

# Retinoids (topical) Prior Authorization Program Summary

## POLICY REVIEW CYCLE

**Effective Date**  
3/1/2023

**Date of Origin**

## FDA APPROVED INDICATIONS AND DOSAGE

<b>Agent(s)</b>	<b>FDA Indication(s)</b>	<b>Notes</b>	<b>Ref#</b>
Adapalene Solution <sup>a</sup> Pads	Topical treatment of acne vulgaris	a - generic available	13 ; 14
Aklief <sup>®</sup> (trifarotene) Cream	Topical treatment of acne vulgaris in patients 9 years of age or older		19
Altreno <sup>®</sup> (tretinoin) Lotion	Topical treatment of acne vulgaris in patients 9 years of age and older		12
Arazlo <sup>™</sup> (tazarotene) Lotion	Topical treatment of acne vulgaris in patients 9 years of age and older		20
Atralin <sup>®</sup> (tretinoin) Gel <sup>a</sup>	Topical treatment of acne vulgaris	a - generic available	1
Differin <sup>®</sup> (adapalene) Cream <sup>a</sup> Gel <sup>a</sup> Lotion	0.1% cream and gel are indicated for the topical treatment of acne vulgaris  0.3% gel and 0.1% lotion are indicated for the topical treatment of acne vulgaris in patients 12 years of age and older	a - generic available	11 ; 16 ; 2 ; 3
Epiduo <sup>®</sup> Forte	Topical treatment of acne vulgaris		26

Agent(s)	FDA Indication(s)	Notes	Ref#
(adapalene/benzoyl peroxide) <sup>a</sup>  Gel			
Epiduo®  (adapalene/benzoyl peroxide) <sup>a</sup>  Gel	Topical treatment of acne vulgaris in patients 9 years of age or older		25
Fabior  (tazarotene)  Foam	Topical treatment of acne vulgaris in patients 12 years of age or older		15
Retin-A®  (tretinoin)  Cream <sup>a</sup>  Gel <sup>a</sup>	Treatment of acne vulgaris	a - generic available	5
Retin-A Micro®  (tretinoin)  Gel microsphere <sup>a</sup>	Topical application in the treatment of acne vulgaris	a - generic available	6
Tazorac®  (tazarotene)  Cream <sup>a</sup>  Gel	0.05% and 0.1% cream are indicated for the topical treatment of plaque psoriasis.  0.1% cream is indicated for the topical treatment of acne vulgaris.  0.05% and 0.1% gel are indicated for the topical treatment of patients with stable plaque psoriasis of up to 20% body surface area involvement.  0.1% gel is indicated for the topical treatment of mild to moderate facial acne vulgaris.	a - generic available	10 ; 9
Twynéo®  (tretinoin and benzoyl peroxide)	Topical treatment of acne vulgaris in adults and pediatric patients 9 years of age and older		24

Agent(s)	FDA Indication(s)	Notes	Ref#
Cream			

See package insert for FDA prescribing information: <https://dailymed.nlm.nih.gov/dailymed/index.cfm>

