



## TOPICAL ACNE AGENTS Preauthorization Criteria for Approval

### Medications and Dosage Forms Included in Criteria

Generic Name	Brand Name	Dosage Form
Adapalene	Differin <sup>®</sup>	topical cream, gel, solution <sup>†</sup>
Tazarotene	Tazorac <sup>®</sup>	topical cream, gel
Tretinoin	Atralin <sup>™</sup>	topical gel
Tretinoin	Avita <sup>®</sup>	topical cream*, gel*
Tretinoin	Retin-A <sup>®</sup>	topical cream*, gel*, liquid <sup>†</sup>
Tretinoin	Retin-A Micro <sup>®</sup>	topical microsphere gel
Tretinoin	Tretin-X	topical cream, gel
Tretinoin/clindamycin	Ziana <sup>™</sup>	topical gel

<sup>†</sup> Formulation discontinued and may not be available

\* Generic products available and

### FDA Approved Indications

#### Atralin<sup>™</sup> 1

Atralin (tretinoin) 0.05% gel is indicated for the topical treatment of acne vulgaris.

#### Avita<sup>®</sup> 2,3

Avita (tretinoin) 0.025% cream and 0.025% gel are indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of this product in the treatment of other disorders have not been established.

#### Differin<sup>®</sup> 4-6

Differin (adapalene) 0.1% cream, and 0.1% and 0.3% gel, are indicated for topical application for the treatment of acne vulgaris.

#### Retin-A<sup>®</sup> 7

Retin-A (tretinoin) cream 0.025%, 0.05%, and 0.1% and gel 0.025% and 0.1% and liquid 0.05%, is indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of the long-term use of this product in the treatment of other disorders have not been established.

#### Retin-A Micro<sup>®</sup> 8

Retin-A Micro (tretinoin gel) microsphere, 0.1% and 0.04%, is indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of the use of this product in the treatment of other disorders have not been established.

#### Tazorac<sup>®</sup> 9,10

Tazorac (tazarotene) cream, 0.05% and 0.1%, are indicated for the topical treatment of patients with plaque psoriasis. Tazorac (tazarotene) cream 0.1% is also indicated for the topical treatment of patients with acne vulgaris.

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.

### **Tretin-X™<sup>11</sup>**

Tretin-X 0.025% and 0.01% gel, and 0.025%, 0.05%, and 0.1% cream, are indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of the long-term use of this product in the treatment of other disorders have not been established.

### **Ziana™<sup>12</sup>**

Ziana gel (tretinoin 0.025%/clindamycin phosphate 1.2%) is indicated for the topical treatment of acne vulgaris in patients 12 years or older.

## **Description**

The purpose of the Topical Acne Products Preauthorization Criteria is to provide approval to patients prescribed retinoid and retinoid-like acne medications that meet requirements based on individual product labeling and/or clinical trials. The Criteria utilizes an age-edit to mitigate pharmacy claims being processed for patients under 40 years of age as these products are generally used for acne vulgaris. For patients 40 years of age or older will proceed through the preauthorization process to evaluate therapy based on product labeling and appropriate diagnoses. The Criteria do not approve these medications or similar medications used in the management of photoaging or photodamaged skin. Preauthorization requests that meet criteria are approved for 12 months.

## **Criteria**

### **Initial and Renewal Evaluation**

1. Is the patient 40 years of age or older?  
If yes, continue to 2.  
If no, approve for 12 months.
2. Is the acne agent under review prescribed for the treatment of acne vulgaris?  
If yes, approve for 12 months.  
If no, continue to 3.
3. Is the medication Tazorac and prescribed for plaque psoriasis?  
If yes, approve for 12 months.  
If no, do not approve.

## **Rationale**

The purpose of the Topical Acne Products Preauthorization Criteria is to provide approval to patients prescribed retinoid and retinoid-like acne medications that meet requirements based on individual product labeling and/or clinical trials. The Criteria will discourage the use of these medications in the management of photoaging or photodamaged skin. The preauthorization includes medications that are FDA approved for the treatment of acne vulgaris<sup>1-12</sup>, and Tazorac which also has an indication for plaque psoriasis.<sup>9,10</sup>

Current evidence suggests that the effectiveness of tretinoin in acne is due primarily to its ability to modify abnormal follicular keratinization.<sup>1-12</sup> Comedones form in follicles with an excess of keratinized epithelial cells. Tretinoin promotes detachment of cornified cells and the enhanced shedding of corneocytes from the follicle. By increasing the mitotic activity of follicular epithelia, tretinoin also increases the turnover rate of thin, loosely-adherent corneocytes. Through these actions, the comedo contents are extruded and the formation of the microcomedo, the precursor lesion of acne vulgaris, is reduced. Additionally, tretinoin acts by modulating the proliferation and differentiation of epidermal cells. These effects are mediated by tretinoin's interaction with a family of nuclear retinoic acid receptors. Activation of these nuclear receptors causes changes in gene expression. The exact mechanisms whereby tretinoin-induced changes in gene

expression regulate skin function are not understood.<sup>8</sup> The mechanism by which tazarotene assists in the treatment of acne vulgaris and psoriasis is unknown.<sup>9-10</sup> Adapalene acts on retinoid receptors. Biochemical and pharmacological profile studies have demonstrated that adapalene is a modulator of cellular differentiation, keratinization, and inflammatory processes all of which represent important features in the pathology of acne vulgaris. Although the exact mode of action of adapalene is unknown, it is suggested that topical adapalene normalizes the differentiation of follicular epithelial cells resulting in decreased microcomedone formation.<sup>4-6</sup>

