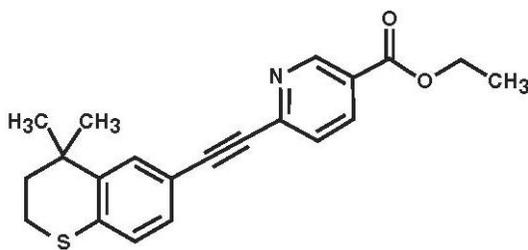


TAZORAC[®]
(tazarotene) Gel, 0.05%
(tazarotene) Gel, 0.1%

FOR DERMATOLOGIC USE ONLY
NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE.

DESCRIPTION

TAZORAC[®] Gel is a translucent, aqueous gel and contains the compound tazarotene, a member of the acetylenic class of retinoids. It is for topical dermatologic use only. The active ingredient is represented by the following structural formula:



TAZAROTENE

Formula: C₂₁H₂₁NO₂S

Molecular Weight: 351.46

Chemical Name: Ethyl 6-[(4,4-dimethylthiochroman-6-yl)ethynyl]nicotinate

Contains:

Active: Tazarotene 0.05% or 0.1% (w/w)

Preservative: Benzyl alcohol 1% (w/w)

Inactives: 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.

CLINICAL PHARMACOLOGY

Tazarotene is a retinoid prodrug which is converted to its active form, the cognate carboxylic acid of tazarotene (AGN 190299), by rapid deesterification in animals and man. AGN 190299 (“tazarotenic acid”) binds to all three members of the retinoic acid receptor (RAR) family: RAR α , RAR β , and RAR γ but shows relative selectivity for RAR β , and RAR γ and may modify gene expression. The clinical significance of these findings is unknown.

Psoriasis: The mechanism of tazarotene action in psoriasis is not defined. Topical tazarotene blocks induction of mouse epidermal ornithine decarboxylase (ODC) activity, which is associated with cell proliferation and hyperplasia. In cell culture and *in vitro* models of skin, tazarotene suppresses expression of MRP8, a marker of inflammation present in the epidermis of psoriasis patients at high levels. In human keratinocyte cultures, it inhibits cornified envelope formation, whose build-up is an element of the psoriatic scale. Tazarotene also induces the expression of a gene which may be a growth suppressor in human keratinocytes and which may inhibit epidermal hyperproliferation in treated plaques. However, the clinical significance of these findings is unknown.

Acne: The mechanism of tazarotene action in acne vulgaris is not defined. However, the basis of tazarotene’s therapeutic effect in acne may be due to its anti-hyperproliferative, normalizing-of-differentiation and anti-

inflammatory effects. Tazarotene inhibited corneocyte accumulation in rhino mouse skin and cross-linked envelope formation in cultured human keratinocytes. The clinical significance of these findings is unknown.

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/cm² 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 ¹⁴C-tazarotene gel. Systemic absorption, as determined from radioactivity in the excreta, was less than 1% of the applied dose (without occlusion) in six psoriatic patients 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_{0-24hr} 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 psoriatic patients, 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_{0-24hr} 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_{0-24hr} 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.

