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**Revised: 01/01/24**

# Subject: Beremagene Geperpavec-svdt (Vyjuvek®) Biological Suspension

**THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.**


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|---|---|---|---|---|---|
| Dosage/ Administration | Position Statement | Billing/Coding | Reimbursement | Program Exceptions | Definitions |
| Related Guidelines | Other | References | Updates | | |


## DESCRIPTION:

Dystrophic epidermolysis bullosa (DEB) is caused by mutations in the *collagen type VII alpha 1 chain (COL7A1)* gene which results in reduced or absent levels of human type VII collagen (COL7) protein. The COL7 molecule arranges into bungles that form anchoring fibrils. The anchoring fibrils hold the epidermis and dermis together to maintain the integrity of the skin. Patients with autosomal dominant DEB have lower than normal functional anchoring fibrils and patients with recessive DEB have no functional anchoring fibrils which manifests as a more severe form the disease. Clinical manifestations of severe disease include fragility of the skin and mucosal surfaces which result in recurrent blisters, chronic wounds, and/or erosions of the skin and/or oral mucosa that result in severe scarring, deformities (e.g. fusion of skin, loss of nails, contractures, hair loss), and infection. Pruritis is common which makes healing difficult if there is trauma from scratching. Esophageal erosions and strictures are a common feature which lead to painful dysphagia and subsequent nutritional deficiencies, electrolyte abnormalities, and anemia. Genitourinary erosions may result in urinary retention and scarring of ocular mucosal membranes can result in vision loss. Patients with the recessive form of DEB are at higher risk of developing aggressive squamous cell carcinomas (SCC) at chronic wound sites and mortality from SCC has been estimated at 84% by 40 years of age. Treatment of DEB is supportive and includes wound care, control of pruritis and pain, preventing infection, nutritional support, and control of any additional presenting symptoms.

Beremagene geperpavec-svdt (Vyjuvek) biological suspension is FDA-approved for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa with mutation(s) in the *COL7A1* gene. Beremagene geperpavec is a genetically modified, herpes-simplex virus type 1 (HSV-1) vector-based non-integrating gene therapy that expresses the COL7 protein. It will not replicate in

the subject's cells and does not integrate into the subject cells' native genetic material. It is mixed with a sterile excipient gel for topical application on wounds. Following topical application, beremagene geperpavec is introduced into keratinocytes and fibroblasts. Once it has entered into the cells, the vector is deposited into the nucleus and transcription of the encoded human *COL7A1* is initiated. This permits production and secretion of COL7 by the cell and production of anchoring fibrils.

The efficacy of beremagene geperpavec was evaluated in a randomized, double-blind, intra-subject placebo-controlled trial over 24 weeks. There were 31 subjects with clinical manifestations consistent with DEB and genetically confirmed mutations in the COL7A1 gene (30 with autosomal recessive DEB and 1 with autosomal dominant DEB). Subjects 6 months of age or older were included if there were two open wounds similar in regard to location and size and if the wound was clean with adequate granulation tissue, excellent vascularization, and no appearance of active infection. Patients were excluded if there was evidence or a history of SCC in the area to be treated, active infection in the area to be treated, or if they had received a skin graft in the past 3 months. Two wounds in each subject were selected and randomized to be treated with either beremagene geperpavec or placebo for 26 weeks until complete wound closure. The size of wound ranged from 2 to 57 $cm^2$ and over 70% of the wounds measured less than 20 $cm^2$. Efficacy was established on the basis of improved wound healing defined as the difference in the proportion of complete wound closure at 24 weeks confirmed at two consecutive study visits 2 weeks apart at assessment time points. Complete (100%) wound closure was defined as durable wound closure evaluated at two consecutive visits two weeks apart. Table 1 shows improvement in the proportion of subjects with complete wound closure with the use of beremagene geperpavec as compared to placebo. The most common adverse reactions were itching, chills, redness, rash, cough, and runny nose.

### Table 1: Summary of Wound Closure Efficacy

| **Wound Closure Assessment Timepoints** | **Complete Wound Closure, n (%) n=31** | | **Treatment difference (95% confidence interval)** | **P-value** |
|---|---|---|---|---|
| | **Beremagene geperpavec** | **Placebo** | | |
| Weeks 22 & 24, or weeks 24 & 26 | 20 (65%) | 8 (26%) | 39% (14,63) | 0.012 |
| Weeks 8 & 10, or weeks 10 & 12 | 21 (68%) | 7 (23%) | 45% (22,69) | 0.003 |

## POSITION STATEMENT:

Initiation of beremagene geperpavec-svdt (Vyjuvek) biological suspension **meets the definition of medical necessity** when **ALL** of the indication- specific criteria are met:

