Clinical Policy: Beremagene Geperpavec (Vyjuvek)

Reference Number: LA.PHAR.592
Effective Date: ~~FDA Approval Date~~
Last Review Date: ~~05.01.23~~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®/™) is a~~n investigational~~ herpes simplex virus type 1 (HSV-1) vector-based gene therapy.

FDA Approved Indication(s) ~~[Pending]~~
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.

~~Limitation(s) of use: [XXX]~~

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® that Vyjuvek is **medically necessary** when the following criteria are met:

~~I.~~ Initial Approval Criteria~~*~~
~~II.~~I. ~~*Criteria will mirror the clinical information from the prescribing information once FDA approved~~

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 ≥ 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. ~~FDA maximum dose.*~~For members 6 months to < 3 years old: 1.6 x 10^9 PFU/week or 0.8 mL/week
   ~~a.~~b. For members ≥ 3 years old: 3.2 x 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.

~~A.~~ **Continued Therapy** *

II.

~~**III.** *Criteria will mirror the clinical information from the prescribing information once FDA-approved~~

~~B.~~**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 x 10^9 PFU/week or 0.8 mL/week
   ~~a.~~b. For members ≥ 3 years old: 3.2 x 10^9 PFU/week or 1.6 mL/week~~FDA maximum dose.*~~

Approval duration: 6 months

Formatted: Font color: Black

~~C.~~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.

~~IV.~~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.

~~V.~~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 ~~[Pending]~~

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

Formatted: Font color: Auto
Formatted: Font color: Auto

- 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- PolyMemb
    - 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	• Where cleansing is required • Chronic wounds	• Stimulates high levels of exudate • Distinct smell does not necessarily indicate infection • Can still be difficult to retain on vertical surfaces	• Change frequently until exudate reduces
Super-absorbent dressings	• Cutimed Siltec • Sorbion Sachet S • Filvasorb/Vilwasorb Pro • Kerramax Care	• High exudate levels	• Can be cut between super-absorbent crystals, which appear in rows (as opposed to cutting across the crystal lattice)	
Soft silicone mesh	• Mepitel • Mepitel One	• Moist wound • Contact layer		

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
	• Adaptic Touch • Cuticell Contact			
Lipido-colloid	• Urgo Tul	• Moist wound, drier wounds and protection of vulnerable healed areas • Used as an alternative to soft silicon (see above) in the presence of over-granulation	• Where retention is difficult (e.g., vertical surfaces)	
Soft silicone foam	• Mepilex • Mepilex Lite • Mepilex Transfer	• Absorption of exudate • Protection • Lightly exuding wounds • To transfer exudate to absorbent dressing • Where conformability is required (e.g. digits, axillae)	• Over-heating • May need to apply over recommended atraumatic primary dressing	
Foam	• Allevyn • UrgoTul Absorb • Aquacel Foam	• Absorption and protection	• May adhere if placed directly on wound bed, use alternative contact layer	
Bordered foam dressings	• Mepilex Border/ Mepliex Border Lite • Biatain Silicone	• Isolated wounds • DDEB and mild RDEB	• Bordered dressings may require removal with SMAR to avoid skin stripping • May require primary contact layer	• Up to 4 days depending on personal choice

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
	Border/ Biatain Border Lite • Allevyn Gentle Border • Allevyn Border Lite • Kerrafoam • UrgoTul Absorb Border		• Poor absorption of highly viscous exudate	
Keratin	• Keragel	• Chronic wounds	• Dilute with blend emollient if stinging occurs	• Reapply with dressing changes

- 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	• PolyMem • PolyMem Max • PolyMem WIC (under a secondary dressing or further layer of PolyMem)	• Infected wounds • Recalitrant wounds	• Can provide initial increase in exudate resulting in further skin damage if not properly controlled • Distinct smell does not necessarily indicate infection • Protect periwound skin	• Change when wet to avoid hypothermia
Enzyme alginogel	• Flaminal Hydro • Flaminal Forte	• Low exudate • High exudate	• Debrides, de-sloughs and antimicrobial • Has some action in modulating excess proteases • Can be used on all wounds apart from third degree burns • Do not use if patient has sensitivity to	• Re-apply at each dressing change at least 2 mm thick

Dressing Type	Brand	Indications	Contraindication/ Comments	Wear Time
			alginates or polyethylene glycol	
Honey		• Sensitive wounds	• Can cause transient stinging or pain due to its acidity and high osmotic 'pull' • In turn this will contribute to high levels of exudate	
Protease modulator	• UrgoTul Start range • Promogran • Promogran Prisma (with silver)	• When excess protease may be present	• Promogran/ Promogran Prisma may cause initial transient stinging • Excess product cannot be saved once opened as it degrades on contact with air • A secondary dressing required and the product may provoke initial heavy exudate	• Frequent dressing changes may be required to avoid maceration

~~VI.~~V. Dosage and Administration ~~[Pending]~~

Indication	Dosing Regimen	Maximum Dose
DEB~~*~~	Apply gel topically to wound(s) once weekly.~~Pending*~~	6 months to < 3 years old: 1.6×10^9 PFU/ week or 0.8 mL/ week ≥3 years old: ~~Pending*~~ 3.2×10^9 PFU/ week or 1.6 mL/ week

Formatted: Font color: Auto

~~VII.~~VI. Product Availability ~~[Pending]~~

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

~~VIII.~~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.

~~1.~~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.
~~2.~~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.
~~3.~~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.
~~4.~~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.
~~5.~~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.
~~6.~~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 ~~[Pending]~~
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.

HCPCS Codes	Description
~~Pending~~J3590	~~Pending~~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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.