Clinical Policy: Beremagene geperpavec-svdt (Vyjuvek)

Reference Number: CP.PHAR.592
Effective Date: 05.19.23
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

Vyjuvek is indicated for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa (DEB) with mutations(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 health plans affiliated with Centene Corporation® that Vyjuvek is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of DEB as evidence by *COL7A1* gene mutation confirmed by genetic testing (*see Appendix E*);
2. Prescribed by or in consultation with a geneticist, dermatologist, or histopathologist;
3. Age ≥ 6 months;
4. Provider attestation that target wounds are clean in appearance with adequate granulation tissue, has excellent vascularization, and does not appear infected;
5. Documentation of size of target wounds at baseline (*see Appendix F*);
6. 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 G*);
7. Member does not have current evidence or history of squamous cell carcinoma in the area that will undergo treatment;
8. Vyjuvek is not prescribed concurrently with Filsuvez®;
9. Dose does not exceed one of the following (a or b):
   a. Age 6 months to < 3 years: 1.6×10^9 plaque forming units (PFU) (0.8 mL) weekly;
   b. Age ≥ 3 years: 3.2×10^9 PFU (1.6 mL) weekly.

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 one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Dystrophic Epidermolysis Bullosa (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in <u>any</u> of the following parameters (a or b):
   a. Decrease in wound size;
   b. Decrease in pain severity for target wound sites associated with dressing changes;
3. Provider attestation that member meets both of the following (a and b):
   a. Continues to have incomplete wound closures that are clean in appearance with adequate granulation tissue, have excellent vascularization, and do not appear infected;
   b. Vyjuvek is not applied on target wounds that have completely healed;
4. Vyjuvek is not prescribed concurrently with Filsuvez;
5. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Age 6 months to < 3 years: 1.6×10^9 PFU (0.8 mL) weekly;
   b. Age ≥ 3 years: 3.2×10^9 PFU (1.6 mL) weekly.

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 one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

COL7A1: collagen type VII alpha 1 chain
DEB: dystrophic epidermolysis bullosa
EB: epidermolysis bullosa
FDA: Food and Drug Administration
HSV-1: herpes simplex virus type 1
IFM: immunofluorescence mapping
PFU: plaque forming units
TEM: transmission electron microscopy

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 EB, 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

Appendix E: Diagnosis Information

- Per 2020 Clinical Practice Guidelines for Laboratory Diagnosis of EB, genetic testing is always recommended for the diagnosis of EB. Methods for clinical diagnosis in EB include immunofluorescence mapping (IFM), transmission electron microscopy (TEM), or genetic testing (e.g., next-generation sequencing, whole-exome sequencing, and Sanger sequencing).
  - IFM is recommended to obtain a rapid diagnosis and prognosis, and to prioritize genetic testing and facilitate interpretation of genetic results.
  - TEM is useful in a limited number of cases and should be performed when IFM and genetic testing do not deliver conclusive results.
- Per 2017 Best Practice Guidelines for Skin and Wound Care in EB, definitive diagnosis is most commonly made from analysis of a skin biopsy using positive immunofluorescence, antigenic mapping, and TEM. 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 (Krystal Biotech and GeneDx collaboration) 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.
- Invitae Epidermolysis Bullosa and Palmoplantar Keratoderma Panel analyzes genes associated with EB. More information can be found on the Invitae website: https://www.invitae.com/en/providers/test-catalog/test-434344.

Appendix F: Dose by Wound Size

Wound Area (cm^2)	Dose (PFU)	Volume (mL)
< 20	4×10^8	0.2
20 to < 40	8×10^8	0.4
40 to 60	1.2×10^9	0.6

**For wound area over 60 cm^2, recommended calculating the total dose based on table above until the maximum weekly dose is reached*

Appendix G: Recommended Wound Care for DEB

Per 2017 Best Practice Guidelines for Skin and Wound Care in EB:

- 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 EB skin and wound care:
  - First choice of dressing for general EB wounds (when available): PolyMemb, Cutimed Siltec (super-absorbent)
  - First choice of dressing for chronic EB wounds (when available): PolyMem, Flaminal Hydro/Forte
- Recommended dressings for general EB skin and wound care:

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 • Adaptic Touch • Cuticell Contact	• Moist wound • Contact layer		
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	• Over-heating • May need to apply over recommended atraumatic primary dressing	

