

PHARMACY COVERAGE GUIDELINE

PICATO® (ingenol mebutate) gel

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Picato (ingenol mebutate) is considered **medically necessary** and will be approved when **ALL** the following criteria are met:
 1. Prescriber is a physician specializing in the patient’s diagnosis or is in consultation with a Dermatologist or Oncologist.
 2. Individual is 18 years of age or older
 3. Individual has a confirmed diagnosis of **ONE** of the following:
 - a. Actinic keratosis with Fitzpatrick Skin Type of 1, 2, or 3

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- b. 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
4. Documented failure, contraindication per FDA label, intolerance, or not a candidate to **ALL** the following:
 - a. Fluorouracil 5%
 - b. Imiquimod cream 5% (generic Aldara)
5. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation.

Initial approval duration: One time only for 1 year

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
 2. **Off-Label Use of Cancer Medications**
-

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 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:

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- Avoid staying in the sun for long periods of time without protection (e.g., sunscreen, clothing, hats).
- Frequently apply 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.
- Avoid sun exposure during noon hours when [ultraviolet](#) light is most powerful.

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.

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

ORIGINAL EFFECTIVE DATE: 09/21/2017 | ARCHIVE DATE: | LAST REVIEW DATE: 08/18/2022 | LAST CRITERIA REVISION DATE: 08/18/2022

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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					

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 (ingenol mebutate) gel product information, revised by Leo Pharma, Inc. 01-2012. Available at <http://fda.gov>. Accessed July 27, 2022. Discontinued on 04-08-2021.

Berman B. Treatment of actinic keratosis. In: UpToDate, Dellavalle RP, Robinson JK, Corona R (Eds), UpToDate, Waltham, MA.: UpToDate Inc. <http://uptodate.com> Topic last updated on July 13, 2021. Accessed July 27, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Squamous Cell Skin Cancer Version 2.2022 – Updated May 02, 2022. Available at <https://www.nccn.org>. Accessed July 27, 2022.

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.