Drug Coverage Policy

Effective Date……12/15/2025
Coverage Policy Number……IP0747
Policy Title……Zevaskyn

Dermatology – Gene Therapy – Zevaskyn

- **Zevaskyn™ (prademagene zamikeracel gene-modified cellular sheets – Abeona)**

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW
*Zevaskyn, an autologous cell sheet-based gene therapy, is indicated for the treatment of wounds with **recessive dystrophic epidermolysis bullosa** (RDEB) in adult and pediatric patients.[1]*

Zevaskyn is composed of autologous cells isolated from skin punch biopsies of patients with mutation in the collagen type VII alpha 1 chain (COL7A1) gene.[1] The cells have been transduced ex vivo with a replication-incompetent retroviral vector (RRV) containing the full length COL7A1 gene. The cell sheets express function collagen VII protein. Up to twelve, 41.25 cm^2 sheets may be manufactured from the patients biopsy and surgically applied.

Disease Overview
Dystrophic epidermolysis bullosa (DEB) can be inherited in a dominant or recessive pattern.[4-6] All subtypes of DEB are caused by mutations in the gene coding COL7A1 leading to extreme skin fragility. The hallmark of DEB is scarring of blisters, both on the skin and on other mucosal surfaces. The estimated incidence and prevalence of DEB vary. The prevalence of all types of DEB in the US has been estimated as approximately 6 per 1 million individuals. The incidence of RDEB in the US has been reported as 3.05 per 1 million live births.

Clinical Efficacy
VIITAL, a Phase III, multicenter, randomized, intrapatient-controlled, pivotal study, assigned patients with RDEB to treat two matched, large wounds; one with Zevaskyn and one with standard of care wound dressings (N = 11 [86 wounds]).[1] Eligible patients were required to be ≥ 6 years of age, have at least 1 pair of matched, large (≥ 20 cm^2), and chronic wounds (open for ≥ 6 months) associated with RDEB. Patients with current or a history of squamous-cell carcinoma at the treatment site or systemic infection were excluded. A total of 86 wounds were treated with Zevaskyn or standard of care. At Month 6, significantly more Zevaskyn- vs. standard of care-treated wounds were healed (35 wounds [81%] vs. 7 wounds [16%], respectively; $P < 0.0001$) and reported pain reduction (-3.07 vs. -0.90, respectively; $P = 0.0002$)[co-primary endpoint]. Secondary endpoints of complete wound healing at Months 3 and 6 were not found to be statistically significant; however, favored Zevaskyn over placebo. At Month 3, 6 wounds (14%) showed complete healing for Zevaskyn vs 0 wounds for standard of care and similar results were seen at Month 6 (7 wounds [16%] vs 0 wounds, respectively).

Dosing Information
The recommended dose is based on the surface area of the wound(s).[1] Up to twelve 41.23 cm^2 sheets of Zevaskyn may be manufactured from the patient biopsies and supplied for use. To administer Zevaskyn, the wound(s) need to be prepared with debridement. Apply full sheets of Zevaskyn onto the wound bed with resorbable sutures. All sheets must be applied in one sterile surgical procedure and the application sites must be covered with non-adhesive dressing. Patients should leave the treated area undisturbed for 5 to 10 days and should be kept dry until the gauze backing falls off (within 2 to 3 weeks).

Guidelines
Zevaskyn is not addressed in available guidelines. According to a position statement by the **European Reference Network for Rare Skin Diseases** (2021), wound care is the cornerstone of treatment for patients with DEB.[2] Careful and complete skin and wound assessment should be undertaken regularly, at least every 6 months. The healing rate of chronic wounds should be closely monitored, by checking wound edges.

The diagnosis of DEB is based on a combination of clinical features, family history, and laboratory findings.[2] Laboratory techniques include immunofluorescence mapping, transmission electron microscopy, and molecular genetic testing. Whenever possible, laboratory diagnosis should be performed in a specialized DEB center. Genetic testing is the gold standard for the diagnosis of DEB, since it provides a definitive diagnosis and classification of the major DEB type and in many cases the subtype.

