



Wellmark Blue Cross and Blue Shield is an Independent Licensee of the Blue Cross and Blue Shield Association.

DRUG POLICY

Keratolytics and Other Topical Dermatological Agents

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Keratolytics and Other Dermatologic Agents Policy is to ensure the medications are being used properly for approved indications and ages to ensure efficacy and safety as well as being cost-effective. This policy includes medications for the topical treatment of actinic keratosis, external genital warts and perianal warts. Many of the drugs are for multiple indications and have different mechanisms of actions.

Zyclara[®] (imiquimod) brand and generic is a Toll-like receptor 7 agonist that activates immune cells. While its exact mechanism of action is unknown, topical application of imiquimod to skin is associated with increases in markers for cytokines and immune cells. It is available in a 2.5% and 3.75% cream formulation.

Zyclara[®] (imiquimod) brand and generic has been approved by the by the Food and Drug Administration (FDA) for the following indications:

- Treatment of clinically typical, visible or palpable actinic keratoses (AK) of the full face or balding scalp in immunocompetent adults (2.5% and 3.75%)
- Treatment of external genital and perianal warts/condyloma acuminata (EGW) in patients 12 years of age and older (3.75% strength only)

Treatment with imiquimod has not been studied for the prevention and transmission of human papilloma virus (HPV). Imiquimod use for children age 2 to 12 with molluscum contagiosum has been evaluated and studies have failed to demonstrate efficacy.

The mechanism of action by which **Klisyri**[®] (tirbanibulin) inhibits microtubules in the treatment of AK lesions is unknown. The safety and efficacy of use of tirbanibulin in children under the age of 18 years has not been established.

Klisyri[®] (tirbanibulin) has been FDA approved for the following indications:

- Treatment of adults with actinic keratosis of the scalp and face.

Fluorouracil blocks the methylation reaction of deoxyuridylic acid to thymidylic acid thus interfering with the formation of DNA and to a lesser extent, RNA. This proposed mechanism of action creates a thymine deficiency that provokes unbalanced growth and cell death.

Fluorouracil solution (2% and 5%) and cream (strengths ranging from 0.5% to 5%) are FDA approved for the following:

- Treatment of adults with multiple actinic or solar keratoses

Carac[®] (fluorouracil) 0.5% cream is FDA approved for the following:

- Treatment of multiple actinic or solar keratoses of the face and anterior scalp.

Condylox[®] (podofilox) is available in a gel and solution formulation. The exact mechanism of action is unknown, treatment results in visible necrosis of wart tissue. The solution is currently available generically.

Condylox[®] (podofilox) gel is FDA approved for the following:

- Treatment of adults with external genital warts (anogenital)
- Treatment of adults with perianal warts

Condylox[®] (podofilox) solution is FDA approved for the following:

- Treatment of adults with external genital warts (anogenital)

Veregen[®] (sinecatechins) 15% ointment is believed to have an antioxidant activity but the current mechanism of action is unknown.

Veregen[®] is FDA approved for the following:

- Treatment of immunocompetent patients 18 years and older for the treatment of external genital warts
- Treatment of immunocompetent patients 18 years and older for the treatment of perianal warts

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Please note: Fluorouracil (2% and 5%) solutions, fluorouracil 5% cream, imiquimod 5% cream, and podofilox 0.5% solution are available without prior authorization.

- I. Carac (fluorouracil 0.5% cream) and generic equivalents may be considered **medically necessary** for the treatment of actinic keratosis (AK) when **all** of the following criteria are met:
 - The patient is 18 years of age and older
 - The patient has a diagnosis of AK
 - The patient has tried and failed cryotherapy, unless otherwise contraindicated
 - The patient has tried and failed OR had an adverse event OR has a contraindication to topical fluorouracil solution or the generic 5% cream unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).

Approval will be for a period of 3 months

Carac (fluorouracil 0.5%) and generic equivalents are considered **not medically necessary** for patient who do not meet the criteria set forth above.

II. Zyclara® (2.5% and 3.75%) brand and generic may be considered **medically necessary** for the treatment of AK when **all** of the following criteria are met:

- The patient is 18 years of age or older
- The patient has a diagnosis of AK
- The patient has tried and failed cryotherapy, unless otherwise contraindicated
- The patient has tried and failed OR had an adverse event OR has a contraindication to topical fluorouracil solution or the generic 5% cream unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).
- The patient has tried and failed OR had an adverse event OR has a contraindication to imiquimod 5% unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).

Approval will be for a period of **3 months**.

III. Zyclara® (3.75%) brand and generic may be considered **medically necessary** for the treatment of external genital warts (EGW) when **all** of the following criteria are met:

- The patient is 12 years of age or older
- The patient has a diagnosis of EGW
- The strength of medication requested is indicated for EGW treatment (3.75%)
- The patient has tried and failed cryotherapy, unless otherwise contraindicated
- The patient has tried and failed OR had an adverse event OR has a contraindication to podofilox solution unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).
- The patient has tried and failed OR had an adverse event OR has a contraindication to imiquimod 5% unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).

Approval will be for a period of **3 months**.

IV. Zyclara (3.75%) brand and generic may be considered medically necessary for the treatment of perianal warts when **all** the following criteria are met:

- The patient is 12 years of age or older
- The patient has a diagnosis of perianal warts
- The strength of medication requested is indicated for perianal warts (3.75%)
- The patient has tried and failed cryotherapy, unless otherwise contraindicated
- The patient has tried and failed OR had an adverse event OR has a contraindication to imiquimod 5% unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).

Approval will be for a period of **3 months**.

Zyclara® brand and generic is considered **not medically necessary** for patients who do not meet the criteria set forth above.

V. Klisyri® 1% ointment may be considered **medically necessary** for the treatment of AK of the face or scalp when **all** the following criteria are met:

- The patient is 18 years of age or older
- The patient has a documented diagnosis of AK
- The patient has tried and failed cryotherapy, unless otherwise contraindicated
- The patient has tried and failed OR had an adverse event OR has a contraindication to topical fluorouracil solution or the generic 5% cream unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).
- The patient has tried and failed OR had an adverse event OR has a contraindication to imiquimod 5% unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).

Approval will be for a period of **one month**.

Klisyri® is considered **not medically necessary** for patients who do not meet the criteria set forth above.

VI. Condylox® gel may be considered **medically necessary** for the treatment of external genital(anogenital) warts when **all** the following criteria are met:

- The patient is 18 years of age or older
- The patient has a documented diagnosis of external genital warts
- The patient has tried and failed cryotherapy, unless otherwise contraindicated
- The patient has tried and failed OR had an adverse event OR has a contraindication to podofilox solution unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).

Approval will be for a period of **3 months**.

VII. Condylox® gel may be considered **medically necessary** for the treatment of perianal warts when **all** the following criteria are met:

- The patient is 18 years of age or older
- The patient has a documented diagnosis of perianal warts
- The patient has tried and failed cryotherapy, unless otherwise contraindicated.
- The patient has tried and failed OR had an adverse event OR has a contraindication to imiquimod 5% unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).

Approval will be for a period of **3 months**.

Condylox® gel is considered **not medically necessary** for patients who do not meet the criteria set forth above.

VIII. Veregen® ointment may be considered **medically necessary** for the treatment of external genital warts when **all** the following criteria are met:

- The patient is 18 years of age or older
- The patient has a documented diagnosis of external genital warts
- The patient has tried and failed cryotherapy, unless otherwise contraindicated
- The patient has tried and failed OR had an adverse event OR has a contraindication to podofilox solution unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).

Approval will be for a period of **6 months**.

IX. Veregen® ointment may be considered **medically necessary** for the treatment of perianal warts when **all** the following criteria are met:

- The patient is 18 years of age or older
- The patient has a documented diagnosis perianal warts
- The patient has tried and failed cryotherapy, unless otherwise contraindicated
- The patient has tried and failed OR had an adverse event OR has a contraindication to Imiquimod 5% unless the patient is currently receiving a positive therapeutic outcome on the requested medications through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs).

Approval will be for a period of **6 months**.

Veregen® is considered **not medically necessary** for patients who do not meet the criteria set forth above.

Quantity Limits

Klisyri (tirbanibulin) 1% ointment – One box of 5 single-use packets per 25 days.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- Code(s), if applicable

REFERENCES

- Klisyri [package insert]. Exton, PA: Almirall LLC; December 2020.
- Zyclara [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; February 2018.
- Carac [package insert]. Bridgewater, NJ : Valeant Pharmaceuticals North America; May 2017.
- Condylox (podofilox) [package insert]. Irvine, CA: Allergan USA Inc; November 2019.
- Veregen (sinecatechins) [package insert]. Melville, NY: PharmaDerm; February 2020.
- Clinical Effectiveness Group (British Association for Sexual Health and HIV). United Kingdom National Guideline on the management of anogenital warts, 2007:
<http://www.bashh.org/documents/86/86.pdf>
- Stockfleth, E, et al. Guidelines for the management of actinic keratoses, 2011 update:
<http://www.euroderm.org/index.php/edf-guidelines>

- Stockfleth E, et al. "Development of a treatment algorithm for actinic keratoses: a European Consensus." European Journal of Dermatology. 2008; 18 (6): 651-9.
- Skin Cancer Foundation. Actinic Keratosis Treatment Options. <http://www.skincancer.org/skin-cancer-information/actinic-keratosis/actinic-keratosis-treatment-options>. Accessed September 30, 2019.
- Actinic Keratosis: Diagnosis, Treatment and Outcome. American Academy of Dermatology. <https://www.aad.org/dermatology-a-to-z/diseases-and-treatments/a---d/actinic-keratosis/diagnosis-treatment>. Accessed September 30, 2019.
- Hept MV, Steeb T, Ruzicka T, Berking C. Cryosurgery combined with topical interventions for actinic keratosis: A systematic review and meta-analysis. Br J Dermatol. 2019;180(4):740-748.
- Workowski KA, Bolan GA; Centers for Disease Control and Prevention (CDC). Sexually transmitted diseases treatment guidelines, 2015 [published correction appears in MMWR Recomm Rep. 2015;64(33):924]. MMWR Recomm Rep. 2015;64(RR-03):1-137.

POLICY HISTORY

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