Some tretinoin and retinoid-like products have been approved for the treatment of photodamaged skin.<sup>13-15</sup> Topical tretinoin has been shown to be effective in the management of reducing fine wrinkling, mottled hyperpigmentation, and skin roughness due to photodamaged skin.<sup>16</sup> Retinoid and retinoid-like products approved for these indications are Renova® (tretinoin) 0.02% cream<sup>14</sup>, Avage® (tazarotene) 0.1% cream<sup>13</sup>, and a combination product Solage® (mequinol 2%/tretinoin 0.01%) topical solution.<sup>15</sup>

The retinoid medications just described are not included in the preauthorization criteria, however, they are approved for the treatment of photoaging or photodamage. These indications are not considered medically necessary and are an excluded benefit. The retinoid agents included in the preauthorization criteria are approved for the treatment of acne vulgaris, but not for the treatment of photoaging or photodamaged skin. Additionally, tazarotene is indicated for the treatment of plaque psoriasis and will be approved for this indication.

### Explanation of PA Criteria

The PA Criteria utilizes an electronic claims edit functionality that automatically adjudicates a pharmacy claim for a retinoid or retinoid-like product in patients younger than 40 years of age. Claims for patients that are 40 years of age or older will reject with a message stating preauthorization is required and a PA request will need to be submitted for evaluation through the PA review process. The age limit edit is based on analyses provided in acne visit and prevalence studies.<sup>17,18</sup> NAMCS data provide evidence that dermatologist visits due to acne is common in ages 15-45 and visits decline drastically in the 40-59 age group.<sup>17</sup> An acne prevalence study found evidence that acne does not decrease during the ages of 24-44 years of age, but falls significantly after the age of 45.<sup>18</sup> A lower age was utilized in the edit to due to conservative assumptions made in the NAMCS analysis<sup>17</sup>, however, those patients 40 years of age or older will be approved for use of the retinoid products in the Criteria if the treatment is for acne vulgaris.

### References

1. Atralin™ (tretinoin) [package insert]. Fort Worth, TX: Coria Laboratories, LTD., August 2007.
2. Avita® (tretinoin) cream [package insert]. Research Triangle Park, NC: Bertek Pharmaceuticals, Inc., October 2001.
3. Avita® (tretinoin) gel [package insert]. Research Triangle Park, NC: Bertek Pharmaceuticals, Inc., November 2001.
4. Differin® (adapalene) cream [package insert]. San Antonio, TX: Galderma Laboratories, L.P., June 2004.
5. Differin® (adapalene) 0.1% gel [package insert]. San Antonio, TX: Galderma Laboratories, L.P., September 2003.
6. Differin® (adapalene) 0.3% gel [package insert]. San Antonio, TX: Galderma Laboratories, L.P., June 2007.
7. Retin-A® (tretinoin) [package insert]. Skillman, NJ: Ortho Dermatological, February 2001.
8. Retin-A Micro® (tretinoin) [package insert]. Skillman, NJ: Ortho Dermatological, May 2002.
9. Tazorac® (tazarotene) cream [package insert]. Irvine, CA: Allergan, May 2004.
10. Tazorac® (tazarotene) gel [package insert]. Irvine, CA: Allergan, January 2004.
11. Tretin-X™ (tretinoin) [package insert]. Mountain Lakes, NJ: Triax Pharmaceuticals, LLC, August 2005.
12. Ziana™ (clindamycin phosphate/tretinoin) [package insert]. Scottsdale, AZ: Medicis, The Dermatology Company, December 2006.
13. Avage® (tazarotene) cream [package insert]. Irvine, CA: Allergan, May 2004.
14. Renova® (tretinoin) cream [package insert]. Los Angeles, CA: OrthoNeutrogena, January 2006.

15. Solagé<sup>®</sup> (mequinol/tretinoin) [package insert]. Princeton, NJ: Barrier Therapeutics, Inc., June 2007.
16. Gilchrest BA. Treatment of photodamage with topical tretinoin: An overview. *J Am Acad Dermatol* 1997;36(3):S27-S36.
17. Stern RS. Medication and medical service utilization for acne 1995-1998. *J Am Acad Dermatol* 2000;43(6):1042-8.
18. Goulden V, Stables GI, Cunliffe WJ. Prevalence of facial acne in adults. *J Am Acad Dermatol* 1999;41(4):577-80.

## Billing/Coding

CODES	NUMBER	DESCRIPTION
GPI	90050003*****	Adapalene
	90050030*****	Tretinoin
	90250070*****	Tazarotene
	9005990265****	Clindamycin phosphate/tretinoin

Type of Service	Prescription Drug	
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Place of Service	Outpatient	
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## Update Information

Date	Action	Reason
07/01/08	Replace PA criteria	New PA criteria

## Preauthorization Criteria History

06/26/08	Reviewed by QMC
07/01/08	Preauthorization criteria original effective date
June 2009	Next Review