BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 08/17/23**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE: 08/15/24**
	CURRENT EFFECTIVE DATE: 08/15/24
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NEXT ANNUAL REVIEW DATE: 3RD QTR 2025	**ARCHIVE DATE:**

GENE THERAPY FOR DYSTROPHIC EPIDERMOLYSIS BULLOSA

- **VYJUVEK™ (beremagene geperpavec-svdt)**

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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Criteria:

Refer to FDA website for current indications and dosage.

- **Criteria for initial therapy:** Vyjuvek (beremagene geperpavec-svdt) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Dermatologist

  2. Individual is 6 months of age or older

  3. Individual has a confirmed diagnosis of dystrophic epidermolysis bullosa (DEB) with **ALL** of the following:

     - Laboratory documentation of mutation in the *collagen type VII alpha 1 chain (COL7A1)* gene
     - Documentation of the number and size of wounds that will be treated
     - Recurrent or chronic open clean wound(s) that meets **ALL** of the following:

       a. Adequate granulation tissue
       b. Excellent vascularization
       c. No active infection
       d. No history of or current squamous cell carcinoma
       e. No history of skin graft in the last 3 months

  4. Vyjuvek will be administered by a healthcare professional

  5. Vyjuvek will not be used in combination with Filsuvez (birch triterpenes) or other gene therapy for DEB

  6. The Attestation for Vyjuvek Treatment form (see below) has been signed by the physician (or designee)

  Initial approval duration: 6 months

  Approval Conditions:
  If an individual meets all coverage guideline criteria and is approved to receive treatment, the requesting provider attests and agrees to submit clinical outcomes data and information.

- Individuals may be referred to a care manager for consideration of additional services such as referral to a physiotherapist for education on health and wellness, including preventing disease, injury, disability, etc.

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- **Criteria for continuation of coverage (renewal request):** Vyjuvek (beremagene geperpavec-svdt) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Dermatologist

  2. Individual meets **ALL** initial criteria above

  3. Individual's condition has responded while on therapy with documentation of **ONE** of the following:

     - Current wound needs additional treatment and has documentation of decrease in wound size and increase in granulation tissue
     - Previously treated wound had complete wound closure and request is for new or recurrent wound(s)

  4. Individual has been adherent with the medication

  5. The Attestation for Vyjuvek Treatment form (see below) has been signed by the physician (or designee) [Note: Signed treatment form only needed once for any treating physician and may not be needed on renewal.]

  Renewal duration: 12 months

  Approval Conditions:
  If an individual meets all coverage guideline criteria and is approved to receive treatment, the requesting provider attests and agrees to submit clinical outcomes data and information.

- Vyjuvek (beremagene geperpavec-svdt) for all other indications not previously listed is considered ***experimental or investigational*** and will not be approved when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *but are not limited to:*

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- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

Attestations for Vyjuvek Treatment

Physician Name: _____

Individual Name: _____ DOB**:** _____

- The Physician is responsible for filling out this form.
- All elements must be initialed, and the form must be signed by the Physician (or designee).
- Incomplete forms will be returned to acquire missing information, initial, signature, or date.
- Return completed form to BCBSAZ.

Physician Agreement:
- Physician to initial by each element and date and sign to show willingness to participate.
- Documentation may include, but is not limited to, chart notes, laboratory test results, claims records, and/or other information.

Initials:

_____ I verify that the patient will be closely followed and monitored for progression of disease

_____ I agree to submit clinical outcomes data and information

Provider (or designee) Signature: _____

Date: _____

Description:

Epidermolysis bullosa (EB) is a rare genetic disorder characterized by skin fragility with blister formation occurring spontaneously or following minor trauma such as gentle pressure or friction. Dystrophic epidermolysis bullosa (DEB) is one of the four major subtypes of EB. DEB is caused by mutations in the COL7A1 gene, which results in reduced or absent levels of biologically active COL7. Collagen VII is the main component of the anchoring fibrils located below the lamina densa of the epidermal basement membrane zone. Hallmark cutaneous symptoms include skin fragility, blisters, scars, and nail changes. Non-cutaneous symptoms include blistering and ulceration in the mucous membranes and upper section of the esophagus, ocular involvement, constipation, anal fissures, and genitourinary tract complications.

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DEB can be either autosomal dominant or recessive and DEB has four subtypes:

- Localized dominant dystrophic epidermolysis bullosa
- Intermediate DDEB
- Intermediate recessive dystrophic epidermolysis bullosa
- Severe RDEB

Vyjuvek (beremagene 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. Collagen VII is the main component of the anchoring fibrils located below the lamina densa of the epidermal basement membrane zone.

Upon topical application to the wounds, Vyjuvek can transduce both keratinocytes and fibroblasts. It enters the cells, and the vector genome is deposited in the nucleus. Once in the nucleus, transcription of the encoded human COL7A1 is initiated. The resulting transcripts allow for production and secretion of COL7 by the cell in its mature form. These COL7 molecules arrange themselves into long, thin bundles that form anchoring fibrils. The anchoring fibrils hold the epidermis and dermis together and are essential for maintaining the integrity of the skin.

Definitions:

Vyjuvek maximum weekly dosing by age:

Age Range	Maximum Weekly Dose (PFU)	Maximum weekly volume (mL)
6 months to < 3 years old	1.6×10^9	0.8
≥ 3 years old	3.2×10^9	1.6

*PFU: plaque forming unit

Vyjuvek dosing per wound size:

Wound Area (cm2)	Dose (PFU)	Volume (mL)
< 20	1.6×10^8	0.2
20 to < 40	8×10^8	0.4
40 to 60	1.2×10^9	0.6

History:	Date:	Activity:
Pharmacy and Therapeutics Committee	08/15/24	Review with revisions: criteria

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Pharmacy and Therapeutics Committee	02/15/24	Revisions to guideline
Pharmacy and Therapeutics Committee	11/16/23	Revisions to guideline
Pharmacy and Therapeutics Committee	08/17/23	Approved guideline
Clinical Pharmacist	08/16/23	Development

Coding:

HCPCS: J3401

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Resources:

Literature reviewed 08/15/24. We do not include marketing materials, poster boards and non-published literature in our review.

1. Guide, SV, Gonzalez ME, Bağci IS, et al. Trial of beremagene geperpavec (B-VEC) for dystrophic epidermolysis bullosa. *N Engl J* Med 2022; 387:2211-2219.

2. Laimer M, Bauer J, Murrell DF. Epidermolysis bullosa: Epidemiology pathogenesis, classification, and clinical features. Hand JL, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated June 3, 2024. Accessed June 10, 2024.

3. Murrell DF. Overview of the management of epidermolysis bullosa. Hand JL, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated January 8, 2024. Accessed June 10, 2024.

4. Vyjuvek (beremagene-geperpavec-svdt). Prescribing information. Krystal Biotech, Inc. May 2023, at DailyMed https://dailymed.nlm.nih.gov/dailymed/. Accessed May 30, 2024.

5. Weisman A, Chan JM, LaPointe C, et al. Physiotherapy for epidermolysis bullosa: clinical practice guidelines. *Orphanet J Rare Dis*. 2021; 16:406-17.

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Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html