

## Clinical Policy: Beremagene Geperpavec (Vyjuvek)

Reference Number: LA.PHAR.592

Effective Date:

Last Review Date: 07.24.23

Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**\*\*Please note: This policy is for medical benefit\*\***

### Description

Beremagene Geperpavec (Vyjuvek<sup>®/TM</sup>) is a herpes simplex virus type 1 (HSV-1) vector-based gene therapy.

### FDA Approved Indication(s)

Vyjuvek is indicated for the treatment of adults and children aged 6 months and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene.

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of Louisiana Healthcare Connections<sup>®</sup> that Vyjuvek is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Recessive Dystrophic Epidermolysis Bullosa (must meet all):

1. Diagnosis of recessive DEB (RDEB) as evidenced by two copies of positive COL7A1 gene mutation by one of the following (a, b, or c; *see Appendix E*):
  - a. Immunofluorescence mapping;
  - b. Transmission electron microscopy;
  - c. Antigenic mapping;
2. Prescribed by or in consultation with a geneticist, dermatologist, or histopathologist;
3. Age  $\geq$  6 months;
4. Provider attestation of at least one cutaneous wound that is clean in appearance with adequate granulation tissue, has excellent vascularization, and does not appear infected;
5. Provider attestation that member is concomitantly receiving standard of care preventative or treatment therapies for wound care (e.g., polymeric membrane, super-absorbent dressings, soft-silicone foam, enzyme alginogel, protease; *see Appendix F*);
6. Member has no evidence of immune response to COL7 as evidenced by immunofluorescence (e.g., member is not positive for anti-COL7 antibodies at baseline);

7. Member does not have current evidence or history of squamous cell carcinoma in the area that will undergo treatment;
8. Dose does not exceed one of the following (a or b):
  - a. For members 6 months to < 3 years old:  $1.6 \times 10^9$  PFU/week or 0.8 mL/week
  - b. For members  $\geq 3$  years old:  $3.2 \times 10^9$  PFU/week or 1.6 mL/week

**Approval duration:** 6 months

**B. Other diagnoses/indications** (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Recessive Dystrophic Epidermolysis Bullosa** (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connection benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters (a or b):
  - a. Decrease in wound size;
  - b. Decrease in pain severity per primary wound site associated with dressing changes;
3. Provider attestation that member continues to have incomplete wound closures that are clean in appearance with adequate granulation tissue, have excellent vascularization, and do not appear infected;
4. If request is for a dose increase, new dose does not exceed one of the following (a or b):
  - a. For members 6 months to < 3 years old:  $1.6 \times 10^9$  PFU/week or 0.8 mL/week
  - b. For members  $\geq 3$  years old:  $3.2 \times 10^9$  PFU/week or 1.6 mL/week

**Approval duration:** 6 months

**B. Other diagnoses/indications** (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – LA.PMN.53 for Medicaid or evidence of coverage documents.

#### **IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

DDEB: dominant dystrophic

epidermolysis bullosa

DEB: dystrophic epidermolysis bullosa

EB: epidermolysis bullosa

FDA: Food and Drug Administration

HSV-1: herpes simplex virus type 1

PFU: Plaque forming units

RDEB: recessive dystrophic  
epidermolysis bullosa

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): None.
- Boxed warning(s): None.

*Appendix D: General Information*

- DEB is a serious, ultra-rare epidermolysis bullosa (EB) subtype caused by mutations in the COL7A1 gene.
- Per 2017 Best Practice Guidelines for Skin and Wound Care in Epidermolysis Bullosa, the most recent classification for EB names four categories of the condition defined by the level of cleavage at the dermal and epidermal junction:
  - EB simplex (EBS)
  - Junctional EB (JEB)
  - Dystrophic EB (DEB)
  - Kindler syndrome
- There are two types of DEB, dominant dystrophic EB (DDEB) and RDEB. RDEB is the more severe form. It is always caused by mutations in the COL7A1 gene, which codes for Type VII collagen.

*Appendix E: Diagnosis Information*

- 2017 Best Practice Guidelines for Skin and Wound Care in Epidermolysis Bullosa, definitive diagnosis is most commonly made from analysis of a skin biopsy using positive immunofluorescence, antigenic mapping, and transmission electron microscopy. Due to rarity of expertise and facilities, diagnosis is generally made using immunofluorescence and antigen mapping.
- No-charge Genetic Testing for Patients with Suspected DEB:
  - The Krystal Decode DEB program is open to all US residents, including residents of Puerto Rico, who have clinical symptoms consistent with EB and have no previously received genetic testing. More information on the Decode DEB program can be found on the Krystal Biotech website: <https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-and-genedx-announce-collaboration-provide-no>.

