

Title: Topical Antineoplastic Agents

Policy #: Rx.01.148

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **mechlorethamine (Valchlor®), bexarotene (Targretin Gel®), ingenol mebutate (Picato®) diclofenac 3% (Solaraze®) and tirbanibulin (Klisyri®)** as provided under the member's prescription drug benefit.

Description:

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. AKs are a concern because the majority of cutaneous squamous cell carcinoma (SCCs) arise from pre-existing AKs, and AKs that will progress to SCC cannot be distinguished from AKs that will spontaneously resolve or persist.

Cutaneous T cell lymphoma (CTCL) describes a heterogeneous group of neoplasms of skin-homing T cells. CTCL represent approximately 75 to 80 percent of all primary cutaneous lymphomas. Mycosis fungoides (MF) and primary cutaneous CD30+ lymphoproliferative disorders (LPD) account for approximately 90 percent of CTCL.

Mechlorethamine (Valchlor®) is indicated for the topical treatment of stage IA and IB mycosis fungoides–type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy.

Mechlorethamine (Valchlor®) is a nitrogen mustard alkylating agent that forms inter- and intrastrand DNA cross-links, resulting in inhibition of DNA synthesis. Topical application allows for skin-directed treatment while minimizing systemic nitrogen mustard exposure.

Bexarotene (Targretin Gel®) is indicated for the topical treatment of cutaneous lesions in patients with cutaneous T-cell lymphoma (CTCL) (Stage IA and IB) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.

Bexarotene (Targretin Gel®) selectively binds and activates retinoid X receptor subtypes (RXR α , RXR β , RXR γ). RXRs can form heterodimers with various receptor partners such as retinoic acid receptors (RARs), vitamin D receptor, thyroid receptor, and peroxisome proliferator activator receptors (PPARs). Once activated, these receptors function as transcription factors that regulate the expression of genes that control cellular differentiation and proliferation. Bexarotene inhibits the growth in vitro of some tumor cell lines of hematopoietic and squamous cell origin. It also induces tumor regression in vivo in some animal models. The exact mechanism of action of bexarotene in the treatment of CTCL is unknown.

Ingenol mebutate (Picato®) is indicated for the topical treatment of actinic keratosis (AK).

Ingenol mebutate (Picato®) is an inducer of cell death. The mechanism of action by which ingenol mebutate gel induces cell death in treating AK lesions is unknown.

Diclofenac 3% gel (Solaraze®) is indicated for the topical treatment of AK.

The mechanism of action of diclofenac 3% gel (Solaraze®) in the treatment of AK is unknown.

Tirbanibulin (Klisyri™) is indicated for the topical treatment of actinic keratosis on the face or scalp.

Tirbanibulin is a microtubule inhibitor. The mechanism of action of KLISYRI for the topical treatment of actinic keratosis is unknown.

Policy:

INITIAL CRITERIA Mechlorethamine (Valchlor®), bexarotene (Targretin®), ingenol mebutate (Picato®) diclofenac 3% (Solaraze®) gel is approved when documentation is provided of an FDA approved indication for the requested drug.

REAUTHORIZATOIN CRITERIA Ingenol mebutate (Picato®) and diclofenac (Solaraze®) are approved when there is documentation of a diagnosis of actinic keratosis at a different treatment site.

Authorization duration:

Diclofenac 3% (Solaraze®) approved for 3 months (initial and reauthorization).

Ingenol mebutate (Picato®) approved for 30 days (initial and reauthorization).

Mechlorethamine (Valchlor®) and bexarotene (Targretin®) approved indefinitely

INITIAL CRITERIA Tirbanibulin (Klisyri®) is approved when BOTH of the following are met:

1. Diagnosis of actinic keratosis; and
2. Inadequate response or inability to tolerate one of the following generics:
 - a. Fluorouracil; or
 - b. Imiquimod; or
 - c. Diclofenac 3% gel

Initial authorization: 30 days

REAUTHORIZATION CRITERIA Tirbanibulin (Klisyri®) is re-approved when there is documentation of a diagnosis of actinic keratosis at a different site.

Reauthorization: 30 days

Black Box Warning as shown in the drug Prescribing Information:

Solaraze® (diclofenac 3%):

Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial and stroke, which can be fatal. This risk may occur in treatment and may increase with duration of use.

Solaraze® is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Jorizzo J. Treatment of actinic keratosis. UpToDate. April 2018. Available at: https://www.uptodate.com/contents/treatment-of-actinic-keratosis?source=search_result&search=actinic%20keratosis&selectedTitle=1~46. Accessed July 23, 2021.

Picato® (ingenol mebutate) [package insert]. Parsippany, NJ. Leo Pharma Inc. June 2017. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=5accc7a5-8209-4680-b0ae-2a6963500419&type=display>. Accessed July 23, 2021.

Solaraze® (diclofenac 3%) [package insert]. Melville, NY. PharmaDerm. April 2016. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=89a7bfd-051f-4d87-a642-96b0df81b8e2&type=display>. Accessed July 23, 2021.

Targretin® (bexarotene) gel [package insert]. Bridgewater, NJ. Valeant. October 2016. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=d35b4697-3f3b-4aa1-b5d9-153993e83811&type=display>. Accessed July 23, 2021.

Valchlor® (mechlorethamine) [package insert]. South San Francisco, CA. Actelion Pharmaceuticals, US. November 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=f522cd6d-aa0f-4b44-92cc-ed952058eea0&type=display#section-1>. Accessed July 23, 2021.

Willemze R. Classification of primary cutaneous lymphomas. UpToDate. August 2018. Available at: <https://www.uptodate.com/contents/classification-of-primary-cutaneous-lymphomas?source=machineLearning&search=CTCL&selectedTitle=7~106§ionRank=1&anchor=H474649238#H474649238>. Accessed July 23, 2020.

Klisyri™ (tirbanibulin) [package insert]. Exton, PA: Almirall; December 2020. Available from: <https://klisyrihcp.com/assets/klisyri-prescribing-information.pdf>. Accessed July 23, 2021.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Valchlor®	mechlorethamine
Targretin®	bexarotene
Picato®	ingenol mebutate
Solaraze®	diclofenac 3%
Klisyri™	Tirbanibulin

Cross References:

Off-Label Use policy Rx.01.33

Policy Version Number:	10.00
P&T Approval Date:	June 10, 2021
Policy Effective Date:	October 01, 2021
Next Required Review Date:	January 9, 2021

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.