Zelsuvmi (berdazimer) topical gel, 10.3%

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Molluscum contagiosum (molluscum) is a widespread skin infection caused by the molluscum virus, a dermatotropic DNA poxvirus. This condition predominantly affects children and is common worldwide. The infection results in small, flesh-colored papules and papulovesicles, measuring 1-4 mm across, which usually have a distinct umbilicated or dimpled center. These papules are typically not accompanied by much inflammation; however, when an inflammatory response is observed, it often signals the start of disease resolution.

- Although molluscum lesions are generally painless, they might itch or become irritated. Scratching or picking at the bumps can lead to autoinoculation, scarring, or secondary bacterial infections.
- The primary mode of molluscum transmission is through direct person-to-person contact or by autoinoculation. Indirect transmission can occur through touching contaminated items like towels, clothes, or toys.
- In immunocompetent individuals, molluscum contagiosum often resolves spontaneously within 6 to 12 months. Treatment may be warranted to decrease spread, relieve symptoms, or reduce duration.
- It is generally recommended that adolescents and adults with sexually transmitted cases of molluscum contagiosum be treated to reduce the spread of the disease to others, including those who may be immunocompromised.
- Immunocompromised individuals are at a higher risk of extensive and persistent disease, and thus commonly treated to prevent a severe infection.

Molluscum contagiosum is often self-limiting in immunocompetent individuals, but decision to treat may be based on risk of inoculation (to self or others via open lesion or sexual transmission in the case of genital lesions). If one chooses to treat molluscum contagiosum, management options include cryotherapy, curettage, Ycanth (cantharidin) topical solution, or podophyllotoxin. Limited data is available for other therapies (e.g., Zelsuvmi [berdazimer], imiquimod, potassium hydroxide, topical retinoids).

Zelsuvmi (berdazimer topical gel, 10.3%) is a new topical treatment for molluscum contagiosum in those 1 year and older. Zelsuvmi (berdazimer topical gel, 10.3%), is a nitric-oxide releasing agent, however the exact mechanism of action is unknown. The Plan has reviewed available evidence for Zelsuvmi (berdazimer topical gel, 10.3%) and determined that it provides modest incremental benefit over vehicle gel for achieving complete clearance of molluscum lesions after 12 weeks of treatment.
Zelsuvmi (berdazimer) is administered as follows:

- Applied once daily to each MC lesion for up to 12 weeks
- Dispense equal amounts (0.5 mL) of gel from Tube A and Tube B
- Each kit provides about 28 applications with the standard 0.5 mL dose
    - Small area each kit lasts ~28 days
    - Large area each kit lasts ~14 days

Definitions

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"Immunocompetent" means having a functional immune system, not weakened by disease or medication.

"Immunosuppression" refers to a state where the immune system is suppressed, either by specific conditions like HIV, medications, or malignancies.

"Molluscum Contagiosum" is a viral skin infection caused by the molluscipox virus resulting in small, raised, typically painless bumps on the skin.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Molloscum Contagiosum (MC)

The Plan considers Zelsuvmi (berdazimer) medically necessary when ALL of the following criteria are met:

1. The member is 1 year of age or older*; AND*
2. The member has a diagnosis of molluscum contagiosum (MC)*; AND*
3. There is documentation the member meets ONE of the following:
    a. The lesion is located in a sensitive area (e.g., facial or genital area)*; or*
    b. The member has sexually transmitted MC*; or*
    c. The member has atopic dermatitis*; or*
    d. The member is immunocompromised (e.g., members with HIV/AIDS, taking immunosuppressive drugs, cancer, transplant, or underdeveloped immunocompetency)*; or*

e. The member has extensive involvement, experiences bleed(s), secondary infection(s), or discomfort (e.g., pain) from the lesion; *AND*

4. There is documentation the member meets ONE of the following:
    a. The lesion did not have complete resolution within six (6) months since diagnosis*; or*
    b. The member is experiencing bleeding, itching, pain, is sexually active, or there are complications such as secondary infection*; AND*
5. No evidence Zelsuvmi (berdazimer) is used concomitantly with any other pharmacologic treatments for MC (see Summary)*; AND*
6. Zelsuvmi (berdazimer) is being prescribed at a dose and frequency that is within FDA approved labeling including the following:
    a. The dose does not exceed one (1) kit per 14 days.

