



PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 9/21/17
LAST REVIEW DATE: 8/15/19
LAST CRITERIA REVISION DATE: 8/15/19
ARCHIVE DATE:

PICATO® (ingenol mebutate) gel

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the [request form](#) in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for therapy:** Picato (ingenol mebutate) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
1. Individual is 18 years of age or older
 2. A confirmed diagnosis of **ONE** of the following:
 - Actinic keratosis with Fitzpatrick Skin Type of 1, 2, or 3
 - Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A
 3. Individual has tried, failed, or has contraindication to **ALL** the following preferred step therapy agents:
 - Imiquimod cream 5% (generic Aldara)
 - Fluorouracil

Initial approval duration: for **one time only** for 1 year

Description:

Picato® (ingenol mebutate) gel is used to treat actinic keratosis, a scaly, crusty lesion on the skin that may be red or yellow in color.

For the treatment of actinic keratosis on the face and scalp Picato gel, 0.015% should be applied to the affected area once daily for 3 consecutive days, using a new tube for each day of treatment. For the treatment of actinic keratosis on the trunk and extremities Picato gel, 0.05% should be applied to the affected area once daily for 2 consecutive days, using a new tube for each day of treatment. The gel is supplied in unit dose laminate tubes, for single use, the 0.015% package contains 3 unit dose tubes per carton and the 0.05% package contains 2 unit dose tubes per carton.

Actinic keratoses (AKs or solar keratoses) are keratotic macules, papules, or plaques resulting from the intraepidermal proliferation of atypical keratinocytes in response to prolonged exposure to ultraviolet radiation. Although most AKs do not progress to squamous cell carcinoma (SCC), AKs are a concern because the majority of cutaneous SCCs arise from pre-existing AKs, and AKs that will progress to SCC cannot be distinguished from AKs that will spontaneously resolve or persist. Because of these factors, most clinicians routinely treat AKs. Improvement in associated symptoms and cosmetic appearance can be additional benefits of treatment.

Treatment options for AK include destructive therapies (e.g., surgery, cryotherapy (liquid nitrogen), dermabrasion, photodynamic therapy [PDT]), topical medications (e.g., topical fluorouracil [5-fluorouracil, 5-FU], and imiquimod, ingenol mebutate), and chemical peels (e.g., trichloroacetic acid). In general, lesion-directed treatments, such as



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cryotherapy and surgical procedures, are the primary approach for isolated lesions. Field-directed therapies, such as topical 5-FU, imiquimod, and ingenol mebutate are particularly useful for treating areas with multiple AKs.

Preventive measures recommended for AK are similar to those for skin cancer:

- Avoid staying in the sun for long periods of time without protection (e.g., sunscreen, clothing, hats).
- Frequently application sunscreens with SPF ratings > 30 that block both UVA and UVB light.
- Wear sun protective clothing such as hats, long-sleeved shirts, long skirts, or trousers.
- Avoiding sun exposure during noon hours when ultraviolet light is the most powerful at that time.

FDA Review:

Ingenol gel (also referred to as PEP005 Gel) applied as indicated was shown to be statistically superior to vehicle gel based on the intent to treat population at significance level of 0.05. About half of the successfully treated patients experienced 'recurrence' of >1 AK lesion in the treated area. Recurrence rate at month 12 was 54% for 108 face/scalp patients studied, and 58% for 38 trunk/extremities patients studied.

The majority of adverse reactions resolved spontaneously, and reactions that required treatment were treated successfully with concomitant medications, and resulted in no serious medical outcomes or permanent side effects. Benefits appear to outweigh risks. The risks associated with use of this product are essentially limited to local adverse reactions, that is, a robust effect which is also likely to lead to the desired product performance.

PEP005 Gel could offer an additional therapeutic option for AK with a shorter duration of treatment course than that of currently available topical products. No comparative trials have been conducted. All topical AK treatments can cause local skin reactions at the treatment area. There are no comparative data on the effect of different management strategies or different methods of removal of AKs, and on incidence, morbidity, or mortality from invasive SCC.

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Definitions:

Fitzpatrick Skin Type (or Fitzpatrick Scale or Fitzpatrick Phototyping Scale):

The Fitzpatrick scale is a numerical classification schema for human skin color. It was developed as a way to estimate the response of different types of skin to ultraviolet light.

Fitzpatrick Skin Type is determined by genetic disposition, reaction to sun exposure, and tanning habits.