Clinical Studies

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

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

| | | TAZORAC® 0.05% Gel | | | | TAZORAC® 0.1% Gel | | | | 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* | <u>2.5</u> | <u>2.6</u> | <u>2.6</u> | <u>2.6</u> | <u>2.5</u> | <u>2.6</u> | <u>2.6</u> | <u>2.6</u> | <u>2.4</u> | <u>2.6</u> | <u>2.6</u> | <u>2.6</u> |
| | C-12* | -1.4 | -1.3 | -1.3 | -1.1 | -1.4 | -1.4 | -1.5 | -1.3 | -0.8 | -0.7 | -0.7 | -0.6 |
| | C-24* | -1.2 | | -1.1 | | -1.1 | | -1.0 | | -0.9 | | -0.7 | |
| Scaling | B* | <u>2.4</u> | <u>2.5</u> | <u>2.5</u> | <u>2.6</u> | <u>2.4</u> | <u>2.6</u> | <u>2.5</u> | <u>2.7</u> | <u>2.4</u> | <u>2.6</u> | <u>2.5</u> | <u>2.7</u> |
| | C-12* | -1.1 | -1.1 | -1.1 | -0.9 | -1.3 | -1.3 | -1.2 | -1.2 | -0.7 | -0.7 | -0.6 | -0.6 |
| | C-24* | -0.9 | | -0.8 | | -1.0 | | -0.8 | | -0.8 | | -0.7 | |
| Erythema | B* | <u>2.4</u> | <u>2.7</u> | <u>2.2</u> | <u>2.5</u> | <u>2.4</u> | <u>2.8</u> | <u>2.3</u> | <u>2.5</u> | <u>2.3</u> | <u>2.7</u> | <u>2.2</u> | <u>2.5</u> |
| | C-12* | -1.0 | -0.8 | -0.9 | -0.8 | -1.0 | -1.1 | -1.0 | -0.8 | -0.6 | -0.5 | -0.5 | -0.5 |
| | C-24* | -1.1 | | -0.7 | | -0.9 | | -0.8 | | -0.7 | | -0.6 | |

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 studies is shown in the following table:

| | TAZORAC® 0.05% Gel | | TAZORAC® 0.1% Gel | | 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 section).

Acne: In two large vehicle-controlled studies, tazarotene 0.1% gel 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 studies are shown in the following table:

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

| | TAZORAC® 0.1% Gel | | 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 studies is shown in the following table:

| | TAZORAC[®] 0.1% Gel | | 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%) |

INDICATIONS AND USAGE

TAZORAC[®] (tazarotene) Gel 0.05% and 0.1% are indicated for the topical treatment of patients with stable plaque psoriasis of up to 20% body surface area involvement.

TAZORAC[®] (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 **TAZORAC[®]** Gel in the treatment of acne previously treated with other retinoids or resistant to oral antibiotics has not been established.

CONTRAINDICATIONS

Retinoids may cause fetal harm when administered to a pregnant woman.

In rats, tazarotene 0.05% gel, administered **topically** during gestation days 6 through 17 at 0.25 mg/kg/day (1.5 mg/m²/day) resulted in reduced fetal body weights and reduced skeletal ossification. Rabbits dosed **topically** with 0.25 mg/kg/day (2.75 mg/m² total body surface area/day) tazarotene gel during gestation days 6 through 18 were noted with single incidences of known retinoid malformations, including spina bifida, hydrocephaly, and heart anomalies. Systemic daily-exposure (AUC_{de}) to tazarotenic acid at topical doses of 0.25 mg/kg/day tazarotene in a gel formulation in rats and rabbits represented 0.62 and 6.7 times, respectively, the AUC_{0-24h} observed in psoriatic patients treated with 2 mg/cm² of tazarotene gel 0.1% (extrapolated for topical application over a 20% body surface area), and 0.78 and 8.4 times, respectively, the maximum AUC_{0-24h} in acne patients treated with 2 mg/cm² of tazarotene gel 0.1% over a 15% (targeted) body surface area.

As with other retinoids, when tazarotene was given **orally** to experimental animals, developmental delays were seen in rats, and teratogenic effects and post-implantation loss were observed in rats and rabbits at AUC_{de} values that were 0.55 and 13.2 times, respectively, the AUC_{0-24h} observed in psoriatic patients treated with 2 mg/cm² of tazarotene gel 0.1% (extrapolated for topical application over a 20% body surface area), and 0.68 and 16.4 times, respectively, the maximum AUC_{0-24h} in acne patients treated with 2 mg/cm² of tazarotene gel 0.1% over a 15% (targeted) body surface area.

