



Horizon BCBSNJ  
 Medical Necessity Guideline

Section           Drugs  
 Policy Number  
 Effective Date   4/28/06  
 Review Date     9/25/06, 11/12/07, 9/26/08

SUBJECT:

DRUG CLASS        Retinoid (topical)

BRAND NAME        Tazorac (all topical)  
 (Generic)           (tazarotene)

**IMPORTANT NOTE:**

*The purpose of this policy is to provide general information applicable to the administration of outpatient prescription drug benefits that Horizon Blue Cross Blue Shield of New Jersey and Horizon Healthcare of New Jersey, Inc. (collectively "Horizon BCBSNJ") insures or administers. **Outpatient prescription drugs are not covered under all Horizon benefit plans.** If the member's contract benefits differ from the pharmacy guideline, the contract prevails. Although a service, supply drug or procedure may be medically necessary, it may be subject to limitations and/or exclusions under a member's benefit plan. If a service, supply drug or procedure is not covered and the member proceeds to obtain the service, supply drug or procedure, the member may be responsible for the cost. Decisions regarding treatment and treatment plans are the responsibility of the physician. This policy is not intended to direct the course of clinical care a physician provides to a member, and it does not replace a physician's or pharmacist's independent professional clinical judgment or duty to exercise special knowledge and skill in the treatment of Horizon BCBSNJ members. Horizon BCBSNJ is not responsible for, does not provide, and does not hold itself out as a provider of medical care. The physician remains responsible for the quality and type of health care services provided to a Horizon BCBSNJ member.*

**Horizon BCBSNJ pharmacy guidelines do not constitute medical advice, authorization, certification, approval, explanation of benefits, offer of coverage, contract or guarantee of payment.**

**FDA-APPROVED INDICATIONS**

Tazorac cream 0.05% and 0.1% are indicated for the topical treatment of patients with plaque psoriasis.

Tazorac cream 0.1% is also indicated for the topical treatment of patients with acne vulgaris.

Tazorac 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 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.

**CRITERIA FOR APPROVAL**

- |  |     |    |
|--|-----|----|
| 1. If applicable, as per the FDA approved package insert, are the physician and patient aware that Tazorac must not be used if the patient is pregnant or may become pregnant? | Yes | No |
| 2. Does the patient have the diagnosis of plaque psoriasis?<br>[Tech only: if the answer to this question is yes, then no further questions are required.]                     | Yes | No |

3. Does the patient have the diagnosis of acne vulgaris?	Yes	No
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Guidelines for Approval					
Duration of Approval			12 months		
Set 1		Set 2			
Yes to question(s)	No to question(s)	Yes to question(s)	No to question		
1	none	1	2		
2		3			

**Horizon BCBSNJ Pharmacy Guideline Development Process:** This Horizon BCBSNJ Pharmacy Guideline (the “Pharmacy Guideline”) has been developed by Horizon BCBSNJ’s Pharmacy Drug Policy Subcommittee, Clinical Issues Subcommittee, and Quality Improvement Committee which include practicing physicians and pharmacists. This guideline is consistent with generally accepted standards of medical and pharmacy practice, and reflects Horizon BCBSNJ’s view of the subject health care services, supplies drugs or procedures, and in what circumstances they are deemed to be medically necessary or experimental/ investigational in nature. This Pharmacy Guideline also considers whether and to what degree the subject health care services, supplies or procedures are clinically appropriate, in terms of type, frequency, extent, site and duration and if they are considered effective for the illnesses, injuries or diseases discussed. Where relevant, this Pharmacy Guideline considers whether the subject prescription drugs are being requested primarily for the convenience of the covered person or the health care provider. It may also consider whether the prescription drugs are more costly than alternative prescription drugs that are at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the relevant illness, injury or disease. In reaching its conclusion regarding what it considers to be the generally accepted standards of medical and pharmacy practice, Horizon BCBSNJ reviews and considers the following: all credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, physician and health care provider specialty society recommendations, the views of physicians and health care providers practicing in relevant clinical areas (including, but not limited to, the prevailing opinion within the appropriate specialty), the findings and directives of the Food and Drug Administration and any other relevant factor as determined by applicable State and Federal laws and regulations.

**BLACK BOX WARNINGS**  
None

**RATIONALE**

The intent of the criteria is to ensure that patients follow selection elements established by Horizon BCBS New Jersey’s medical policies.

Tazorac cream is approved for the treatment of acne vulgaris and plaque psoriasis. Tazorac gel is indicated for the topical treatment of patients with stable plaque psoriasis of up to 20% body surface area involvement and for the topical treatment of patients with facial acne vulgaris of mild to moderate severity. Horizon BCBSNJ has chosen to allow Tazorac in those patients with a diagnosis of acne vulgaris or plaque psoriasis as first line therapy. Horizon BCBSNJ has chosen to add a safety question into the criteria regarding the contraindicated use of Tazorac in pregnancy. Therefore a negative pregnancy test will not be required.

