

## 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.

Zelsuvmi (berdazimer topical gel, 10.3%) is a new topical treatment for molluscum contagiosum in patients 1 year and older. 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. Overall, Zelsuvmi (berdazimer topical gel, 10.3%) has not been conclusively proven superior to standard treatments or active non-intervention for this self-limited condition.

### Definitions

“**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.

### Policy Statement on Zelsuvmi (berdazimer topical gel, 10.3%) Efficacy

While Zelsumi (berdazimer sodium) gel 10.3% represents a novel topical treatment option for molluscum contagiosum, the available evidence from the clinical trials is not consistent or robust enough to consider it proven or medically necessary at this time. Across the three phase 3 studies, efficacy results were mixed, with one trial showing clear benefit, and two failing to demonstrate a significant treatment effect. Even in the positive trial, the magnitude of benefit over vehicle gel was modest (e.g. 32.4% vs 19.7% in NI-MC-304, a 12.8% difference).

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%).

- Key secondary endpoint (complete clearance at Week 8): Berdazimer statistically superior (19.6% vs 11.6%, p=0.0012).
- 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%).
- 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%).

### Medical Necessity Criteria for Zelsuvmi (berdazimer topical gel, 10.3%)

The Plan considers Zelsuvmi (berdazimer topical gel, 10.3%) to be not medically necessary for treatment of molluscum contagiosum or any other indication, as available evidence is insufficient to determine that it provides a significant net health benefit over standard therapies or active non-intervention.

### Experimental or Investigational / Not Medically Necessary

Zelsuvmi (berdazimer topical gel, 10.3%) for any indication is considered experimental, investigational, and not medically necessary as current evidence is insufficient to support conclusions regarding long-term efficacy and safety compared with standard treatment options for molluscum contagiosum. The modest benefit provided by Zelsuvmi (berdazimer topical gel, 10.3%) is not clearly superior to active non-intervention for this self-limited condition in light of potential risks. Therefore, the Plan considers Zelsuvmi to be unproven, and not medically necessary.

### References

1. Basdag H et al: Molluscum contagiosum: to treat or not to treat? Experience with 170 children in an outpatient clinic setting in the northeastern United States. *Pediatr Dermatol.* 32(3):353-7, 2015
2. Browning JC, Cartwright M, Thorla I Jr, Martin SA, Olayinka-Amao O, Maeda-Chubachi T. A Patient-Centered Perspective of Molluscum Contagiosum as Reported by B-SIMPLE4 Clinical

Trial Patients and Caregivers: Global Impression of Change and Exit Interview Substudy Results. *Am J Clin Dermatol*. 2023 Jan;24(1):119-133. doi: 10.1007/s40257-022-00733-9. Epub 2022 Oct 26. PMID: 36287306; PMCID: PMC9870829.

3. Forbat E et al: Molluscum contagiosum: review and update on management. *Pediatr Dermatol*. 34(5):504-15, 2017
4. James WD et al: Epidermal nevi, neoplasms, and cysts. In: James WD et al, eds: *Andrews' Diseases of the Skin*. Elsevier; 2020:636-85.e7
5. Maeda-Chubachi T, Hebert D, Messersmith E, Siegfried EC. SB206, a Nitric Oxide-Releasing Topical Medication, Induces the Beginning of the End Sign and Molluscum Clearance. *JID Innov*. 2021 May 5;1(3):100019. doi: 10.1016/j.xjidi.2021.100019. PMID: 34909721; PMCID: PMC8659381.
6. Petersen BW et al: Other poxviruses that infect humans: parapoxviruses (including orf virus), molluscum contagiosum, and Yatapoxviruses. In: Bennett JE et al, eds: *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 9th ed. Elsevier; 2020:1818-21
7. Sugarman JL, Hebert A, Browning JC, Paller AS, Stripling S, Green LJ, Cartwright M, Enloe C, Wells N, Maeda-Chubachi T. Berdazimer gel for molluscum contagiosum: An integrated analysis of 3 randomized controlled trials. *J Am Acad Dermatol*. 2024 Feb;90(2):299-308. doi: 10.1016/j.jaad.2023.09.066. Epub 2023 Oct 5. PMID: 37804936.
8. van der Wouden JC et al: Interventions for nongenital molluscum contagiosum in persons without immune deficiency. *JAMA Dermatol*. 154(2):203-4, 2018
9. Zelsuvmi (berdazimer) [prescribing information]. Wilmington, DE: EPIH SPV LLC; January 2024.

#### Clinical Guideline Revision / History Information

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