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
		absorbent dressing • Where conformability is required (e.g., digits, axillae)		
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 Border/ Biatain Border Lite • Allevyn Gentle Border • Allevyn Border Lite • Kerrafoam • UrgoTul Absorb Border	• Isolated wounds • DDEB and mild RDEB	• Bordered dressings may require removal with SMAR to avoid skin stripping • May require primary contact layer • Poor absorption of highly viscous exudate	• Up to 4 days depending on personal choice
Keratin	• Keragel	• Chronic wounds	• Dilute with blend emollient if stinging occurs	• Reapply with dressing changes

- Recommended dressings for chronic EB wounds based on consensus opinion

Dressing Type	Brand	Indications	Contraindication/ Comments	Wear Time
Polymeric membrane	• PolyMem • PolyMem Max • PolyMem WIC (under a	• Infected wounds • Recalitrant wounds	• Can provide initial increase in exudate resulting in further skin damage if not properly controlled	• Change when wet to avoid hypothermia

Dressing Type	Brand	Indications	Contraindication/ Comments	Wear Time
	secondary dressing or further layer of PolyMem)		• Distinct smell does not necessarily indicate infection • Protect periwound skin	
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 alginates or polyethylene glycol	• Re-apply at each dressing change at least 2 mm thick
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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
DEB	**Age 6 months to < 3 years:**	**Age 6 months to < 3 years:**

Indication	Dosing Regimen	Maximum Dose
	1.6×10^9 PFU (0.8 mL) topically once weekly **Age ≥ 3 years:** 3.2×10^9 PFU (1.6 mL) topically once weekly	1.6×10^9 PFU/ weekly **Age ≥ 3 years:** 3.2×10^9 PFU/ weekly

VI. Product Availability

Biological suspension in a single dose vial (1 mL extractable volume) mixed into excipient gel vial: 5×10^9 PFU/mL

VII. References

1. Vyjuvek Prescribing Information. Pittsburgh, PA: Krystal Biotech, Inc.; May 2023. Available at: https://www.krystallabel.com/pdf/vyjuvek-us-pi.pdf. Accessed July 6, 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 July 6, 2023.
3. Guide S, Gonzalez ME, Bağcı IS, et al. Trial of beremagene geperpavec (B-VEC) for dystrophic epidermolysis bullosa. N Engl J Med. 2022;387(24):2211-2219. doi:10.1056/NEJMoa2206663.
4. 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.
5. Has C, Liu L, Bolling MC, Charlesworth AV, et al. Clinical practice guidelines for laboratory diagnosis of epidermolysis bullosa. Br J Dermatol. 2020 Mar;182(3):574-592. doi: 10.1111/bjd.18128.
6. 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.
7. 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.

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.

HCPCS Codes	Description
J3401	Beremagene geperpavec-svdt for topical administration, containing nominal 5×10^9 pfu/mL vector genomes, per 0.1 mL

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	10.04.22	11.22
For initial criteria, clarified "member is not positive for anti-COL7 antibodies at baseline" with addition of "no evidence of immune response to COL7 as evidenced by immunofluorescence" aligning with other RDEB policy.	12.01.22	02.23
RT1: drug is now FDA approved – policy updated per FDA labeling; updated indication from "recessive" DEB indication to DEB per PI; updated diagnosis criteria to require confirmation of *COL7A1* gene mutation via genetic testing only; for initial approval criteria, added requirement for documentation of size of target wounds at baseline; updated verbiage from "one wound" to "target wounds"; removed "member has no as evidence of immune response to COL7 as evidence by immunofluorescence" from initial criteria as requirement was not part of exclusion criteria of phase 3 study and based on results from the post-hoc analysis; for continued therapy, added "Vyjuvek is not applied on target wounds that have completely healed" to ensure member is not using therapy for closed wounds and updated wording from "primary wound" to "target wounds"; updated maximum dosing criteria as reflected in PI; updated Appendix E with laboratories that offer DEB testing; added Appendix F as reference for dose by wound size; references reviewed and updated.	07.18.23	08.23
Added HCPCS code [J3401]	10.27.23	
Added exclusion of concomitant use with Filsuvez.	03.05.24	05.24

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. The Health Plan 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. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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 the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. 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.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.