Vyjuvek (beremagene geperpavec-svdt)
PAM – 087

Iowa Medicaid Program	Prior Authorization	**Effective Date**	01/01/2023
Revision Number	1	**Last Reviewed**	10/18/2024
Reviewed By	Medicaid Medical Director	**Next Review**	10/17/2025
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	10/18/2024

Overview

Medication: [1]	beremagene geperpavec-svdt
Brand Name:	Vyjuvek™
Pharmacologic Category:	Dermatological agents; herpes-simplex virus type 1 (HSV-1) vector-based gene therapy
FDA-Approved Indication(s):	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
How Supplied:	Carton contains one single-dose vial of Vyjuvek™ biological suspension and one single-dose vial of excipient gel

Dosage and Administration:

- Prepare gel at pharmacy for immediate use within 8 hours of application.
- Only a healthcare professional should apply Vyjuvek™ gel either at a healthcare professional setting (e.g., clinic) or the home setting.
- Apply to wound(s) once weekly; dosing is based on age.
- Apply gel to wounds until they are closed before selecting new wound(s) to treat. Prioritize weekly treatment to previously treated wounds if they re-open.
- Vyjuvek is a replication deficient HSV-1-based gene therapy. Follow universal biohazard precautions for handling.

Maximum Weekly Dose by Age		
Age Range	Maximum Weekly Dose (plaque forming units; PFU)	Maximum Weekly Volume (mL) *
6 months to < 3 years	1.6×10^9	0.8
≥ 3 years old	3.2×10^9	1.6
* max weekly volume after mixing Vyjuvek biological suspension with excipient gel		

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, recommend calculating the total dose based on this table until the maximum weekly dose is reached.		

Benefit Category: Medical

Descriptive Narrative

Epidermolysis bullosa (EB) is a clinically and genetically heterogeneous inherited skin fragility disorder characterized by disruption of the skin's structure at the dermoepidermal junction or in the basal layer of the epidermis, resulting in increased cutaneous vulnerability to mechanical stress. The variant type (biallelic versus monoallelic), number (monogenic, digenic inheritance), and location within the gene or gene segment, as well as the spectrum of associated quantitative (absence, reduction) or qualitative (gradual loss of function) alterations of protein expression, result in considerable genetic heterogeneity with complex genotype-phenotype correlations.

The genes involved in the pathogenesis of EB are also partly expressed in other epithelial tissues and mesenchymal tissues, resulting in the occurrence of primary extracutaneous manifestations and relevant complications, especially in the severe forms of EB. Complications may involve other organs and systems (e.g., the heart and musculoskeletal system). Onset of epidermolysis bullosa is at birth or shortly after. The exception occurs in mild cases of epidermolysis bullosa simplex, which may remain undetected until adulthood or occasionally remain undiagnosed.

Dystrophic Epidermolysis Bullosa

Dystrophic epidermolysis bullosa (DEB) is characterized by blistering of the skin and mucosal membranes that heal with scarring. The 2020 consensus classification recognizes four major subtypes and several rare dominant or recessive subtypes of DEB:

1. Localized dominant dystrophic epidermolysis bullosa (DDEB; previously encompassing nails only, pretibial, and acral DDEB);
2. Intermediate DDEB (previously known as generalized DDEB);
3. Intermediate recessive dystrophic epidermolysis bullosa (RDEB; previously known as RDEB generalized intermediate, non-Hallopeau-Siemens RDEB);
4. Severe RDEB (previously RDEB generalized severe, Hallopeau-Siemens RDEB).

All DEB subtypes are caused by variants in the *COL7A1* gene on chromosome 3p21.31, encoding the alpha-1 chain of type VII collagen. More than 600 distinct variants in the *COL7A1* gene have been identified in DEB. Although a few variants are recurrent in some populations due to the founder effect, most families carry unique variants ("private variants"). DEB can be inherited in a dominant or recessive manner. RDEB is generally more severe than DDEB, although there is considerable phenotypic overlap between subtypes, and RDEB may present with a milder phenotype in some cases.

Clinical hallmarks of DEB are skin fragility, blistering, scarring, nail changes, and milia formation in areas of healed blistering. Since collagen VII is also expressed in noncutaneous stratified epithelia, blistering can also occur in the mucosae.[2] The onset of disease is usually at birth or during infancy, with generalized blistering as a common presentation. With increasing age, an evolution to localized blistering is present.[3]

According to the United States National Epidermolysis Bullosa Registry, the incidence and prevalence of dominant dystrophic epidermolysis bullosa were found to be 2.12 and 1.49 cases per 1 million live births, respectively. The incidence and prevalence of recessive dystrophic epidermolysis bullosa were found to be 3.05 and 1.35 cases per 1 million live births, respectively.[4]

Guidelines

General principles in the management of epidermolysis bullosa include:

1. Supportive care – Treatment is largely supportive and includes wound care, control of infection, nutritional support, and prevention and treatment of complications. Care plans should be individualized according to age, severity, symptoms, complications, and patient priorities.
2. Monitoring – Laboratory and imaging monitoring is an important aspect of the management of patients with EB. Patients with EB require regular monitoring for complications and sequelae.
3. Skin and wound care –
    a. Bathing – Bathing in normal water is painful for patients with severe forms of epidermolysis bullosa (EB) and open wounds. Pain can be greatly reduced by bathing with salt water that approximates isotonic saline for bathing.
    b. Wound dressing – Nonstick or nonadherent silicone dressings and foam dressings that absorb exudates are ideal as primary dressings for EB wounds. They can be covered with absorbent padding and left in place for several days (the frequency of change depends upon the patient's preference, time availability, amount of exudate, and presence of infection).
4. Foot care – Foot blistering from friction or minor trauma is common in all types of EB. Rupture of blisters at their lowest point to allow gravitational drainage is recommended.
5. Prevention and management of infection – Bacterial colonization of EB wounds is common. Wounds that are "critically colonized" (i.e., active multiplication of organisms without invasion) or frankly infected fail to heal. In critically colonized wounds, the bacterial load can be reduced with topical agents. Wounds with frank infection usually require systemic antibiotics. The choice of antibiotic therapy should be based on bacterial culture results.