## CLINICAL RATIONALE

Acne	<p>The American Academy of Dermatology suggests several options for treatment of acne vulgaris in adolescents and young adults. Recommendations for topical acne therapies include benzoyl peroxide or combination with topical antibiotics (e.g., erythromycin or clindamycin) as monotherapy for mild acne, or in conjunction with topical retinoid, or systemic antibiotic therapy for moderate to severe acne. Topical antibiotics are not recommended as monotherapy due to risk of bacterial resistance, and due to increased efficacy when used in combination with benzoyl peroxide. Clindamycin 1% solution or gel is currently the preferred topical antibiotic for acne therapy. Erythromycin 2% available in multiple formulations but has reduced efficacy compared to clindamycin due to resistance of cutaneous Staphylococci and P acnes.(16,17)</p> <p>Topical adapalene, tretinoin, and benzoyl peroxide can be safely used in the management of preadolescent acne in children. Azelaic acid is useful as an adjunctive acne treatment and is recommended in the treatment of post-inflammatory dyspigmentation. Topical dapsone 5% gel is recommended for inflammatory acne, particularly in adult females with acne. There is limited data to support sulfur, nicotinamide, resorcinol, sodium sulfacetamide, aluminum chloride, and zinc in the treatment of acne. If topical antibiotic treatment is to be prolonged for more than a few weeks, topical benzoyl peroxide should be added, or used in combination products.(16,17) Topical retinoids (e.g., tretinoin, adapalene, and tazarotene) can be used to treat both inflamed and noninflamed acne lesions, alone or in combination with antibiotics, or for maintenance treatment. Many dermatologists now use them as first-line treatment. It is not clear that any one of these agents is more effective versus others. Retinoid/antimicrobial combinations are more effective than either component alone, but simultaneous application of tretinoin and benzoyl peroxide can cause oxidation of tretinoin and loss of effectiveness.(18)</p> <p>Topical retinoids are vitamin A derivatives used for acne treatment. Retinoids bind to a set of retinoic acid receptors: tretinoin to alpha, beta, and gamma, while tazarotene and adapalene bind to beta and gamma. This confers slight differences in activity, tolerability, and efficacy. Retinoids are the core of topical therapy for acne because they are comedolytic, resolve the precursor microcomedone lesion, and are anti-inflammatory. Retinoids have been found to enhance any topical acne regimen and allow for maintenance of clearance after discontinuation of oral therapy. Retinoid use may be limited by side effects, including dryness, peeling, erythema, and irritation, which can be mitigated by reduced frequency of application. Higher concentrations may be more efficacious, but have greater side effects. Some studies support greater efficacy of tazarotene over adapalene and tretinoin, and adapalene over tretinoin, but the concentrations and formulations of the agents used were varied. Data suggests that adapalene is better tolerated than multiple concentrations of tretinoin, but this data used older formulations. Overall, the limitations of the existing studies prohibit direct efficacy comparisons of topical retinoids.(16)</p> <p>American Academy of Pediatrics (2013)</p> <ul style="list-style-type: none"> <li>• Topical retinoids (tretinoin, adapalene, tazarotene) may be used as monotherapy or in combination products and in regimens of care for all types and severities of acne in children and adolescents of all ages. Isotretinoin is recommended for severe, scarring, and/or refractory acne in adolescents and may be used in younger patients. Extensive counseling, particularly regarding the avoidance of pregnancy as well as careful monitoring of potential side effects and toxicities, is recommended.</li> </ul>
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	<ul style="list-style-type: none"> <li>The guideline recommends concomitant use of benzoyl peroxide with the fixed-combination of tretinoin and clindamycin, to avoid potential development of bacterial resistance.(17)</li> </ul> <p>For additional clinical information see the Prime Therapeutics Formulary Chapter 14.5C Acne Agents: Retinoids and Retinoid-Like Agents.</p>
Additional Information	<p>The age limit of 40 years or older as the edit parameter has been based on analysis of National Ambulatory Medical Care Survey (NAMCS) data (1990-1994)(21) and (1990-2004).(22) In the initial analysis, acne-related treatment with tretinoin was equal to non-acne conditions around 44 years of age.(21) The second analysis confirmed that there was a “minute probability” of non-acne-related use of topical retinoids in the population aged 40 years and younger.(22) The authors of the NAMCS data evaluations suggest a minimum age of 40 years as a cut-off to determine coverage of retinoid agents for acne.(21,22) These analyses were consistent with a study of the prevalence of acne in adults in the United Kingdom (UK).(23) Data from the UK study indicated the prevalence of acne did not substantially decline between the ages of 24 and 44 years of life but fell significantly after 45 years of age.(23)</p>
Safety (1-15,19,20,24-26)	<p><i>Adapalene</i></p> <p>Adapalene is contraindicated for use in individuals who are hypersensitive to adapalene or any of the components in the vehicle.</p> <p><i>Aklief</i></p> <p>Aklief does not have any FDA labeled contraindications for use.</p> <p><i>Altreno</i></p> <p>Altreno does not have any FDA labeled contraindications for use.</p> <p><i>Arazlo</i></p> <p>Arazlo is contraindicated in pregnancy.</p> <p><i>Atralin</i></p> <p>Atralin does not have any FDA labeled contraindications for use.</p> <p><i>Differin</i></p> <p>Differin is contraindicated for use in individuals who are hypersensitive to adapalene or any of the components in the vehicle.</p> <p><i>Epiduo</i></p> <p>Epiduo does not have any FDA labeled contraindications for use.</p> <p><i>Epiduo Forte</i></p> <p>Epiduo Forte is contraindicated in patients with a history of hypersensitivity reactions to benzoyl peroxide or any components of the formulation in Epiduo Forte.</p> <p><i>Fabior</i></p> <p>Fabior is contraindicated in pregnancy.</p>

