Pharmacy Policy Bulletin: J-0212 Zyclara (imiquimod) – Commercial and Healthcare Reform	
Number: J-0212	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** 1. Other Managed Prior Authorization = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0212-011	**Original Date:** 05/01/2019
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Zyclara (imiquimod) cream 2.5%, 3.75%
FDA-Approved Indication(s):	• **2.5% and 3.75% cream**: Topical treatment of clinically typical, visible or palpable actinic keratoses (AK) of the face or balding scalp in immunocompetent adults. • **3.75% cream only**: Topical treatment of external genital and perianal warts (EGW) also known as condyloma acuminata in patients 12 years or older.

Background:	• Imiquimod is a topical agent for the treatment of AK and external genital and perianal warts. Despite destruction of human papillomavirus (HPV) warts, imiquimod does not completely eliminate HPV. Imiquimod, an immune response modifier, is a Toll-like receptor 7 agonist that activates immune cells. Topical application to the skin is associated with increases in markers for cytokines and immune cells. • The 2021 American Academy of Dermatology (AAD) guidelines strongly recommend topical fluorouracil or topical imiquimod for the treatment of AK. Conditional recommendations were made for the use of photodynamic therapy (PDT) or topical diclofenac 3% for the treatment of AK, both individually and as part of combination therapy regimens. Field-directed therapies, such as topical fluorouracil, topical imiquimod, and PDT, are particularly useful for treating areas with multiple AK lesions. • The 2021 Centers for Disease Control and Prevention (CDC) Guidelines for Sexually Transmitted Infections recommend imiquimod 3.75% or 5%; podofilox 0.5% solution; or sinecatechins 15% ointment for the treatment of external anogenital warts. • Prior authorization is utilized to ensure appropriate diagnosis. Step therapy contains criteria for prior utilization of products that are cost-effective and guideline recommended. • Prescribing Considerations: ○ Zyclara (imiquimod) 2.5% or 3.75% cream for AK is used for two 2-week treatment cycles separated by a 2-week no-treatment period.

	○ Zyclara (imiquimod) 3.75% cream is used for external genital/perianal warts until total clearance or for up to 8 weeks. ○ Zyclara (imiquimod) are for topical use only; not for oral, ophthalmic, intra-anal, or intravaginal use.

Approval Criteria

I. Initial Authorization

A. Actinic Keratosis

When a benefit, coverage of Zyclara (imiquimod) cream 2.5% or 3.75% may be covered when all of the following criteria are met **(1. through 4.)**:

1. The member is 18 years of age or older.
2. The member has a diagnosis of actinic keratosis (ICD-10: L57.0).
3. The member has experienced therapeutic failure or intolerance to plan-preferred generic imiquimod 5% cream.
4. The member has experienced therapeutic failure or intolerance to one (1) of the following plan-preferred agents **(a. or b.)**:
   a. fluorouracil 5% topical cream
   b. fluorouracil topical solution

B. External Genital Warts

When a benefit, coverage of Zyclara (imiquimod) cream 3.75% may be covered when all of the following criteria are met **(1., 2., and 3.)**:

1. The member is 12 years of age or older.
2. The member has a diagnosis of condyloma acuminata (external genital warts and perianal warts) (ICD-10: A63.0; B07; B07.8).
3. The member has experienced therapeutic failure or intolerance to plan-preferred generic imiquimod 5% cream.

II. Reauthorization

When a benefit, reauthorization of a non-preferred imiquimod product may be approved when all of the following criteria are met **(A. and B.)**:

A. The prescriber attests that the member has experienced positive clinical response to therapy.
B. The prescriber attests that the member requires additional courses of treatment.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 16 week authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Zyclara [package insert]. Bridgewater, NJ: Bausch Health US, LLC; September 2024.
2. Geisse JK, Rich P, Pandya A, et al. Imiquimod 5% Cream for the Treatment of Superficial Basal Cell Carcinoma: A Double-Blind, Randomized, Vehicle-Controlled Study. *J Am Acad Dermatol*. 2002;47(3):390-8.
3. Hengge UR, Esser S, Schultewolter T, et al. Self-Administered Topical 5% Imiquimod for the Treatment of Common Warts and Molluscum Contagiosum. *Br J Dermatol*. 2000;143(5):1026-31.
4. Hazra A, Collison MW, Davis AM. CDC sexually transmitted infections treatment guidelines, 2021. *JAMA*. 2022;327(9):870.
5. Treatment Options for Actinic Keratosis. American Family Physician. Available at: https://www.aafp.org/afp/2007/0901/p667.html. Accessed July 2, 2025.
6. Werner RN, Stockfleth E, Connolly SM, et al. Evidence- and consensus-based (S3) Guidelines for the Treatment of Actinic Keratosis - International League of Dermatological Societies in cooperation with the European Dermatology Forum - Short version. *J Eur Acad Dermatol Venereol* 2015; 29:2069.
7. Eisen DB, Asgari MM, Bennett DD, et al. Guidelines of care for the management of actinic keratosis. *J Am Acad Dermatol*. 2021.
8. Gilson R, Nugent D, Werner RN, Ballesteros J, Ross J. 2019 IUSTI-Europe guideline for the management of anogenital warts. *J Eur Acad Dermatol*. 2020;34(8):1644-1653.