1. Dystrophic Epidermolysis Bullosa (DEB)
    a. Member meets **ALL** of the following - documentation must be provided:
        i. Mutation in the collagen type VII alpha 1 chain (COL7A1) gene
        ii. Wound to be treated is open and clean with adequate granulation tissue, excellent vascularization, and no appearance of active infection

b. The member does not have current evidence or a history of squamous cell carcinoma in the area to be treated

c. The member does not have evidence of an active systemic infection

d. The member has not received a skin graft in the past 3 months

e. Treatment is prescribed by or in consultation with a specialist (dermatologist, geneticist)

f. The dose does not exceed one single dose vial (containing $5x10^9$ plaque forming units(PFU) per mL) every 7 days

**Approval duration**: 6 months

Continuation of beremagene geperpavec-svdt (Vyjuvek) biological suspension **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. An authorization or reauthorization for beremagene geperpavec has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of dystrophic epidermolysis bullosa, **OR** the member has previously met **ALL** indication-specific criteria.
2. Member meets **ALL** of the following – documentation must be provided:
   a. Mutation in the collagen type VII alpha 1 chain (COL7A1) gene
   b. Wound to be treated is open and clean with adequate granulation tissue, excellent vascularization, and no appearance of active infection
3. The member had a beneficial response to treatment with evidence of improved wound healing (closure or reduction in wound area from baseline).
4. The member does not have current evidence or a history of squamous cell carcinoma in the area to be treated.
5. The member does not have evidence of an active systemic infection.
6. The member has not received a skin graft in the past 3 months.
7. Treatment is prescribed by or in consultation with a specialist (dermatologist, geneticist).
8. The dose does not exceed one single dose vial (containing $5x10^9$ plaque forming units (PFU) per mL) every 7 days.

**Approval duration**: 6 months

## DOSAGE/ADMINISTRATION:

**THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.**

**FDA-approved –** 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.

| Age Range | Maximum weekly dose (plaque forming units; PFU) | Maximum weekly volume (mL) after mixing with excipient gel |
|---|---|---|

| | | |
|---|---|---|
| 6 months to less than 3 years old | $1.6 \times 10^9$ | 0.8 |
| 3 years old or greater | $3.2 \times 10^9$ | 1.6 |

Apply on wounds once a week in droplets spaced evenly within the wound, approximately 1cm-by-1cm apart. The table below provides a reference on dose per approximate size of the wound. See prescribing information on preparation, handling, and administration.

| Wound area ($cm^2$)* | Dose (plaque forming units; PFU) | Volume (mL) |
|---|---|---|
| Less than 20 | $4 \times 10^8$ | 0.2 |
| 20 to less than 40 | $8 \times 10^8$ | 0.4 |
| 40 to 60 | $1.2 \times 10^9$ | 0.6 |
| *For wound area over 60 $cm^2$, recommend calculating the total dose based on this table until maximum weekly dose is reached. | | |

**Drug Availability**

Biological suspension, mixed into excipient gel, for topical application supplied as a 1.0 mL extractable volume in a single dose vial at a nominal concentration of 5×10 PFU/mL. The excipient gel is supplied as a 1.5 mL fill volume in a separate single use vial. The biological suspension (1 mL) is mixed into the excipient gel vial prior to administration.

## PRECAUTIONS:

**Boxed Warning**

None

**Contraindications**

None

**Precautions/Warnings**

- Avoid direct contact with treated wounds and dressings of treated wounds for approximately 24 hours following application. Clean the affected area if accidental exposure occurs.

## BILLING/CODING INFORMATION:

The following codes may be used to describe:

### HCPCS Coding

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|---|---|
| J3401 | Beremagene geperpavec-svdt for topical administration, containing nominal 5 x 10^9 pfu/ml vector genomes, per 0.1 ml |

## ICD-10 Diagnosis Codes That Support Medical Necessity

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|---|---|
| Q81.2 | Epidermolysis bullosa dystrophica |

## REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

## PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

**Medicare Part D:** Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

**Medicare Advantage:** No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

## DEFINITIONS:

None

## RELATED GUIDELINES:

None

## OTHER:

None

## REFERENCES:


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5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2023 [cited Jul 26, 2023]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
6. Vyjuvek (beremagene geperpavec-svdt) biological suspension. Krystal Biotech, Inc. Pittsburgh, PA. July 2023.

7. Wounds International consensus guidelines: Skin and wound care in epidermolysis bullosa. 2017. Available at af13d6_01ed147ab87e49c584c20a917c47f19f.pdf (usrfiles.com).

## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 08/09/23.

## GUIDELINE UPDATE INFORMATION:

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|---|---|
| 09/15/23 | New Medical Coverage Guideline. |
| 01/01/24 | Revision: Added HCPCS code J3401 and deleted code J3590. |