6. Pain and itch management –
    a. Pain is a constant feature of epidermolysis bullosa (EB). Medications to treat pain should be chosen based on the severity of the pain.
    b. Chronic pruritus is a prominent debilitating feature of EB. Measures that may be helpful include antihistamines, antidepressants, and oral gabapentin or pregabalin.
7. Management of nutritional compromise – All patients with severe forms of epidermolysis bullosa (EB), particularly recessive dystrophic epidermolysis bullosa (RDEB) or junctional epidermolysis bullosa (JEB), have nutritional compromise and require nutritional support.
8. Related problems requiring clinical management may include anemia, osteopenia or osteoporosis, ocular lesions, oral and dental lesions, delayed puberty, esophageal strictures, mitten deformity, squamous cell carcinoma, and chronic ulcers.

Affected families should be offered genetic consultation so that they can better understand their reproductive risks and options, such as prenatal diagnosis and preimplantation genetic testing. Affected individuals and family members may benefit from updated genetic consultation prior to their reproductive years.[5]

Criteria

Prior authorization is required.

Vyjuvek™ is considered medically necessary when **ALL** of the following are met:
1. Diagnosis of dystrophic epidermolysis bullosa (DEB) and member has mutations in the collagen type VII alpha 1 chain *(COL7A1)* gene (confirmed by genetic testing); **AND**
2. Member is 6 months of age or older; **AND**
3. Member does not have current evidence or a history of squamous cell carcinoma or active infection in the area that will undergo treatment; **AND**
4. Documentation that member is receiving standard of care wound therapy; **AND**
5. Will not be used in combination with Filsuvez® (birch triterpenes); **AND**
6. Prescribed by, or in consultation with, a dermatologist, geneticist, histopathologist, or wound care specialist with expertise in the treatment of DEB; **AND**
7. Request meets one of the following (a, b, or c):
    a. Member is age 6 months to < 3 years, and regimen prescribed does not exceed 1.6×10^9 plaque forming units (PFU) (0.8 mL) once weekly; or
    b. Member is 3 years of age or older, and regimen prescribed does not exceed 3.2×10^9 PFU (1.6 mL) once weekly; or
    c. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Vyjuvek™ is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by (including but not limited to) improvement in any of the following:
    a. Reduction in the number of wounds and/or decrease in wound size; and/or
    b. Increase in granulation tissue; and/or
    c. Decrease in pain severity for wound sites associated with dressing changes; **AND**
3. Member has not experienced any serious adverse events or complications that would undermine the benefit of therapy; **AND**
4. Documentation that member continues to have incomplete wound closures, and that Vyjuvek™ is not applied on target wounds that have completely healed; **AND**
5. Will not be used in combination with Filsuvez® (birch triterpenes); **AND**
6. Prescribed by, or in consultation with, a dermatologist, geneticist, histopathologist, or wound care specialist with expertise in the treatment of DEB; **AND**
7. Request meets one of the following (a, b, or c):
    a. Member is age 6 months to < 3 years, and regimen prescribed does not exceed 1.6 x 10^9 plaque forming units (PFU) (0.8 mL) once weekly; or
    b. Member is 3 years of age or older, and regimen prescribed does not exceed 3.2 x 10^9 PFU (1.6 mL) once weekly; or
    c. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits*	• 6 months to < 3 years of age: 1.6 x 10^9 PFU (0.8 mL) once weekly • 3 years of age or older: 3.2 x 10^9 PFU (1.6 mL) once weekly	

* PFU = plaque forming units

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J3401	Beremagene geperpavec-svdt for topical administration, containing nominal 5 x 10^9 PFU/ml vector genomes, per 0.1 mL

ICD-10	Description
Q81.2	Epidermolysis bullosa dystrophica

NDC (and strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units /Pkg
Carton NDC: 82194-0510-02 Carton contains: 1 mL vial of Vyjuvek™ (5 x 10^9 PFU/mL) (82194-0501-01) and 1.5 mL vial of excipient gel (82194-0001-01)	Krystal Biotech, Inc. (82194)	0.1 mL	1	EA	25

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Vyjuvek™ prescribing information (05/2023). Krystal Biotech, Inc.: Pittsburgh, PA. Available online: www.vyjuvekhcp.com. Accessed June 25, 2024.

[2] Laimer M, Murrell DF. Epidermolysis bullosa: Epidemiology, pathogenesis, classification, and clinical features. Corona R, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed August 27, 2024.

[3] Marinkovich MP. Epidermolysis Bullosa Treatment & Management. James WD, chief editor. Medscape. Drugs and Diseases: Dermatology.

[4] Fine JD. Epidemiology of Inherited Epidermolysis Bullosa Based on Incidence and Prevalence Estimates From the National Epidermolysis Bullosa Registry. JAMA Dermatol. 2016 Nov 1;152(11):1231-1238. PMID: 27463098.

[5] Murrell DF. Overview of the management of epidermolysis bullosa. Corona R, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed August 27, 2024.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]
Signature			

Change Date	Changed By	Description of Change	Version
10/18/2024	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee