Keratolytics and Other Topical Dermatological Agents

**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 keratoses, external genital warts and perianal warts. Many of the drugs are for multiple indications and have different mechanisms of actions.

**Zyclara® (imiquimod)** 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)** 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 molliscum contagiosum has been evaluated and studies have failed to demonstrate efficacy.

The mechanism of action by which **Picato® (ingenol mebutate)** produces cell death in the treatment of AK lesions is unknown. The safety and efficacy of use of ingenol in children under the age of 18 years has not been established.

**Picato® (ingenol mebutate)** has been FDA approved for the following indications:

- Treatment of adults with actinic keratoses of the trunk and extremities (0.05% strength) and the scalp and face (0.015% strength).

**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

Tolak® (fluorouracil) 4% cream is FDA approved for the following:
- Treatment of adults with actinic keratosis lesions of the face, ears, and 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 antioxidate 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

**POLICY**

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

I. Carac (fluorouracil 0.5% cream), Fluoroplex (fluorouracil 1% cream), Tolak (fluorouracil 4% 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 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%), Fluoroplex (fluorouracil 1% cream), Tolak (fluorouracil 4% cream), 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%) 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 cryotherapy, unless otherwise contraindicated to topical fluorouracil 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.

III. Zyclara® (3.75%) 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%) 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® is considered not medically necessary for patients who do not meet the criteria set forth above.

V. Picato® 0.015% gel may be considered medically necessary for the treatment of AK of the scalp and face 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 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**.

VI. Picato® 0.05% gel may be considered **medically necessary** for the treatment of AK of the trunk and extremities 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 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**.

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

VII. 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**.

VIII. 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.
IX. 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**.

X. Veregen® ointment may be considered **medically necessary** for the treatment of perianal 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.

**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**

- Fluoroplex [package insert], West Chester, PA: Aqua Pharmaceuticals; August 2016.
• Condylox [prescribing information]. Parsippany, NJ: Watson Medical, March 2011
• Actinic Keratosis Treatment and Management. Medscape.
• Tolak (fluorouracil 4% cream) [prescribing information]. Sanford, FL: Hill Dermaceuticals; September 2015.

POLICY HISTORY

Policy #: 05.01.35
Original Effective Date: April 2010
Reviewed: September 2017
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