoiding uninvolved skin.
2. If undue irritation (redness, peeling, or discomfort) occurs, reduce frequency of application or temporarily interrupt treatment. Treatment may be resumed once irritation subsides *[see Dosage and Adminstration (2.1)]*.
3. Moisturizers may be used as frequently as desired.
4. Patients with psoriasis may use a cream or lotion to soften or moisten skin at least 1 hour before applying tazarotene gel.
5. Avoid contact with the eyes. If tazarotene gel gets in or near eyes, rinse thoroughly with water. Seek medical attention if eye irritation continues.
6. Tazarotene gel is for topical use only. Do not apply to eyes, mouth, or other mucous membrane. Not for ophthalmic, oral, or intravaginal use.
7. Wash hands thoroughly after applying tazarotene gel.

Manufactured for:
Solaris Pharma Corporation
Bridgewater, NJ 08807

Pharmacist: Please cut or tear at dotted line and provide this patient

package insert to your customer

PATIENT INFORMATION
Tazarotene (taz-AR-oh-teen) Gel, 0.05% and 0.1%

Important information: Tazarotene gel is for use on skin only. Do not use tazarotene gel in your eyes, mouth, or vagina.

What is the most important information I should know about tazarotene gel?
Tazarotene gel may cause birth defects if used during pregnancy.

- **Females must not be pregnant when they start using tazarotene gel or become pregnant during treatment with tazarotene gel.**
- For females who can become pregnant:
  - Your doctor will order a pregnancy test for you within 2 weeks before you begin treatment with tazarotene gel to be sure that you are not pregnant. Your doctor will decide when to do the test.
  - Begin treatment with tazarotene gel during a normal menstrual period.
  - Use an effective form of birth control during treatment with tazarotene gel. Talk with your doctor about birth control options that may be used to prevent pregnancy during treatment with tazarotene gel.
  - **Stop using tazarotene gel and tell your doctor right away if you become pregnant while using tazarotene gel.**

What is tazarotene gel?

- Tazarotene gel, 0.05% and 0.1% is a prescription medicine used on the skin (topical) to treat people with stable plaque psoriasis on up to 20% of your body surface.
- Tazarotene gel, 0.1% is also used on the skin to treat people with mild to moderate facial acne vulgaris.

It is not known if tazarotene gel is:

- safe and effective for use in children under 12 years of age.
- effective for the treatment of acne in people who have been treated with retinoid medicines or have acne that does not respond to treatment with oral antibiotics.
- safe if used over more than 20% of your body for the treatment of psoriasis or acne.

Who should not use tazarotene gel?
Do not use tazarotene gel if you:

- are pregnant or plan to become pregnant. See "What is the most important information I should know about tazarotene gel?" at the beginning of this leaflet.
- are allergic to tazarotene or any of the ingredients in tazarotene gel. See the end of this leaflet for a complete list of ingredients in tazarotene gel.

What should I tell my doctor before using tazarotene gel?
Before you use tazarotene gel, tell your doctor about all of your medical conditions, including if you:

- have eczema or any other skin problems
- are breastfeeding or plan to breastfeed. It is not known if tazarotene gel passes into your breast milk. Talk to your doctor about using tazarotene gel while breastfeeding.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
Certain medicines, vitamins, or supplements may make your skin more sensitive to sunlight.
Also, tell your doctor about any cosmetics you use, including moisturizers, creams, lotions, or products that can dry out your skin.
Keep a list of your medicines to show to your doctor and pharmacist when you get a new medicine.

How should I use tazarotene gel?

- Use tazarotene gel exactly as your doctor tells you to use it.

- Apply tazarotene gel 1 time each day, in the evening.
- **Do not** get tazarotene gel in your eyes, on your eyelids, or in your mouth. If tazarotene gel gets in or near your eyes, rinse them well with water. Call your doctor or get medical help if you have eye irritation that does not go away.
- Wash your hands after applying tazarotene gel.

