Molina Clinical Policy
Zevaskyn (prademagene zamikeracel): MEDICARE
Policy No. 471b

Last Approval: 06/25/2025
Next Review Due By: June 2026

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of the Federal government or CMS for Medicare. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Prademagene zamikeracel is a gene-cell therapy for the treatment of recessive dystrophic epidermolysis bullosa (RDEB). The epidermolysis bullosa (EB) group of disorders are inherited dermatologic disorders associated with skin fragility and blistering. The primary pathology is due to a lack of functional anchoring fibrils that connect the dermis and epidermis together. Those with the severest forms of EB may manifest secondary sequelae that can include skin infections, scarring deformities (scarring that fuses fingers into “mitten hands” and contractures), ocular corneal erosions leading to vision loss and skin cancers that may be lethal. The severity is based on the subtype and variable expressivity of EB. There are four major types of EB: EB simplex (EBS), junctional EB (JEB), Kindler EB (KEB), and dystrophic EB (DEB) in addition to EB related disorders. There are approximately 200 children born every year with EB in the United States (Hayes 2025).

The DEB group is further subdivided by inheritance pattern, dominant or recessive. It is the recessive form of DEB that is potentially treatable by prademagene zamikeracel. RDEB is typically more severe than the dominant form of DEB (DDEB) although there is some phenotypic overlap. Both RDEB and DDEB are caused by mutations in the collagen gene, COL7A1. The recessive form requires both copies of the COL7A1 gene to be dysfunctional or mutated. Type VII collagen helps bind the dermis to the outer epidermis at the basement membrane. Absence of this protein leads to blistering and other sequelae noted above. While initial diagnosis is typically clinical due to visible manifestations, subsequent biopsy, immunofluorescence, and genetic testing is used for prognostication, treatment, and planning purposes (Has 2020).

Current therapies for the majority of EB subtypes are supportive with few targeted therapies. However, in 2023, Vyjuvek a gene therapy for RDEB, was approved. This is a multidose, topical gene therapy directly applied to wounds related to RDEB. Prademagene (Zevaskyn) is now a second therapy for RDEB. Prademagene zamikeracel adds a functional copy of the COL7A1 gene back to the patient’s own keratinocytes. Prademagene is genetically engineered as a sheet of skin cells. Once the patient’s keratinocytes are transduced with the COL7A1 gene, the sheets of keratinocytes begin expressing a normal COL7A1 protein that helps keep dermis & epidermis skin layers together allowing chronic wounds to heal. It takes approximately 26 days to manufacture a graft and about a week of inpatient stay to foster engraftment. The process begins with a keratinocyte isolation from the patient’s skin biopsy, followed by cell culture to grow sufficient cell number, then transduction of the normal col7A1 gene via viral vector, and final cell culture adjusted to allow sheets of skin cells to be produced.

RELATED POLICIES

MCP policy No 439: Vyjuvek (beremagene geperpavec)

COVERAGE POLICY

All Gene Therapy requests require Molina Medical Director review.

Zevaskyn (prademagene zamikeracel) may be **considered medically necessary** when the following criteria are met:

1. A diagnosis of recessive dystrophic epidermolysis bullosa (confirmed by genetic testing)
2. Documentation of pathogenic biallelic COL7A1 gene mutations consistent with recessive dystrophic epidermolysis bullosa
3. At least one clinical feature of RDEB (recessive dystrophic epidermolysis bullosa) including but not limited to blistering, scarring and skin wounds
4. Age 6 years or older
5. Positive expression of the non-collagenous region 1 of the type 7 collagen protein (NC1+) in the skin (NC1 the most antigenic region of collagen VII. EB patients that are NC1[+] are less likely to develop autoimmune reactions to grafted keratinocytes that express functional type VII collagen)
6. At least 40 cm^2 areas of chronically wounded area on the trunk and/or extremities (open erosions)
7. Able to undergo adequate anesthesia during application
8. Negative pregnancy test and not breast-feeding
9. Women of childbearing potential must use a reliable birth control method throughout the duration of the treatment and for 6 months post treatment
10. Must be on stable pain medication regimen at least 30 days prior to therapy
11. Absence of active infection with human immunodeficiency virus (HIV), hepatitis B or hepatitis C
12. Absence of evidence of systemic infection
13. No evidence or a history of squamous cell carcinoma (SCC) in the area that will undergo treatment
14. No evidence of immune response to C7 by indirect immunofluorescence (IIF) on skin biopsy
15. Absence of active drug or alcohol addiction
16. Hypersensitivity to vancomycin or amikacin
17. Clinical event or laboratory abnormality grade 3 or higher on the National Cancer Institute [NCI] toxicity scale. (Abnormalities such as esophageal strictures, anemia, low albumin, and pain/itch are expected in RDEB patients. These abnormalities will not exclude a participant. [9]NCI Common Terminology Criteria for Adverse Events version 5)

Limitations and Exclusions

QUANTITY LIMITATIONS: The recommended dose of ZEVASKYN is based on the surface area of the wound(s). One sheet of ZEVASKYN covers an area of 41.25 cm^2. Up to twelve ZEVASKYN sheets may be manufactured from the patient biopsies and supplied for potential use.

