Clinical Policy: Beremagene geperpavec-svdt (Vyjuvek)

Reference Number: PA.CP.PHAR.592
Effective Date: 08/2023
Last Review Date: 07/2023

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 PA Health & Wellness® 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. 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

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Diagnosis (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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 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. 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. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53

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

< 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	• Where retention is difficult (e.g., vertical surfaces)	

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
		(see above) in the presence of over-granulation		
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 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

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
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 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 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	• When excess protease may be present	• Promogran/ Promogran Prisma may cause initial transient stinging	• Frequent dressing changes may be required to

Dressing Type	Brand	Indications	Contraindication/ Comments	Wear Time
	• Promogran Prisma (with silver)		• 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	avoid maceration

V. Dosage and Administration

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

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
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