If the above prior authorization criteria are met, the requested product will be authorized for up to 12-weeks.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Molloscum Contagiosum (MC)

The Plan considers Zelsuvmi (berdazimer) medically necessary when ALL of the following criteria are met:

1. The member meets the above Initial Indication-Specific Criteria; *AND*
2. There is documentation the member has previously experienced a complete or partial clearance of MC lesions with Zelsuvmi (berdazimer); *AND*
3. There is documentation that additional courses of therapy are required for recurrence of MC.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-weeks.[s]

Experimental or Investigational or Unproven / Not Medically Necessary[s]

Zelsuvmi (berdazimer topical gel, 10.3%) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, unproven, or not medically necessary. Non-covered indications include, but are not limited to, the following:

- Condylomata Acuminata, another term for genital warts, referring specifically to the raised, cauliflower-like appearance that these warts can have. They are caused by HPV and are not the same as molluscum contagiosum.

- Genital Warts, warts that appear on the genitalia and are caused by certain strains of HPV. They are not the same as molluscum contagiosum.
- Papilloma Viral Infection, benign tumors that arise from epithelial tissues and are caused by various types of the human papillomavirus (HPV).
- Sexually Transmitted Disease (STD), a broad category of diseases that are primarily transmitted through sexual contact. Both molluscum contagiosum and genital warts (caused by HPV) can be considered STDs, but the term STD includes many other diseases as well, such as chlamydia, gonorrhea, and HIV, to name a few. This does not apply to cases of molloscum contagiosum that are sexually transmitted.
- Verruca (Warts), another term for warts. These are caused by HPV and are distinct from molluscum contagiosum.
- Verruca Vulgaris, i.e., common warts, typically seen on the hands and fingers. They are caused by the human papillomavirus (HPV) and are not the same as molluscum contagiosum.

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Appendix A

Efficacy was studied in 3 clinical trials B-SIMPLE 4, B-SIMPLE 2, and B-SIMPLE 1

- B-SIMPLE 4 (N=891) (NCT04535531):
    - Primary endpoint (complete clearance at Week 12): Berdazimer statistically superior to vehicle (32.4% vs 19.7%, p<0.0001).
        - Treatment difference: 12.8% (95% CI: 7.1% to 18.6%, number needed to treat [NNT] = 8)
    - Key secondary endpoint (complete clearance at Week 8): Berdazimer statistically superior (19.6% vs 11.6%, p=0.0012).
        - Treatment difference: 7.5% (95% CI: 3.0-12.0%, NNT = 14)
    - In an assessment of the Global Impression of Change (GIC) of patients and caregivers who completed B-SIMPLE 4, complete clearance at 12 weeks was reported in 40% of participants (consistent with investigator reports), versus 20% in those who received the vehicle control. Most (82%) of participants reported that their MC was either very much improved or much improved at week 12, versus 60% who received the control (again, consistent with investigator reports). In a subset of 30 participants, most (26/30) reported being very satisfied with their disease changes during the trial duration and 23/30 stated the changes in lesion counts were meaningful despite most (22/28) experienced less than complete lesion clearance at 12 weeks.
- B-SIMPLE 2 (N=355) (NCT03927703):
    - Primary endpoint (complete clearance at Week 12): Berdazimer NOT statistically significant compared to vehicle (30.0% vs 20.3%, p=0.0510).
        - Treatment difference: 9.2% (95% CI: -0.04% to 18.4%).
    - Secondary endpoint (complete clearance at Week 8): Berdazimer statistically superior (13.9% vs 5.9%, treatment difference of 7.8%, NNT = 13).

- B-SIMPLE 1 (N=352) (NCT03927716):
    - Primary endpoint (complete clearance at Week 12): Berdazimer NOT statistically significant compared to vehicle (25.8% vs 21.6%, p=0.3637).
        - Treatment difference: 4.3% (95% CI: -5.0% to 13.6%).
    - Secondary endpoint (complete clearance at Week 8): Berdazimer NOT statistically superior (15.3% vs 10.3%).
- In a post-hoc analysis of B-SIMPLE -4, 2, and 1 (n=1598), the primary endpoint of complete clearance at 12 weeks was assessed in those with or without atopic dermatitis (AD). While those with AD experienced clinically greater clearance on Zelsuvmi (berdazimer) than the vehicle control group (35% versus 27.4%), this was not statistically significant (Odds Ratio [OR] = 1.3, 95% CI, 0.7-2.5). Those without AD experienced a slightly lower clearance rate between Zelsuvmi (berdazimer) and the vehicle control which was statistically significant (29.1% vs 18.9%; OR=1.8, 95% CI 1.4-2.4; NNT = 10). Zelsuvmi (berdazimer) had a higher risk of causing erythema than the vehicle control, which may be difficult to distinguish between a side effect and AD symptoms.

Clinical Guideline Revision / History Information

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