Follow these instructions for applying tazarotene gel:

- **If you have psoriasis:**
  - If you shower or bathe before applying tazarotene gel, your skin should be dry before applying the gel.
  - You may use a cream or lotion to soften or moisten your skin at least 1 hour before you apply tazarotene gel.
  - Apply a thin layer of tazarotene gel to cover only the psoriasis lesions.
- **If you have acne:**
  - Gently wash and dry your face before applying tazarotene gel.
  - Apply a thin layer of tazarotene gel to cover only the acne lesions.
- If you swallow tazarotene gel, call your doctor or go to the nearest hospital emergency room right away.

What should I avoid while using tazarotene gel?

- Avoid sunlight, including sunlamps, during treatment with tazarotene gel. Tazarotene gel can make you more sensitive to the sun, and the light from sunlamps and tanning beds. You could get a severe sunburn. Use sunscreen and wear a hat and clothes that cover your skin if you have to be in sunlight.
- Talk to your doctor if you get a sunburn during treatment with tazarotene gel. If you get a sunburn, do not use tazarotene gel until your sunburn is healed.
- Avoid using cosmetics or topical medicines that may make your skin more sensitive to sunlight or make your skin dry.
- Avoid using tazarotene gel on unaffected skin or skin with eczema because it may cause severe irritation.

What are the possible side effects of tazarotene gel?
Tazarotene gel may cause serious side effects, including:

- **Skin irritation and allergic reactions (hypersensitivity).** Tazarotene gel may cause increased skin irritation (including blistering and skin peeling) and allergic reactions (including hives). Tell your doctor if you develop itching, burning, redness, blistering or peeling of your skin during treatment with tazarotene gel. If you develop skin irritation or hives, your doctor may tell you to temporarily stop using tazarotene gel until your skin heals, tell you to use tazarotene gel less often, or change your tazarotene gel dose. Also, wind or cold weather may be more irritating to your skin while you are using tazarotene gel.
- **Sensitivity to sunlight and risk of sunburn.** See "What should I avoid while using tazarotene gel?"

The most common side effects of tazarotene gel in people with plaque psoriasis include itching, burning, redness, worsening of psoriasis, irritation and skin pain.
The most common side effects of tazarotene gel in people with acne include peeling, burning, dry skin, redness and itching.
These are not all the possible side effects of tazarotene gel. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store tazarotene gel?

- Store tazarotene gel at 68°F to 77°F (20°C to 25°C).
- Keep tazarotene gel and all medicines out of the reach of children.

General information about the safe and effective use of tazarotene gel.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use tazarotene gel for a condition for which it was not prescribed. Do not give tazarotene gel to other people, even if they have the same

symptoms you have. It may harm them. You can ask your doctor or pharmacist for information about tazarotene gel that is written for health professionals.

What are the ingredients in tazarotene gel?
Active ingredient: tazarotene
Inactive ingredients: ascorbic acid, benzyl alcohol, butylated hydroxyanisole, butylated hydroxytoluene, carbomer homopolymer type B, edetate disodium, hexylene glycol, poloxamer 407, polyethylene glycol 400, polysorbate 40, purified water, and tromethamine

Manufactured for:
Solaris Pharma Corporation
Bridgewater, NJ 08807

Rev: 03/2023

For more information, call 1-833-919-0527 or go to www.solaris-pharma.com

This Patient Information has been approved by the U.S. Food and Drug Administration

17.2 FDA-Approved Patient Labeling

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SPL PATIENT PACKAGE INSERT SECTION

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PACKAGE LABEL PRINCIPAL DISPLAY PANEL