In a study of the effect of oral tazarotene on fertility and early embryonic development in rats, decreased number of implantation sites, decreased litter size, decreased numbers of live fetuses, and decreased fetal body weights, all classic developmental effects of retinoids, were observed when female rats were administered 2 mg/kg/day from 15 days before mating through gestation day 7. A low incidence of retinoid-related

malformations at that dose was reported to be related to treatment. This dose produced an AUC_{de} that was 1.7 times the AUC_{0-24h} observed in psoriatic patients treated with 2 mg/cm² tazarotene gel 0.1% (extrapolated for topical application over a 20% body surface area) and 2.1 times the maximum AUC_{0-24h} in acne patients treated with 2 mg/cm² of tazarotene gel 0.1% over a 15% (targeted) body surface area.

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 THESE 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 IT IS NOT KNOWN WHAT LEVEL OF EXPOSURE IS REQUIRED FOR TERATOGENICITY IN HUMANS (SEE CLINICAL PHARMACOLOGY: PHARMACOKINETICS).

There were thirteen reported pregnancies in patients who participated in clinical trials for topical tazarotene. Nine of the patients were found to have been treated with topical tazarotene, and the other four had been treated with vehicle. One of the patients 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 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.

TAZORAC[®] Gel is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, treatment should be discontinued and the patient apprised of the potential hazard to the fetus. Women of child-bearing potential should be warned of the potential risk and use adequate birth-control measures when **TAZORAC**[®] Gel is used. The possibility that a woman of child-bearing potential is pregnant at the time of institution of therapy should be considered. A negative result for pregnancy test having a sensitivity down to at least 50 mIU/mL for human chorionic gonadotropin (hCG) should be obtained within 2 weeks prior to **TAZORAC**[®] Gel therapy, which should begin during a normal menstrual period (see also PRECAUTIONS: Pregnancy: Teratogenic Effects).

TAZORAC[®] Gel is contraindicated in individuals who have shown hypersensitivity to any of its components.

WARNINGS

See CONTRAINDICATIONS section. Women of child-bearing potential should be warned of the potential risk and use adequate birth-control measures when **TAZORAC**[®] Gel is used. The possibility that a woman of child-bearing potential is pregnant at the time of institution of therapy should be considered. A negative result for pregnancy test having a sensitivity down to at least 50 mIU/mL for hCG should be obtained within 2 weeks prior to **TAZORAC**[®] Gel therapy, which should begin during a normal menstrual period.

PRECAUTIONS

General

TAZORAC[®] Gel should be applied only to the affected areas. For external use only. Avoid contact with eyes, eyelids, and mouth. If contact with eyes occurs, rinse thoroughly with water. The safety of use of **TAZORAC**[®] Gel over more than 20% of body surface area has not been established in psoriasis or acne.

Retinoids should not be used on eczematous skin, as they may cause severe irritation.

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 **TAZORAC**[®] Gel. Patients must be warned to use sunscreens (minimum SPF of 15) and protective clothing when using **TAZORAC**[®] Gel. Patients with sunburn should be advised not to use **TAZORAC**[®] 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 **TAZORAC**[®] Gel and ensure that the precautions outlined in the Information for Patients subsection are observed.

TAZORAC[®] 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.

Some individuals may experience excessive pruritus, burning, skin redness or peeling. If these effects occur, the medication should either be discontinued until the integrity of the skin is restored, or the dosing should be reduced to an interval the patient can tolerate. However, efficacy at reduced frequency of application has not been established. Alternatively, patients with psoriasis who are being treated with the 0.1% concentration can be switched to the lower concentration.

Weather extremes, such as wind or cold, may be more irritating to patients using **TAZORAC**[®] Gel.

Information for Patients

See attached Patient Package Insert.

Drug Interactions

Concomitant dermatologic 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 use of **TAZORAC**[®] Gel is begun.

In a study 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 ethynyl estradiol, concomitant use of tazarotene did not affect the pharmacokinetics of norethindrone and ethynyl estradiol over a complete cycle.

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

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 (AUC_{de}) in the rat equivalent to 0.32 times the AUC_{0-24h} observed in psoriatic patients treated with 2 mg/cm² of tazarotene gel 0.1% (extrapolated for topical application over a 20% body surface area), and 0.38 times the maximum AUC_{0-24h} in acne patients treated with 2 mg/cm² of tazarotene gel 0.1% over a 15% (targeted) body surface area.