**ADDITIONAL INFORMATION**

Tazarotene is a retinoid prodrug which is converted to its active form, the cognate carboxylic acid of tazarotene by rapid deesterification in animals and man.

Psoriasis: The mechanism of tazarotene action in psoriasis is not defined. Topical tazarotene blocks induction of mouse epidermal ornithine decarboxylase 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 comedocyte accumulation in rhino mouse skin and cross-linked envelope formation in cultured human keratinocytes. The clinical significance of these findings is unknown.

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

For Psoriasis: It is recommended that treatment start with Tazorac 0.05%, with strength increased to 0.1% if tolerated and medically indicated. Apply Tazorac once a day, in the evening, to psoriatic lesions, using enough ( $2\text{mg}/\text{cm}^2$ ) 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 Tazorac. If emollients are used, they should be applied at least an hour before application of Tazorac. Because unaffected skin may be more susceptible to irritation, application of tazarotene to these areas should be carefully avoided. Tazorac 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 0.1% ( $2\text{mg}/\text{cm}^2$ ) once a day, in the evening, to the skin where acne lesions appear. Use enough to cover the entire affected area. Tazorac was investigated for up to 12 weeks during clinical trials for acne.

### **CONTRAINDICATIONS/WARNINGS/PRECAUTIONS**

#### **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  $0.25\text{ mg}/\text{kg}/\text{day}$  ( $1.5\text{ mg}/\text{m}^2/\text{day}$ ) resulted in reduced fetal body weights and reduced skeletal ossification. Rabbits dosed **topically** with  $0.25\text{ mg}/\text{kg}/\text{day}$  ( $2.75\text{ mg}/\text{m}^2$  total body surface area/day) tazarotene gel during gestation days 6 through 16 were noted with single incidences of known retinoid malformations, including spina bifida, hydrocephaly, and heart anomalies. Systemic daily-exposure (AUC) to tazarotenic acid at topical doses of  $0.25\text{ mg}/\text{kg}/\text{day}$  tazarotene in a gel formulation in rats and rabbits represented 0.62 and 6.7 times, respectively, the  $\text{AUC}_{0-24\text{h}}$  observed in psoriatic patients treated with  $2\text{mg}/\text{cm}^2$  of tazarotene gel 0.1% (extrapolated for topical application over 20% body surface area), and 0.78 and 8.4 times, respectively the maximum  $\text{AUC}_{0-24\text{h}}$  in acne patients treated with  $2\text{ mg}/\text{cm}^2$  of tazarotene gel 0.1% over 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 SHOULD 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.

Tazorac 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 childbearing potential should be warned of the potential risk and use adequate birth-control measures when Tazorac is used. The possibility that a woman of childbearing 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 therapy, which should begin during a normal menstrual period.

Tazorac is contraindicated in individuals who have shown hypersensitivity to any of its components.

**Warnings:**

**Pregnancy Category X.** Women of childbearing potential should be warned of the potential risk and use adequate birth-control measures when Tazorac is used. The possibility that a woman of childbearing potential is pregnant at the time of institution of the 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 therapy, which should begin during a normal menstrual period. 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.

**Precautions:**

Tazorac should only be applied 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 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. Patients must be warned to use sunscreens (minimum SPF of 15) and protective clothing when using Tazorac. Patients with sunburn should be advised not to use Tazorac 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 and ensure that the precautions outlined in the Information for Patients subsection are observed.

Tazorac 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.

The safety and efficacy of tazarotene have not been established in pediatric patients under the age of 12 years.

Of the total number of subjects in clinical studies of tazarotene gels 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 for the treatment of acne has not been clinically evaluated in persons over the age of 65.

**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 is begun.

**REFERENCES**

1. Tazorac Gel Product Information. Allergan. January 2004.
2. Tazorac Cream Product Information. Allergan. October 2001.
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5. Mason C, Oftedahl G, Neely C, et al. Health Care Guideline: Acne Management. Institute for Clinical Systems Improvement. Second Edition; September 2003.
6. American Academy of Dermatology. Guidelines of Care for Acne Vulgaris. [www.aad.org](http://www.aad.org). Accessed 10/22/2004.
7. American Academy of Dermatology. Guidelines of Care for Psoriasis. [www.aad.org](http://www.aad.org). Accessed 10/22/2004.
8. National Psoriasis Foundation. Psoriasis and Psoriatic Arthritis. A Treatment Guide for the Health Insurance Industry. <http://www.psoriasis.org/treatment/psoriasis>. Accessed 11/05/2004.

*Pharmacy Guidelines can be highly technical and are designed for use by the Horizon BCBSNJ professional staff in making coverage determinations. Members referring to this policy should discuss it with their treating physician or pharmacist, and should refer to their specific benefit plan for the terms, conditions, limitations and exclusions of their coverage.*

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