Vyjuvek® (Beramagene Geperpavec-Svdt)

Policy Number: CS2024D00127E
Effective Date: July 1, 2024

➲ Instructions for Use

Table of Contents **Page**

Commercial Policy
• Vyjuvek® (Beramagene Geperpavec-Svdt)

Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

State	Policy/Guideline
Indiana	None
Kansas	None
Louisiana	Refer to the state's Medicaid clinical policy
North Carolina	None
Ohio	Vyjuvek® (Beramagene Geperpavec-Svdt) (for Ohio Only)
Texas	Refer to drug-specific criteria found within the Texas Medicaid Provider Procedures Manual

Coverage Rationale

Vyjuvek (beramagene geperpavec-svdt) is proven and medically necessary for the treatment of wounds in patients with dystrophic epidermolysis bullosa (DEB) who meet all of the following criteria:

- For **initial therapy**, **all** of the following:
  - Patient is aged at least 6 months and older; **and**
  - Diagnosis of dystrophic epidermolysis bullosa (DEB); **and**
  - Submission of medical records (e.g., chart notes, laboratory values) confirming a mutation in the collagen type VII alpha 1 chain (*COL7A1*) gene; **and**
  - Patient has at least **one** recurrent or chronic open wound that meets all of the following criteria:
    - Adequate granulation tissue
    - Excellent vascularization
    - No evidence of active wound infection
    - No evidence or history of squamous cell carcinoma

    and
  - Vyjuvek is prescribed by, or in consultation with, a dermatologist with expertise in the treatment of DEB; **and**
  - Vyjuvek is not being used in combination with Filsuvez (birch triterpenes) on the same wound(s); **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be issued for no more than 12 months and no more than 52 doses
- For **continuation of therapy**, **all** of the following:
  - Patient has been previously treated with Vyjuvek therapy; **and**

- Patient had a positive clinical response to Vyjuvek therapy (e.g., decrease in wound size, increase in granulation tissue, complete wound closure); **and**
- Wound(s) being treated to meet **all** of the following criteria:
  - Adequate granulation tissue; **and**
  - Excellent vascularization; **and**
  - No evidence of active wound infection; **and**
  - No evidence or history of squamous cell carcinoma

  and
- Vyjuvek is prescribed by, or in consultation with, a dermatologist with expertise in the treatment of DEB; **and**
- Vyjuvek is not being used in combination with Filsuvez (birch triterpenes) on the same wound(s); **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Reauthorization will be issued for no more than 12 months and no more than 52 doses

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J3401	Beremagene geperpavec-svdt for topical administration, containing nominal 5 x 10 < sup > 9 </sup > PFU/ml vector genomes, per 0.1 ml

Diagnosis Code	Description
Q81.2	Epidermolysis bullosa dystrophica

Background

Dystrophic epidermolysis bullosa (DEB) is an ultra-rare genetic connective tissue disorder caused by mutations in the collagen type VII alpha 1 chain (*COL7A1*) gene.[1-2] The *COL7A1* gene codes for type VII collagen (C7), a major component of structures in the skin called anchoring fibrils found in the epidermal basement membrane located between the epidermis (top layer of skin) and dermis (underlying layer). Mutations in the *COL7A1* gene disrupt adhesion of the epidermis to the dermis. Patients with EB completely lack or are deficient in *COL7A1*, resulting in skin fragility and multiple recurring wounds that are difficult to manage. Over time, repeated blistering and fibrosis can lead to squamous-cell carcinoma, life-threating infections, and limb deformities. DEB may be inherited as a dominant or recessive trait; generally, RDEB is more severe than dominant disease (DDEB); however, there is considerable phenotypic overlap between types. DEB affects approximately 9,000 people globally, including approximately 3,000 people in the U.S. and approximately 3,000 in Europe. The current standard of care is supportive treatment with wound care and prevention of infection.

Vyjuvek is a topical gene therapy that uses a herpes simplex virus (HSV-1) to introduce a normal copy of the *COL7A1* gene to patients' skin cells. Once Vyjuvek enters the nucleus of transduced cells, the vector genome is deposited episomally and as a result, *COL7A1* transcripts are generated, allowing the cell to produce and secrete functional *CO7A1* protein necessary for the formation of anchoring fibrils that bind the dermis and epidermis together, and blistered skin to be replaced with healthy skin. The *COL7A1* gene does not incorporate itself into patients' chromosomes; therefore, patients must be treated with Vyjuvek repeatedly in order to continue producing healthy skin.