In evaluation of photo co-carcinogenicity, median time to onset of tumors was decreased and the number of tumors increased in hairless mice following chronic topical dosing with intercurrent exposure to ultraviolet radiation at tazarotene concentrations of 0.001%, 0.005%, and 0.01% in a gel formulation for up to 40 weeks.

A long-term topical application study 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; untreated control animals were not completely evaluated. Systemic exposure (AUC_{0-12h}) at the

highest dose was 2 times the AUC_{0-24h} observed in psoriatic patients treated with 2 mg/cm² of tazarotene gel 0.1% (extrapolated for topical application over a 20% body surface area), and 2.5 times the maximum AUC_{0-24h} in acne patients treated with 2 mg/cm² of tazarotene gel 0.1% over a 15% (targeted) body surface area.

Tazarotene was found to be non-mutagenic in the Ames assay using Salmonella and *E. coli* and did not produce structural chromosomal aberrations in a human lymphocyte assay. Tazarotene was also 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 of up to 0.125 mg/kg/day. Based on data from another study, the systemic drug exposure (AUC_{de}) in the rat would be equivalent to 0.31 times the AUC_{0-24h} observed in psoriatic patients treated with 2 mg/cm² of tazarotene gel 0.1% (extrapolated for topical application over a 20% body surface area), and 0.38 times the maximum AUC_{0-24h} in acne patients treated with 2 mg/cm² of tazarotene gel 0.1% over a 15% (targeted) body surface area.

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 an AUC_{de} that was 0.95 times the AUC_{0-24h} observed in psoriatic patients treated with 2 mg/cm² of tazarotene gel 0.1% (extrapolated for topical application over a 20% body surface area), and 1.2 times the maximum AUC_{0-24h} in acne patients treated with 2 mg/cm² of tazarotene gel 0.1% over a 15% (targeted) body surface area.

No effect on parameters of mating performance or fertility was observed in female rats treated for 15 days prior to mating and continuing through day 7 of gestation 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 2 mg/kg/day (see CONTRAINDICATIONS). This dose produced an AUC_{0-24h} which was 1.7 times that observed in psoriatic patients treated with 2 mg/cm² of tazarotene gel 0.1% (extrapolated for topical application over a 20% body surface area), and 2.1 times the maximum AUC_{0-24h} in acne patients treated with 2 mg/cm² of tazarotene gel 0.1% over a 15% (targeted) body surface area.

Reproductive capabilities of F1 animals, including F2 survival and development, were not affected by topical administration of tazarotene gel to female F0 parental rats from gestation day 16 through lactation day 20 at the maximum tolerated dose of 0.125 mg/kg/day. Based on data from another study, the systemic drug exposure (AUC_{de}) in the rat would be equivalent to 0.31 times the AUC_{0-24h} observed in psoriatic patients treated with 2 mg/cm² of tazarotene gel 0.1% (extrapolated for topical application over a 20% body surface area), and 0.38 times the maximum AUC_{0-24h} in acne patients treated with 2 mg/cm² of tazarotene gel 0.1% over a 15% (targeted) body surface area.

Pregnancy

Teratogenic Effects

See CONTRAINDICATIONS section. Women of child-bearing potential should use adequate birth-control measures when TAZORAC[®] Gel is used. The possibility that a woman of child-bearing potential is pregnant at the time of institution of therapy should be considered. A negative result for pregnancy test having a sensitivity down to at least 50 mIU/mL for hCG should be obtained within 2 weeks prior to TAZORAC[®] Gel therapy, which should begin during a normal menstrual period. There are no adequate, well-controlled studies in pregnant women. 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 it is not known what level of exposure is required for teratogenicity in humans (see CLINICAL PHARMACOLOGY: Pharmacokinetics).

Nursing Mothers

After single topical doses of ¹⁴C-tazarotene to the skin of lactating rats, radioactivity was detected in milk, suggesting that there would be transfer of drug-related material to the offspring via milk. It is not known whether this drug is excreted in human milk. Caution should be exercised when tazarotene is administered to a nursing woman.