100 g Tube Carton Label for Tazarotene Gel, 0.05%

NDC 73473-309-10

Tazarotene Gel, 0.05%
For Dermatologic Use Only
Not for Ophthalmic Use
Rx Only

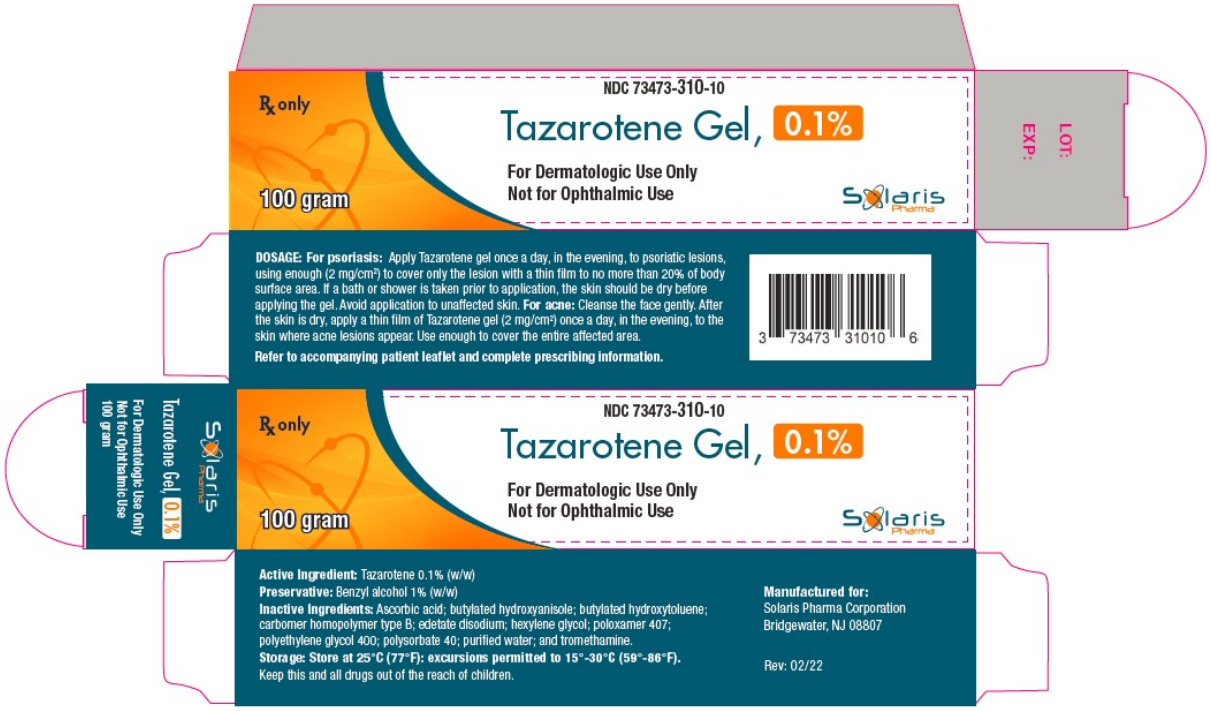
100 gram

100 g Tube Carton Label for Tazarotene Gel, 0.1%

NDC 73473-310-10

Tazarotene Gel, 0.1%
For Dermatologic Use Only
Not for Ophthalmic Use
Rx Only

100 gram



TAZAROTENE
tazarotene gel

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:73473-309
Route of Administration	CUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TAZAROTENE (UNII: 81BDR9Y8PS) (TAZAROTENE - UNII:81BDR9Y8PS)	TAZAROTENE	0.5 mg in 1 g

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:73473-309-30	1 in 1 CARTON	01/03/2025	
1		30 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:73473-309-10	1 in 1 CARTON	01/03/2025	
2		100 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	ANDA213644	01/03/2025	

TAZAROTENE

tazarotene gel

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:73473-310
Route of Administration	CUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TAZAROTENE (UNII: 81BDR9Y8PS) (TAZAROTENE - UNII:81BDR9Y8PS)	TAZAROTENE	1 mg in 1 g

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:73473-310-30	1 in 1 CARTON	01/03/2025	
1		30 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:73473-310-10	1 in 1 CARTON	01/03/2025	
2		100 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	ANDA213644	01/03/2025	

Labeler - Solaris Pharma Corporation (079904672)

Revised: 1/2025 Solaris Pharma Corporation