	<p><i>Retin-A</i></p> <p>Use of Retin-A should be discontinued if hypersensitivity to any of the ingredients is noted.</p> <p><i>Retin-A Micro</i></p> <p>Retin-A Micro does not have any FDA labeled contraindications for use.</p> <p><i>Tazorac</i></p> <p>Tazorac is contraindicated in the following:</p> <ul style="list-style-type: none"> <li>• Pregnancy</li> <li>• Individuals who have a known hypersensitivity to any of its components.</li> </ul> <p><i>Twyneo</i></p> <p>Twyneo cream is contraindicated in patients with a history of hypersensitivity reaction to benzoyl peroxide or any components of Twyneo cream.</p>
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## REFERENCES

Number	Reference
1	Atralin prescribing information. Bausch Health US, Inc. July 2016.
2	Differin Gel 0.3% prescribing information. Galderma Laboratories, LP. February 2018.
3	Differin Gel 0.1% prescribing information. Galderma Laboratories, LP. July 2019.
4	Retin-A prescribing information. Bausch Health US Inc. September 2019.
5	Retin-A Micro prescribing information. Bausch Health US, Inc. October 2017.
6	Avita Cream prescribing information. Mylan Pharmaceuticals, Inc. July 2018.
7	Avita Gel prescribing information. Mylan Pharmaceuticals, Inc. August 2018.
8	Tazorac Gel prescribing information. Allergan, Inc. April 2018.
9	Tazorac Cream prescribing information. Allergan, Inc. July 2017.
10	Differin Cream prescribing information. Galderma Laboratories, LP. February 2018.
11	Altreno lotion prescribing information. Bausch Health Companies, Inc. March 2020.
12	Adapalene solution 0.1% prescribing information. Allegis Pharmaceuticals. March 2020.
13	Adapalene swab topical solution 0.1%. Rochester Pharmaceuticals. November 2020.
14	Fabior prescribing information. Mayne Pharma. June 2018.
15	Differin Lotion 0.1% prescribing information. Galderma Laboratories, LP. February 2018.
16	Zaenglein AL, Pathy AL, Schlosser BL et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016;75:945-73. <a href="https://www.jaad.org/article/S0190-9622(15)02614-6/fulltext">https://www.jaad.org/article/S0190-9622(15)02614-6/fulltext</a>
17	Eichenfield L, Krakowski A, Piggott C, et al. Evidence-based recommendations for the diagnosis and treatment of pediatric acne. Pediatrics. 2013;131;S163-S186.
18	Drugs for Acne. Medical Letter. 2016;58(1487):13-15.
19	Aklief prescribing information. Galderma Laboratories, L.P. October 2019.
20	Arazlo prescribing information. Bausch Health Companies Inc. May 2021.
21	McConnel RC, Fleisher AB, Williford PM, Feldman SR. Most topical tretinoin treatment is for acne vulgaris through the age of 44 years: An analysis of the National Ambulatory Medical Care Survey, 1990-1994. J Am Acad Dermatol 1998;38:221-226.

Number	Reference
22	Balkrishnan R, Bhosle MJ, Camacho F, Fleischer Jr AB, Feldman SR. Prescribing patterns for topical retinoids: Analyses of 15 years of data from the National Ambulatory Medical Care Survey. J Dermatol Treat. 2010;21:193-200.
23	Goulden V, Stables GI, Cunliffe WJ. Prevalence of acne in adults. J Am Acad Dermatol 1999;41(4):577-580.
24	Twynéo prescribing information. Galderma Labs LP. July 2021.
25	Epiduo prescribing information. Galderma Laboratories, L.P. February 2018.
26	Epiduo Forte prescribing information. Galderma Laboratories, L.P. June 2018.

## POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
	Adapalene Soln 0.1%	0.1 %	M ; N ; O ; Y	N		02-01-2023
Adapalene treatment ; Differin	adapalene gel	0.1 % ; 0.3 %	M ; N ; O ; Y	O ; Y		
Aklief	trifarotene cream	0.005 %	M ; N ; O ; Y	N		
Altreno	tretinoin lotion	0.05 %	M ; N ; O ; Y	N		
Arazlo	tazarotene (acne) lotion	0.045 %	M ; N ; O ; Y	N		
Atralin ; Avita ; Retin-a	tretinoin gel	0.01 % ; 0.025 % ; 0.05 %	M ; N ; O ; Y	O ; Y		
Avita ; Retin-a	tretinoin cream	0.025 % ; 0.05 % ; 0.1 %	M ; N ; O ; Y	N ; O ; Y		
Differin	adapalene cream	0.1 %	M ; N ; O ; Y	O ; Y		
Differin	adapalene lotion	0.1 %	M ; N ; O ; Y	M ; N		
Epiduo ; Epiduo forte	Adapalene-Benzoyl Peroxide Gel ; adapalene-benzoyl peroxide gel	0 ; 0.1 % ; 0.3 %	M ; N ; O ; Y	N ; O ; Y		02-01-2023
Fabior	tazarotene (acne) foam	0.1 %	M ; N ; O ; Y	N		
Plixda	Adapalene Pads 0.1%	0.1 ; 0.1 %	M ; N ; O ; Y	M ; N		02-01-2023
Retin-a micro ; Retin-a micro pump	tretinoin microsphere gel	0.04 % ; 0.06 % ; 0.08 % ; 0.1 %	M ; N ; O ; Y	N ; O ; Y		
Tazorac	Tazarotene Cream 0.1%	0.1 %	M ; N ; O ; Y	O ; Y		
Twynéo	tretinoin-benzoyl peroxide cream	0.1 %	M ; N ; O ; Y	N		

## CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Differin	adapalene cream	0.1 %	Commercial ; HIM ; ResultsRx
Adapalene treatment ; Differin	adapalene gel	0.1 % ; 0.3 %	Commercial ; HIM ; ResultsRx
Plixda	Adapalene Pads 0.1%	0.1 ; 0.1 %	Commercial ; HIM ; ResultsRx
	Adapalene Soln 0.1%	0.1 %	Commercial ; HIM ; ResultsRx
Epiduo ; Epiduo forte	Adapalene-Benzoyl Peroxide Gel ; adapalene-benzoyl peroxide gel	0 ; 0.1 % ; 0.3 %	Commercial ; HIM ; ResultsRx
Aklief	trifarotene cream	0.005 %	Commercial ; HIM ; ResultsRx
Altreno	tretinoin lotion	0.05 %	Commercial ; HIM ; ResultsRx
Arazlo	tazarotene (acne) lotion	0.045 %	Commercial ; HIM ; ResultsRx
Atralin ; Avita ; Retin-a	tretinoin gel	0.01 % ; 0.025 % ; 0.05 %	Commercial ; HIM ; ResultsRx
Avita ; Retin-a	tretinoin cream	0.025 % ; 0.05 % ; 0.1 %	Commercial ; HIM ; ResultsRx
Differin	adapalene lotion	0.1 %	Commercial ; HIM ; ResultsRx
Fabior	tazarotene (acne) foam	0.1 %	Commercial ; HIM ; ResultsRx
Retin-a micro ; Retin-a micro pump	tretinoin microsphere gel	0.04 % ; 0.06 % ; 0.08 % ; 0.1 %	Commercial ; HIM ; ResultsRx
Tazorac	Tazarotene Cream 0.1%	0.1 %	Commercial ; HIM ; ResultsRx
Twynéo	tretinoin-benzoyl peroxide cream	0.1 %	Commercial ; HIM ; ResultsRx

## PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Brand Retinoids	<p><b>Brand Retinoid products</b> will be approved when ALL of the following are met:</p> <ol style="list-style-type: none"> <li>1. The patient is 40 years of age or over <b>AND</b></li> <li>2. The patient is not using the requested agent for treatment of wrinkles, stretch marks, age spots, or skin lightening <b>AND</b></li> <li>3. ONE of the following:               <ol style="list-style-type: none"> <li>A.The patient has tried and had an inadequate response to a generic topical retinoid <b>OR</b></li> <li>B.The patient has an intolerance or hypersensitivity to a generic topical retinoid <b>OR</b></li> <li>C.The patient has an FDA labeled contraindication to ALL generic topical retinoids</li> </ol> </li> </ol> <p><b>Length of Approval:</b> 12 months</p>
Generic Retinoids	<p><b>Generic Retinoid products</b> will be approved when BOTH of the following are met:</p> <ol style="list-style-type: none"> <li>1. The patient is 40 years of age or over <b>AND</b></li> <li>2. The patient is not using the requested agent for treatment of wrinkles, stretch marks, age spots, or skin lightening</li> </ol> <p><b>Length of Approval:</b> 12 months</p>