Pediatric Use

The safety and efficacy of **TAZORAC**[®] Gel have not been established in pediatric patients under the age of 12 years.

Geriatric Use

Of the total number of subjects in clinical studies of tazarotene gels, 0.05% and 0.1% 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 **TAZORAC**[®] Gel compared with those 65 years of age and younger. Currently there is no other reliable clinical experience on the differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals can not be ruled out. Tazarotene gel for the treatment of acne has not been clinically evaluated in persons over the age of 65.

ADVERSE REACTIONS

In human dermal safety studies, tazarotene 0.05% and 0.1% gels did not induce allergic contact sensitization, phototoxicity or photoallergy.

Psoriasis: The most frequent adverse events reported with **TAZORAC**[®] Gel 0.05% and 0.1% were limited to the skin. Those occurring in 10 to 30% of patients, in descending order, included pruritus, burning/stinging, erythema, worsening of psoriasis, irritation, and skin pain. Events occurring in 1 to 10% of patients 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 patients over the 4th to 12th months as compared to the first three months of a 1 year study. In general, the incidence of adverse events with **TAZORAC**[®] Gel 0.05% was 2 to 5% lower than that seen with **TAZORAC**[®] Gel 0.1%.

Acne: The most frequent adverse events reported with **TAZORAC**[®] Gel 0.1% in the treatment of acne occurring in 10 to 30% of patients, in descending order, included desquamation, burning/stinging, dry skin, erythema and pruritus. Events occurring in 1 to 10% of patients included irritation, skin pain, fissuring, localized edema and skin discoloration.

Postmarketing Experience

The following adverse reactions have been identified during postapproval use of tazarotene. 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.

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.

OVERDOSAGE

Excessive topical use of **TAZORAC**[®] Gel may lead to marked redness, peeling, or discomfort (see PRECAUTIONS: General).

TAZORAC[®] Gels 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.

DOSAGE AND ADMINISTRATION

General: Application may cause excessive irritation in the skin of certain sensitive individuals. In cases where it has been necessary to temporarily discontinue therapy, or the dosing has been reduced to a lower concentration (in patients with psoriasis) or to an interval the patient can tolerate, therapy can be resumed, or the drug concentration or frequency of application can be increased as the patient becomes able to tolerate the treatment. Frequency of application should be closely monitored by careful observation of the clinical therapeutic response and skin tolerance [see *Precautions*].

Tazorac Gel, 0.05% and 0.1%, are for topical use only. Tazorac Gel, 0.05% and 0.1%, are not for ophthalmic, oral, or intravaginal use.

Avoid accidental transfer of Tazorac Gel, 0.05% and 0.1%, into eyes, mouth, or other mucous membranes. If contact with mucous membranes occurs, rinse thoroughly with water [see *Precautions*].

Efficacy has not been established for less than once daily dosing frequencies.

For Psoriasis: It is recommended that treatment start with **TAZORAC**[®] 0.05% Gel, with strength increased to 0.1% if tolerated and medically indicated. Apply **TAZORAC**[®] Gel once a day, in the evening, to psoriatic lesions, using enough (2 mg/cm²) to cover only the lesion with a thin film to 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 **TAZORAC**[®] Gel. Because unaffected skin may be more susceptible to irritation, application of tazarotene to these areas should be carefully avoided. **TAZORAC**[®] Gel was investigated for up to 12 months during clinical trials for psoriasis.

For Acne: Cleanse the face gently. After the skin is dry, apply a thin film of **TAZORAC**[®] Gel 0.1% (2 mg/cm²) once a day, in the evening, to the skin where acne lesions appear. Use enough to cover the entire affected area. **TAZORAC**[®] Gel was investigated for up to 12 weeks during clinical trials for acne.