*Appendix F: Recommended Wound Care for DEB*

- Wounds should be dressed with nonadherent silicone dressings, foam dressings that absorb exudates, and nonadherent silicone-based tape. Diluted bleach baths or compresses, topical antiseptics, and topic antibiotics are used as preventative measures against bacterial infections.
- Standard of Care for wound care per 2017 Best Practice Guidelines for skin and wound care in epidermolysis bullosa:
  - First choice of dressing when available:
    - Chronic or acute wounds- PolyMem
    - Sugar-absorbent- Cutimed Siltec
- Recommended dressings for DEB per 2017 Best Practice Guidelines for skin and wound care in epidermolysis bullosa:

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
Polymeric membrane	PolyMem	<ul style="list-style-type: none"> <li>• Where cleansing is required</li> <li>• Chronic wounds</li> </ul>	<ul style="list-style-type: none"> <li>• Stimulates high levels of exudate</li> <li>• Distinct smell does not necessarily indicate infection</li> <li>• Can still be difficult to retain on vertical surfaces</li> </ul>	<ul style="list-style-type: none"> <li>• Change frequently until exudate reduces</li> </ul>
Super-absorbent dressings	<ul style="list-style-type: none"> <li>• Cutimed Siltec</li> <li>• Sorbion Sachet S</li> <li>• Filvasorb/Vilwasorb Pro</li> <li>• Kerramax Care</li> </ul>	<ul style="list-style-type: none"> <li>• High exudate levels</li> </ul>	<ul style="list-style-type: none"> <li>• Can be cut between super-absorbent crystals, which appear in rows (as opposed to cutting across the crystal lattice)</li> </ul>	
Soft silicone mesh	<ul style="list-style-type: none"> <li>• Mepitel</li> <li>• Mepitel One</li> <li>• Adaptic Touch</li> <li>• Cuticell Contact</li> </ul>	<ul style="list-style-type: none"> <li>• Moist wound</li> <li>• Contact layer</li> </ul>		
Lipido-colloid	<ul style="list-style-type: none"> <li>• Urgo Tul</li> </ul>	<ul style="list-style-type: none"> <li>• Moist wound, drier wounds and protection of vulnerable healed areas</li> <li>• Used as an alternative to</li> </ul>	<ul style="list-style-type: none"> <li>• Where retention is difficult (e.g., vertical surfaces)</li> </ul>	

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
		soft silicon (see above) in the presence of over- granulation		
Soft silicone foam	<ul style="list-style-type: none"> <li>• Mepilex</li> <li>• Mepilex Lite</li> <li>• Mepilex Transfer</li> </ul>	<ul style="list-style-type: none"> <li>• Absorption of exudate</li> <li>• Protection</li> <li>• Lightly exuding wounds</li> <li>• To transfer exudate to absorbent dressing</li> <li>• Where conformability is required (e.g. digits, axillae)</li> </ul>	<ul style="list-style-type: none"> <li>• Over-heating</li> <li>• May need to apply over recommended atraumatic primary dressing</li> </ul>	
Foam	<ul style="list-style-type: none"> <li>• Allevyn</li> <li>• UrgoTul Absorb</li> <li>• Aquacel Foam</li> </ul>	<ul style="list-style-type: none"> <li>• Absorption and protection</li> </ul>	<ul style="list-style-type: none"> <li>• May adhere if placed directly on wound bed, use alternative contact layer</li> </ul>	
Bordered foam dressings	<ul style="list-style-type: none"> <li>• Mepilex Border/ Meplix Border Lite</li> <li>• Biatain Silicone Border/ Biatain Border Lite</li> <li>• Allevyn Gentle Border</li> <li>• Allevyn Border Lite</li> <li>• Kerrafoam</li> </ul>	<ul style="list-style-type: none"> <li>• Isolated wounds</li> <li>• DDEB and mild RDEB</li> </ul>	<ul style="list-style-type: none"> <li>• Bordered dressings may require removal with SMAR to avoid skin stripping</li> <li>• May require primary contact layer</li> <li>• Poor absorption of highly viscous exudate</li> </ul>	<ul style="list-style-type: none"> <li>• Up to 4 days depending on personal choice</li> </ul>

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
	<ul style="list-style-type: none"> <li>• UrgoTul Absorb Border</li> </ul>			
Keratin	<ul style="list-style-type: none"> <li>• Keragel</li> </ul>	<ul style="list-style-type: none"> <li>• Chronic wounds</li> </ul>	<ul style="list-style-type: none"> <li>• Dilute with blend emollient if stinging occurs</li> </ul>	<ul style="list-style-type: none"> <li>• Reapply with dressing changes</li> </ul>

- First choice of treatment when available: PolyMem, Flaminal Hydro/Forte
- Treatment of choice for chronic wounds based on consensus opinion per 2017 Best Practice Guidelines for skin and wound care in epidermolysis bullosa:

Dressing Type	Brand	Indications	Contraindication/ Comments	Wear Time
Polymeric membrane	<ul style="list-style-type: none"> <li>• PolyMem</li> <li>• PolyMem Max</li> <li>• PolyMem WIC (under a secondary dressing or further layer of PolyMem)</li> </ul>	<ul style="list-style-type: none"> <li>• Infected wounds</li> <li>• Recalcitrant wounds</li> </ul>	<ul style="list-style-type: none"> <li>• Can provide initial increase in exudate resulting in further skin damage if not properly controlled</li> <li>• Distinct smell does not necessarily indicate infection</li> <li>• Protect periwound skin</li> </ul>	<ul style="list-style-type: none"> <li>• Change when wet to avoid hypothermia</li> </ul>
Enzyme alginogel	<ul style="list-style-type: none"> <li>• Flaminal Hydro</li> <li>• Flaminal Forte</li> </ul>	<ul style="list-style-type: none"> <li>• Low exudate</li> <li>• High exudate</li> </ul>	<ul style="list-style-type: none"> <li>• Debrides, de-sloughs and antimicrobial</li> <li>• Has some action in modulating excess proteases</li> <li>• Can be used on all wounds apart from third degree burns</li> <li>• Do not use if patient has sensitivity to alginates or polyethylene glycol</li> </ul>	<ul style="list-style-type: none"> <li>• Re-apply at each dressing change at least 2 mm thick</li> </ul>
Honey		<ul style="list-style-type: none"> <li>• Sensitive wounds</li> </ul>	<ul style="list-style-type: none"> <li>• Can cause transient stinging or pain due to its acidity and high osmotic 'pull'</li> <li>• In turn this will contribute to high levels of exudate</li> </ul>	

Dressing Type	Brand	Indications	Contraindication/ Comments	Wear Time
Protease modulator	<ul style="list-style-type: none"> <li>• UrgoTul</li> <li>• Start range</li> <li>• Promogran</li> <li>• Promogran Prisma (with silver)</li> </ul>	<ul style="list-style-type: none"> <li>• When excess protease may be present</li> </ul>	<ul style="list-style-type: none"> <li>• Promogran/ Promogran Prisma may cause initial transient stinging</li> <li>• Excess product cannot be saved once opened as it degrades on contact with air</li> <li>• A secondary dressing required and the product may provoke initial heavy exudate</li> </ul>	<ul style="list-style-type: none"> <li>• Frequent dressing changes may be required to avoid maceration</li> </ul>

## V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
DEB	Apply gel topically to wound(s) once weekly.	<u>6 months to &lt; 3 years old:</u> $1.6 \times 10^9$ PFU/ week or 0.8 mL/ week <u>≥3 years old:</u> $3.2 \times 10^9$ PFU/ week or 1.6 mL/ week

## VI. Product Availability

Carton: 1 mL single-dose, single-use vial of Vyjuvek ( $5 \times 10^9$  PFU/mL) and 1.5 mL of excipient gel in a separate single-use, single-dose vial.

## VII. References

1. Vyjuvek Prescribing Information. Pittsburgh, PA: Krystal Biotech, Inc; March 2021. Available at: <https://www.krystallabel.com/pdf/vyjuvek-us-pi.pdf>. Accessed July 24, 2023.
2. ClinicalTrials.gov. The objective of this study is to compare the efficacy and safety of Beremagene Geperpavec (B-VEC) topical gel with that of placebo for the treatment of dystrophic epidermolysis bullosa (DEB). Available at: <https://www.clinicaltrials.gov/ct2/show/NCT04491604>. Accessed October 4, 2022.
3. Denyer J, Pillay E, Clapham J, et al. Best practice guidelines for skin and wound care in epidermolysis bullosa. An International Consensus. Wounds International, 2017.
4. Mellerio JE, El Hachem M, Bellon N, et al. Emergency management in epidermolysis bullosa: consensus clinical recommendations from the European reference network for rare skin diseases. Orphanet J Rare Dis. 2020 Jun 6;15(1):142.



5. El Hachem M, Zambruno G, Bourdon-Lanoy E, et al. Multicentre consensus recommendations for skin care in inherited epidermolysis bullosa. Orphanet J Rare Dis. 2014 May 20;9:76.
6. Marinkovic MP, Gonzalez ME, Guide S, et al. PowerPoint presented: GEM-3: A Phase 3 study of Beremagene Geperpavec (B-VEC), an investigational, topical gene therapy, for the treatment of dystrophic epidermolysis bullosa (DEB). Krystal Biotech, Inc. September 2022; Pittsburgh, PA.
7. Marinkovic MP, Gonzalez ME, Guide S, et al. GEM-3: Phase 3 safety and immunogenicity results of Beremagene Geperpavec (B-VEC), an investigational, topical gene therapy for dystrophic epidermolysis bullosa. Poster presented at: Society for Investigative Dermatology (SID) 2022 Annual Meeting. May 2022; Portland, OR.

### Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPSC Codes	Description
J3590	Unclassified biologics

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.01.23	
Updated policy based on FDA-approved indications. Added dosing regimen. References reviewed and updated.	07.24.23	

### Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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