Genetic Disposition:

Genetic Score	0	1	2	3	4
Eye color	Light blue, grey, or green	Blue, grey, or green	Blue	Dark brown	Brownish black
Hair color (natural)	Sandy red	Blond	Chestnut/Dark Blond	Dark brown	Black
Skin color (non-exposed area)	Reddish	Very pale	Pale with beige tint	Light brown	Dark brown
Freckles on non-exposed skin	Many	Several	Few	Incidental	None
Total Genetic Score					

Reaction to Sun Exposure:

Sun Exposure Score	0	1	2	3	4
What happens when you stay in the sun too long	Painful redness, blistering, peeling	Blistering followed by peeling	Burns sometimes followed by peeling	Rare burns	Never had burns
To what degree do you turn brown	Hardly or not at all	Light color tan	Reasonable tan	Tan very easy	Turn dark Brown quickly
Do you turn brown within several hours after sun exposure	Never	Seldom	Sometimes	Often	Always
How does your face react to sun exposure	Very sensitive	Sensitive	Normal	Very resistant	Never had a problem
Total Sun Exposure Score					

Tanning Habits:

Tanning Habits Score	0	1	2	3	4
When did you last expose your body to sun (or artificial sunlamp/tanning cream)	More than 3 months ago	2-3 months ago	1-2 months ago	Less than a month ago	Less than 2 weeks ago
Did you expose the area to be treated to the sun	Never	Hardly ever	Sometimes	Often	Always
Total Tanning Habits Score					

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Skin Type Score:

Genetic Score	
Sun Exposure Score	
Habits Score	
Total Skin Type Score	

Fitzpatrick Skin Type:

Total Skin Type Score	Fitzpatrick Skin Type	
0-7	Type 1	Highly sensitive, always burns, never tans. Example: Red hair with freckles
8-16	Type 2	Very sun-sensitive, burns easily, tans minimally. Example: Fair skinned, fair haired Caucasians
17-25	Type 3	Sun sensitive skin, sometimes mild burns, slowly tans to light brown, tans uniformly. Example: Darker Caucasians.
25-30	Type 4	Minimally sun sensitive, burns minimally, always tans to moderate brown. Example: Mediterranean type Caucasians, some Hispanics
> 30	Type 5	Sun insensitive skin, very rarely burns, tans well, tans very easily to dark brown. Example: Some Hispanics, some Blacks
> 30	Type 6	Sun insensitive, never burns, deeply pigmented dark brown to darkest brown. Example: Darker Blacks

Resources:

Picato. Package Insert. Revised by manufacturer 6/2017. Accessed 7/19/18.

Picato. Package Insert. Revised by manufacturer 10/2016. Accessed 9/05/17.

McIntyre W, Downs M, Bedwell S. Treatment options for actinic keratoses. *Am Fam Physician*. 2007;76:667-672.

Berman B, Bienstock L, Kuritsky L, et al. Actinic keratoses: Sequelae and treatments. Recommendations from a consensus panel. *J Fam Pract*. 2006;55(5):suppl 1-8.

Picato Dossier. Leo Pharma. February 28, 2012.

Siller G, Gebauer K, Welburn P, et al.: PEP005 (ingenol mebutane) gel, a novel agent for the treatment of actinic keratosis: Results of a randomized, double blind, vehicle controlled, multicenter, phase IIa study. 2009 *Austral J Dermatol*; 50:16-22.

Anderson L, Schmieder GJ, Werschler WP, et al.: Randomized, double-blind, double dummy, vehicle controlled study of ingenol mebutane gel 0.25% and 0.05% for actinic keratosis. *J Am Acad Dermatol* 2009; 60: 934-943.



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Martin G and Swanson N: Clinical findings using ingenol mebutane gel to treat actinic keratosis. J Am Acad Dermatol 2013; 68: S39-S48.

Micali G, Lacarrubba F, Nasca MR, et al.: Topical pharmacotherapy for skin cancer. J Am Acad Dermatol 2014; 70: 979.e1-12.

NCCN Clinical Practice Guidelines in Oncology: Squamous Cell Skin Cancer. Version 2.2018, Oct 5, 2017. https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf

UpToDate: Epidemiology, natural history, and diagnosis of actinic keratosis. Current through Jul 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/epidemiology-natural-history-and-diagnosis-of-actinic-keratosis?search=actinic%20keratosis&source=search_result&selectedTitle=2~93&usage_type=default&display_rank=2

UpToDate: Treatment of actinic keratosis. Current through Jul 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-actinic-keratosis?search=actinic%20keratosis&source=search_result&selectedTitle=1~93&usage_type=default&display_rank=1

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.
