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Coverage Policy Number IP0367

Topical Medications for Actinic Keratosis

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for topical medications for actinic keratosis.

- Aldara™ (imiquimod) 5% cream
- Carac® (fluorouracil) 0.5% cream
- imiquimod 3.75% (A-rated and authorized generics for Zyclara) cream pump
- Klisyri® (tirbanibulin)
- Zyclara® (imiquimod) 2.5% cream pump
- Zyclara® (imiquimod) 3.75% cream and cream pump

Medical Necessity Criteria

Non-Covered Product	Diagnosis
Carac (fluorouracil 0.5% cream)	The following (1): 1. Actinic keratosis

Non-Covered Product	Diagnosis
Klisyri (tirbanibulin)	The following (1): 1. Actinic keratosis on the face or scalp
Aldara (imiquimod) 5% cream	For **ANY** of the following (1, 2 or 3): 1. Actinic keratosis 2. External genital and perianal warts (condyloma acuminata) 3. Superficial basal cell carcinoma (sBCC)
imiquimod 3.75% (A-rated and authorized generics for Zyclara) cream pump **Zyclara** (imiquimod) 3.75% cream and cream pump	For **EITHER** of the following (1 or 2): 1. Actinic keratosis 2. External genital and perianal warts (condyloma acuminata)
Zyclara (imiquimod) 2.5% cream pump	The following (1): 1. Actinic keratosis

Coverage for topical medications for actinic keratosis varies across plans and may require the use of preferred products. Refer to the customer's benefit plan document for coverage details.

Non-covered drugs are considered medically necessary when there is documentation of ONE of the following:

A. The individual has had inadequate efficacy to the number of covered alternatives according to the table below

OR

B. The individual has a contraindication according to FDA label, significant intolerance, or is not a candidate* for the covered alternatives according to the table below

**Note: Not a candidate due to being subject to a warning per the prescribing information (labeling), having a disease characteristic, individual clinical factor[s], other attributes/conditions, or is unable to administer and requires this dosage formulation)*

Employer Group Non-Covered Products and Preferred Covered Alternatives by Drug List:

Non-Covered Product	Standard / Performance	Value / Advantage	Cigna Total Savings	Legacy
Carac (fluorouracil 0.5% cream)	The following (1): 1. fluorouracil 0.5% cream (generic for Carac) ±			
Klisyri (tirbanibulin)	**BOTH** of the following (1 and 2): 1. fluorouracil-containing topical product 2. imiquimod 5% cream			
Aldara (imiquimod) 5% cream **imiquimod** 3.75% (A-rated and authorized generics	The following (1): 1. generic imiquimod 5% cream±			

Non-Covered Product	Standard / Performance	Value / Advantage	Cigna Total Savings	Legacy
for Zyclara) cream pump **Zyclara** (imiquimod) 2.5% cream pump **Zyclara** (imiquimod) 3.75% cream and cream pump				

[±]*Where applicable, documentation that individual has tried the generic product AND cannot take due to a formulation difference in the inactive ingredient(s) [for example, difference in dyes, fillers, preservatives] between the brand and the generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction.*

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Topical medications for actinic keratosis are considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.

Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Topical medications for actinic keratosis are considered not medically necessary for ANY other use.

Background

OVERVIEW
The various topical fluorouracil and imiquimod products, Klisyri, and Picato are indicated for the treatment of **actinic keratosis**.[1-7] Imiquimod 5% cream (Aldara, generic), Zyclara 3.75% cream, and imiquimod 3.75% cream are also indicated for the treatment of external genital and perianal warts/condyloma cuminata in patients ≥ 12 years of age.[1,6] Imiquimod 5% cream, fluorouracil 5% cream (Efudex, generic), and fluorouracil 5% solution are also indicated for the treatment of superficial basal cell carcinoma in certain patients.[1,3] Note that as of October 2020, Picato is no longer being marketed or manufactured, but there may be existing stock in the pharmacies.

Guidelines
The National Comprehensive Cancer Network (NCCN) Guidelines for Squamous Cell Skin Cancer (version 1.2023 – March 10, 2023) note that accepted treatment modalities for actinic keratoses include cryotherapy, topical 5-fluorouracil (preferred) with or without calcipotriol (calcipotriene), topical imiquimod, Klisyri, photodynamic therapy, and curettage and electrodesiccation.[8] For hyperkeratotic actinic keratoses, pretreatment with topical tazarotene,

curettage, or topical keratolytics (topical urea, lactic acid, and salicyclic acid) prior to the listed therapies may be considered. Other modalities that may be considered include topical diclofenac (category 2B), chemical peel, and ablative skin resurfacing (e.g., laser, dermabrasion).

References

1. Aldara® cream [prescribing information]. Bridgewater, NJ: Valeant; April 2018.
2. Carac® cream [prescribing information]. Bridgewater, NJ: Bausch Health; May 2021.
3. Efudex® topical solution and cream [prescribing information]. Bridgewater, NJ: Bausch Health; October 2021.
4. Fluorouracil 0.5% cream [prescribing information]. Morgantown, VA: Mylan; January 2019.
5. Picato® gel [prescribing information]. Madison, NJ: LEO Pharma; February 2020.
6. Zyclara® cream [prescribing information]. Bridgewater, NJ. Bausch Health; June 2020.
7. Klisyri® ointment [prescribing information]. Malvern, PA: Almirall; August 2021.
8. The NCCN Squamous Cell Skin Cancer Clinical Practice Guidelines in Oncology (version 1.2023 – March 10, 2023). © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 6, 2023.