Clinical Evidence

Proven

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.[1-2] 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 (excipient gel) weekly for 26 weeks. The study enrolled 31 subjects (20 males and 11 females), including 30 subjects with autosomal recessive DEB and one subject 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 gel-treated wounds ranged from 2 to 52 cm^2, with 71% of wounds < 20 cm^2 and 26% from 20 to < 40 cm^2. The mean age of the subjects was 17 years (1 year to 44 years), including 61% pediatric subjects (n = 19, age from 1 year to < 17 years). Sixty-four percent of subjects were White; 19% were Asian, and the remainder were American Indian or Alaska Native. 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 (100%) wound closure was defined as durable wound closure evaluated at two consecutive visits two weeks apart. At 6 months, complete wound healing occurred in 67% of the wounds exposed to B-VEC as compared with 22% of those exposed to placebo [difference, 46 percentage points; 95% confidence interval (CI), 24 to 68; p = 0.002]. Complete wound healing at 3 months occurred in 71% of the wounds exposed to B-VEC as compared with 20% of those exposed to placebo (difference, 51 percentage points; 95% CI, 29 to 73; p < 0.001). The mean change from baseline to week 22 in pain severity during wound-dressing changes was -0.88 with B-VEC and -0.71 with placebo (adjusted least-squares mean difference, -0.61; 95% CI, -1.10 to -0.13); similar mean changes were observed at Weeks 24 and 26.

A total of 18 patients (58%) had at least one adverse event (Table 4). The majority of adverse events were mild or moderate in severity, as assessed by the investigators. Five serious adverse events occurred in 3 patients: 1 patient was hospitalized three times, once for diarrhea and twice for severe anemia; 1 patient was hospitalized for treatment of cellulitis; and 1 patient was hospitalized for a positive blood culture related to a hemodialysis catheter. None of the serious adverse events were considered to be related to B-VEC or placebo by the investigators. One adverse event, mild erythema, was considered to be related to B-VEC. No adverse events led to discontinuation of B-VEC or placebo. The most common adverse events were pruritus, chills, and squamous-cell carcinoma of the skin, each of which occurred in 3 patients (10%). All three cases of squamous-cell carcinoma occurred at wound sites that had not been exposed to B-VEC or placebo.

To determine potential immunogenicity, levels of antibodies against HSV-1 and C7 before and after treatment were assessed. Because of the difficulty of venipuncture in these patients, 22 of 31 patients (71%) had baseline serum samples. Among the patients with baseline samples, 14 of 22 patients (64%) had antibodies against HSV-1, a finding consistent with the prevalence of seropositivity in the U.S. population, 21 and 1 of 22 patients (5%) had antibodies against C7. Among the patients with baseline samples, 19 had samples at both baseline and week 26, including the patient who had antibodies against C7. By week 26, seroconversion had occurred in 6 of 8 patients (75%) with no antibodies against HSV-1 at baseline (Fig. S4) and in 13 of 18 (72%) with no antibodies against C7 at baseline. No clinically significant immunologic reactions were reported. Treatment response to B-VEC was not associated with baseline HSV-1 serostatus (Table S5) or C7 seroconversion (Table S6).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Vyjuvek (beramagene geperpavec-svdt) 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 and older with dystrophic epidermolysis bullosa with mutation(s) in the collagen type VII alpha 1 chain (*COL7A1*) gene.[1]

References

1. Vyjuvek package insert]. Pittsburg, PA: Krystal Biotech, Inc.; May 2023.
2. Guide SV, Gonzalez ME, Bağcı IS, Agostini B, Chen H, Feeney G, Steimer M, Kapadia B, Sridhar K, Quesada Sanchez L, Gonzalez F, Van Ligten M, Parry TJ, Chitra S, Kammerman LA, Krishnan S, Marinkovich MP. Trial of Beremagene Geperpavec (B-VEC) for Dystrophic Epidermolysis Bullosa. N Engl J Med. 2022 Dec 15;387(24):2211-2219. doi: 10.1056/NEJMoa2206663. PMID: 36516090.
3. A Phase III Efficacy and Safety Study of Beremagene Geperpavec (B-VEC, Previously "KB103") for the Treatment of Dystrophic Epidermolysis Bullosa (DEB). ClinicalTrials.gov identifier: NCT04491604. Updated February 17, 2023. https://classic.clinicaltrials.gov/ct2/show/study/NCT04491604. Accessed January 30, 2024.
4. Open Label Treatment of Beremagene Geperpavec (B-VEC). ClinicalTrials.gov identifier: NCT04917874. Updated April 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04917874. Accessed January 30, 2024.
5. Filsuvez [package insert]. Boston, MA: Chiesi Global Rare Diseases; January 2024.

Policy History/Revision Information

Date	Summary of Changes
07/01/2024	**Coverage Rationale** • Revised coverage criteria for initial therapy; added criterion requiring Vyjuvek is not used in combination with Filsuvez (birch triterpenes) on the same wound(s) **Supporting Information** • Updated *References* section to reflect the most current information • Archived previous policy version CS2024D00127D

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state, or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state, or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state, or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state, or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.