HOW SUPPLIED

TAZORAC[®] (tazarotene) Gel is 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.

| | | |
|-------|---------------------------------------|--------------------------------------|
| | TAZORAC [®] Gel 0.05% | TAZORAC [®] Gel 0.1% |
| 30 g | NDC 0023-8335-03 | NDC 0023-0042-03 |
| 100 g | NDC 0023-8335-10 | NDC 0023-0042-10 |

Storage: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Revised: 07/2017

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Irvine, CA 92612
Made in the U.S.A.



PATIENT INFORMATION
TAZORAC® (TAZ-or-ac)
(tazarotene)
Gel, 0.05% and 0.1%

Important information: TAZORAC Gel is for use on skin only. Do not use TAZORAC Gel in your eyes, mouth, or vagina.

What is the most important information I should know about TAZORAC Gel?

TAZORAC Gel may cause birth defects if used during pregnancy.

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

What is TAZORAC Gel?

- TAZORAC 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.
- TAZORAC Gel 0.1% is also used on the skin to treat people with mild to moderate facial acne vulgaris.

It is not known if TAZORAC 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.
- effective when used less than 1 time a day.
- safe if used over more than 20% of your body for the treatment of psoriasis or acne.

Who should not use TAZORAC Gel?

Do not use TAZORAC Gel if you:

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

What should I tell my doctor before using TAZORAC Gel?

Before you use TAZORAC 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 TAZORAC Gel passes into your breast milk. Talk to your doctor about using TAZORAC 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.

How should I use TAZORAC Gel?

- Use TAZORAC Gel exactly as your doctor tells you to use it.
- Apply TAZORAC Gel 1 time each day, in the evening.
- **Do not** get TAZORAC Gel in your eyes, on your eyelids, or in your mouth. If TAZORAC 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 TAZORAC Gel.

Follow these instructions for applying TAZORAC Gel:

- **If you have psoriasis:**
 - If you shower or bathe before applying TAZORAC 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 TAZORAC Gel.
 - Apply a thin layer of TAZORAC Gel to cover only the psoriasis lesions.
- **If you have acne:**
 - Gently wash and dry your face before applying TAZORAC Gel.
 - Apply a thin layer of TAZORAC Gel to cover only the acne lesions.
- If you swallow TAZORAC Gel, call your doctor or go to the nearest hospital emergency room right away.

What should I avoid while using TAZORAC Gel?

- Avoid sunlight, including sunlamps, during treatment with TAZORAC Gel. TAZORAC 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 TAZORAC Gel. If you get a sunburn, do not use TAZORAC 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 TAZORAC Gel on unaffected skin or skin with eczema because it may cause severe irritation.

What are the possible side effects of TAZORAC Gel?

TAZORAC Gel may cause serious side effects, including:

- **Skin irritation.** TAZORAC Gel may cause increased skin irritation. Tell your doctor if you develop itching, burning, redness, or peeling of your skin during treatment with TAZORAC Gel. If you develop skin irritation, your doctor may tell you to temporarily stop using TAZORAC Gel until your skin heals, tell you to use TAZORAC Gel less often, or if you are being treated for psoriasis with the 0.1% strength, may change your TAZORAC Gel dose. Also, wind or cold weather may be more irritating to your skin while you are using TAZORAC Gel.
- **Sensitivity to sunlight and risk of sunburn.** See "What should I avoid while using TAZORAC Gel?"

The most common side effects of TAZORAC Gel in people with plaque psoriasis include itching, burning, redness worsening of psoriasis, irritation and skin pain.

The most common side effects of TAZORAC Gel in people with acne vulgaris include peeling, burning, dry skin, redness and itching.

These are not all the possible side effects of TAZORAC 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 TAZORAC Cream?

- Store TAZORAC Gel at 77°F (25°C).
- Keep TAZORAC Gel and all medicines out of the reach of children.

General information about the safe and effective use of TAZORAC Gel.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use TAZORAC Gel for a condition for which it was not prescribed. Do not give TAZORAC 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 TAZORAC Gel that is written for health professionals.

What are the ingredients in TAZORAC 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 by: Allergan Sales, LLC., Waco, Texas
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Irvine, CA 92612
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For more information, call 1-800-678-1605 or go to www.tazorac.com

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

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