BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 9/21/17**
SECTION: DRUGS	**LAST REVIEW DATE: 9/20/18**
	LAST CRITERIA REVISION DATE: 9/20/18
	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.

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.**

PICATO® (ingenol mebutate) gel (cont.)

Criteria:

- **Criteria for initial therapy:** Picato (ingelol mebutane) 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 actinic keratosis

  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 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.

PICATO® (ingenol mebutate) gel (cont.)

- 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.

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.

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

PICATO® (ingenol mebutate) gel (cont.)

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.

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

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