LOUISIANA BLUE

beremagene geperpavec-svdt (Vyjuvek™)

Policy # 00864
Original Effective Date: 02/12/2024
Current Effective Date: 02/10/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider beremagene geperpavec-svdt (Vyjuvek™)‡ for the treatment of dystrophic epidermolysis bullosa to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for beremagene geperpavec-svdt (Vyjuvek) will be considered when the following criteria are met:

- Initial (6 months)
  - Patient has a diagnosis of dystrophic epidermolysis bullosa (DEB) with genetic testing confirming pathogenic variant in the *collagen type VII alpha 1 chain* (*COL7A1*) gene; AND
  - Patient is greater than or equal to 6 months of age; AND
  - Patient has open DEB skin wounds and application of Vyjuvek is limited to open DEB skin wounds only; AND
  - Patient has at least one clinical feature of DEB (e.g., blistering, wounds, scarring); AND
  - Patient does not have any of the following:
    - Current evidence or history of squamous cell carcinoma in the area that will undergo treatment; OR
    - Recent skin graft in the past 3 months; OR
    - Presence of active infection in the area to be treated; AND

    *(Note: These specific patient selection criteria are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Dosing does not exceed maximum weekly dose of 2.5 mL (1 vial) per week, or 10 mL (4 vials) every 28 days.

- Continuation
  - Patient has received an initial authorization for Vyjuvek; AND
  - Wounds are improving according to the treating provider; AND
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Dosing does not exceed maximum weekly dose of 2.5 mL (1 vial) per week, or 10 mL (4 vials) every 28 days.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of beremagene geperpavec-svdt (Vyjuvek) when the patient has evidence or history of squamous cell carcinoma, active infection, or recent skin graft in the area to be treated to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of beremagene geperpavec-svdt (Vyjuvek) when the treated wounds are not improving to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of beremagene geperpavec-svdt (Vyjuvek) when patient selection criteria are not met (except those noted above as **not medically necessary****) to be **investigational.***

Background/Overview

Vyjuvek is a herpes-simplex virus type-1 (HSV-1) vector-based gene therapy indicated for the treatment of wounds in patients ≥6 months of age with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the *collagen type VII alpha 1 chain* (*COL7A1*) gene. It is formulated as a gel containing a live, replication defective HSV-1 based vector that has been genetically modified to express the human type VII collagen (COL7) protein. This protein is defective or deficient in patients with DEB. Vyjuvek is dosed weekly by application of the gel by a healthcare professional to open wound(s). The maximum weekly dose is 1.6×10^9 plaque forming units (PFUs) in patients less than 3 years of age or 3.2×10^9 PFUs in patients greater than or equal to 3 years of age. It may not be possible to treat all wounds at each visit. Vyjuvek should be applied until wound(s) are closed before selecting new wound(s) to treat.

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DEB is a rare skin condition that can be inherited in a dominant (DDEB) or recessive (RDEB) pattern, with RDEB typically being more severe. Both subtypes are caused by mutations in the *COL7A1* gene leading to reduced or absent production of the protein COL7, a crucial component of anchoring fibrils which attach the epidermis to the dermis. This deficiency leads to extreme skin fragility that varies in severity depending on if the mutation predisposes to mild or severe disease and whether the patient has completely absent or reduced COL7. The hallmark symptom of DEB is scarring of blisters, both on the skin and on other mucosal surfaces. Secondary extracutaneous complications are common in more severe forms of RDEB. Pain and itching can be constant and also reduce quality of life. Skin and oral mucosal scarring or nail loss can be irreversible and progressive, becoming more pronounced with age. RDEB forms are usually more generalized and characterized by scarring, leading to progressive fusion of fingers and toes resulting in mitten deformities and joint contracture, as well as by major involvement of the mucous membranes (oral cavity and esophagus). Anemia, reduced bone mineral density, renal impairment, and the development of squamous cell carcinoma are also potential complications of severe RDEB. However, there is variability. Early onset and aggressive squamous cell carcinoma at chronic wound sites is typical of RDEB; aggressive squamous-cell cancer is the leading cause of death in patients with DEB.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Vyjuvek was approved in May 2023 for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the *collagen type VII alpha 1 chain (COL7A1)* gene.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Vyjuvek gel in subjects one year of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the *COL7A1* gene was evaluated in one randomized, double-blind, intra-subject placebo-controlled trial. All study subjects had clinical manifestations consistent with DEB and genetically confirmed mutation(s) in the *COL7A1* gene. Two comparable wounds in each subject were selected and randomized to receive either topical application of Vyjuvek gel or the placebo weekly for 26 weeks.

The study enrolled 31 subjects, including 30 subjects with autosomal recessive DEB and one subjected with autosomal dominant DEB. The size of the Vyjuvek gel-treated wounds ranged from 2 to 57 cm^2, with 74% of wounds <20 cm^2 and 19% from 20 to <40 cm^2. The size of the placebo-treated wounds ranged from 2 to 52 cm^2, with 71% of wounds <20 cm^2 and 26% from 20 to <40 cm^2.

Efficacy was established on the basis of improved wound healing defined as the difference in the proportion of complete (100%) wound closure at 24 Weeks confirmed at two consecutive study visits 2 weeks apart, assessed at Weeks 22 and 24 or at Weeks 24 and 26, between the Vyjuvek gel-treated and the placebo gel-treated wounds. Efficacy was supported by the difference in the proportion of complete wound closure assessed at Weeks 8 and 10 or at Weeks 10 and 12 between the Vyjuvek gel-treated and the placebo gel-treated wounds. Complete wound closure was defined as durable wound closure evaluated at two consecutive visits two weeks apart. At Weeks 22&24 or 24&26, 65% (n=20) of the Vyjuvek gel-treated wounds met criteria for complete wound closure compared to 26% (n=8) of the placebo gel-treated wounds (p=0.012). At Weeks 8&10 or 10&12, 68% (n=21) of the Vyjuvek gel-treated wounds met criteria for complete wound closure compared to 23% (n=7) of the placebo gel-treated wounds (p=0.003).

References

1. Vyjuvek [package insert]. Krystal Biotech, Inc. Pittsburgh, PA. Updated July 2023.
2. Vyjuvek Drug Evaluation. Express Scripts. Updated May 2023.

Policy History

Original Effective Date: 02/12/2024
Current Effective Date: 02/10/2025
01/04/2024 Medical Policy Committee review
01/10/2024 Medical Policy Implementation Committee approval. New policy.
01/02/2025 Medical Policy Committee review
01/08/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 01/2026

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3401
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

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**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.