Continuation of Therapy

Repeat administration of Zevaskyn to the same area is considered **experimental, investigational, and unproven** due to insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

The FDA approval of Prademagene was based on a compilation of data from phase 3 and phase 1/2a trials. The phase 3 trial (NCT04227106) results are not published in a peer reviewed journal at this time. The phase 3 trial was presented at an international conference in 2023. Those results indicated improved wound healing and decreased wound pain. The abstract authored by Tang (2023), described the phase 3 trial and results. In brief, the phase 3 trial (VIITAL) was a randomized, intra-patient controlled trial of prademagene for the treatment of RDEB patients, with ages ranging from 6 years to 40 years. The trial looked at the safety and efficacy of prademagene applied to 43 randomized, chronic wounds in 11 patients. Intra-patient controls were matched wounds (in the same patient) for a total of 43 control wounds. Control wounds were managed with standard of care wound treatment. Prademagene treated wounds had ≥50% healing from baseline (BL) vs 16.3% (7/43) of control wounds (P<0.0001) at 24 weeks. Wound healing in the prademagene treated group was ≥75% from BL in 65.1% of treated wounds vs 7.0% of controls (P<0.0001). Complete wound healing was achieved in 16.3% of Prademagene treated wounds vs 0% of controls (P=0.0160). Pain scores were assessed on a 0-10 scale and were reduced for the treatment group as compared to the controls. Prademagene was well tolerated and did not have serious treatment-related adverse events.

Eichstadt (2019) reported results from the phase 1/2a clinical trial (NCT0126337). That trial was a Phase 1/2a, single center, open label, study to evaluate the efficacy and safety of Prademagene in patients diagnosed with RDEB. Sheets of autologous keratinocytes were genetically engineered with COL7A1 gene then grown and transplanted onto 6 wound sites per person in a total of 7 people. These 42 wound sites were followed for a mean of 2.7 years and compared to untreated chronic wounds. Wounds selected for treatment had been present for mean of 11.2 years. Median age of participants were 28.7 years

The primary endpoint was The Investigator Global Assessment (IGA) of wound healing at various time points at graft sites. At 6 months 95% of treated wounds (36 of 38) had 50% or greater wound healing versus 0% of untreated controls. At year 2, 71% (27 of 38) treated wounds had 50% or greater healing compared with 17% of control wounds. Patient reported outcomes were recorded for pain, itch and wound durability. Participants reported improvement at treated sites for all subjective measures and a reduced ease of blistering at treated sites at all measured time points.

No serious adverse events were reported. Common adverse events were infection (n=2), pruritis (n=3) and pain around the treated sites (n=1). While there was evidence of a localized immune response to the expressed COL7A1 protein in one participant, there were no systemic responses and even the one person with a local immune response never developed systemic immunity. Two participants developed squamous cell carcinomas, but all tumors were distant to the grafted tissue. Squamous cell cancers are the leading cause of death in RDEB, and the squamous cell cancers may have been related to disease progression.

So et al. (2022) reported 5-year follow-up results (mean 5.9 years) from phase 1/2a clinical trial (NCT0126337). After six months of treatment with prademagene 92.9% of wounds healed by greater than or equal to 50%, however, at year five only 70% of wounds had greater than 50% wound healing. Significant improvement in patient report outcomes such as pain and itch at grafted sites remained improved. At 5 years there were no serious adverse events related to treatment. The authors note that at 70% of wounds with 50% or more healing prademagene appears to be durable.

Two additional trials are underway. NCT05708677 is the long-term extension trial for those with RDEB previously treated with prademagene. NCT05725018 is a phase 3b study for patients 12 months of age and older.

National/Specialty Organizations

The **National Institute for Health and Care Excellence (NICE)** does not have published guidelines on prademagene yet. Other subspecialty organizations have not included prademagene in their guidelines either.

CODING & BILLING INFORMATION

HCPCS (Healthcare Common Procedure Coding System)

HCPCS	Description
C9399	Unclassified drugs or biologicals [when specified as ZEVASKYN (prademagene zamikeracel)]
J3590	Unclassified biologics [when specified as ZEVASKYN (prademagene zamikeracel)]

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

06/25/2025 New policy. IRO Peer Review on June 3, 2025, by a practicing physician board-certified in Dermatology.

REFERENCES

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8. Zevaskyn (Prademagene Zamikeracel) Prescribing information. United States Food and Drug Administration (FDA). April 2025. ZEVASKYN_Final_Label_30Apr2025.pdf