An **international consensus best practice guideline** on skin and wound care in epidermolysis bullosa (EB) [2017] notes that EB is a lifelong disease that requires specialist intervention and consideration to minimize complications and improve quality of life.[3] Management should take place in a specialized center by a multi-disciplinary team, ideally. Definitive diagnosis is most commonly made from analysis of skin biopsy using positive immunofluorescence, antigenic mapping, and transmission electron microscopy. These key diagnostic tools help confirm diagnosis and indicate the particular subtype of EB. Due to the rarity of expertise and facilities, diagnosis is generally made using immunofluorescence and antigen mapping. Some laboratories are moving towards molecular diagnosis from exome sequencing of a panel of known skin fragility genes. Experienced clinicians can often make a provisional diagnosis on clinical observations, but a definitive diagnosis will always be required.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of Zevaskyn. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Zevaskyn as well as the monitoring required for adverse events and long-term efficacy, approval requires Zevaskyn to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of Zevaskyn as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and/or other information.

Zevaskyn is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Dystrophic Epidermolysis Bullosa; Recessive.** Approve a single application (up to 12 sheets) if the patient meets ALL of the following (A, B, and C):
   - **A)** The diagnosis is confirmed by genetic testing showing a pathogenic variant in both alleles in the collagen type VII alpha 1 chain (COL7A1) gene **[documentation required]**; AND
   - **B)** Patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient has at least one clinical feature of recessive dystrophic epidermolysis bullosa **[documentation required]**; AND
       Note: Examples of clinical features of recessive dystrophic epidermolysis bullosa include but are not limited to blistering, wounds, and scarring.
     - **ii.** Patient has one or more open wound(s) that will be treated (i.e., "target wound[s]); AND
     - **iii.** Target wound(s) meets ALL of the following, according to the prescriber (a, b, c and d):
       - **a)** Target wound(s) is clean in appearance and does not appear to be infected; AND
       - **b)** Target wound(s) has adequate granulation tissue and vascularization; AND
       - **c)** Target wound(s) is chronic wound(s) (present ≥ 6 months); AND

d) The prescriber attests that there is no evidence or clinical suspicion of squamous cell carcinoma identified at the target wound(s); AND

e) The prescriber attests that the medication has NOT been previously applied to the target wound(s); AND

C) The medication is prescribed by or in consultation with a dermatologist or wound care specialist.

Dosing. Approve one application of up to 12 gene-modified cellular sheets.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Zevaskyn for any other use is considered not medically necessary. Criteria will be updated as newly published data are available.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals (Code effective until 12/31/2025)
J3389	Topical administration, prademagene zamikeracel, per treatment (Code effective 1/1/2026)
J3490	Unclassified drugs (Code effective until 12/31/2025)
J3590	Unclassified biologic (Code effective until 12/31/2025)

References

1. Zevaskyn™ gene-modified cellular sheets [prescribing information]. Cleveland, OH: Abeona Therapeutics; April 2025.
2. Has C, El Hachem M, Buckova H, et al. Practical management of epidermolysis bullosa: consensus clinical position statement from the European Reference Network for Rare Skin Diseases. *J Eur Acad Derm Venereol.* 2021;35:2349-2360.
3. Denyer J, Pillay E, Clapham J. Best practice guidelines for skin and wound care in epidermolysis bullosa. An International Consensus. *Wounds International.* 2017. Available at: https://af13d689-15eb-4199-8733-e91a7bb8ae3f.usrfiles.com/ugd/af13d6_01ed147ab87e49c584c20a917c47f19f.pdf. Accessed on: May 8, 2025.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy.	08/15/2025
Selected Revision	**Dystrophic Epidermolysis Bullosa; Recessive:** The requirement the prescriber attests that the medication has not been previously applied to the target wound(s) was added. The requirement "squamous cell carcinoma has been considered for the target wound(s)" was modified to "the prescriber attests that there is no evidence or clinical suspicion of squamous cell carcinoma at the target wound(s)". Coding Information: **Added HCPCS: C9399 & J3490**	10/15/2025
Selected Revision	Coding Information **Added** HCPCS: J3389 with a note "Code effective 1/1/2026" **Updated** the description for C9399, J3490 & J3590 to include the note "Code effective until 12/31/2025"	12/15/2025

The policy effective date is in force until updated or retired.