PRIOR AUTHORIZATION POLICY

POLICY: Dermatology – Gene Therapy – Vyjuvek Prior Authorization Policy
- Vyjuvek™ (beremagene geperpavec-svdt topical gel – Krystal Biotech)

REVIEW DATE: 06/26/2024

OVERVIEW

Vyjuvek, a herpes-simplex virus type-1 (HSV-1) vector-based gene therapy, is indicated for the treatment of wounds with **dystrophic epidermolysis bullosa** (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene in patients ≥ 6 months of age.[1]

Vyjuvek is a live, replication defective HSV-1-based vector that has been genetically modified to express the human type VII collagen (COL7) protein.[1] Mutation(s) in the COL7A1 gene result in reduced or absent levels of biologically active COL7 in patients with DEB. COL7 protein is a crucial component of anchoring fibrils that are essential for maintaining skin integrity. Application of Vyjuvek to wounds results in transcription of the encoded human COL7A1 and production and secretion of COL7 by the cell in its mature form. The COL7 molecules form anchoring fibrils that hold the epidermis and dermis together.

Disease Overview

DEB usually presents at birth and is divided into two major types depending on the pattern of inheritance: recessive DEB (RDEB) and dominant DEB (DDEB).[6] All subtypes of DEB are caused by mutations in the gene coding COL7A1 leading to extreme skin fragility.[4,6] The hallmark of DEB is scarring of blisters, both on the skin and on other mucosal surfaces.[4]

Clinical Efficacy

GEM-3, a Phase III, double-blind, placebo-controlled, intrapatient randomized, pivotal study, assigned patients with DEB to treat two similarly sized wounds; one with Vyjuvek and one with placebo for 26 weeks (N = 31).[2] Eligible patients were ≥ 6 months of age presenting with a clinical diagnosis of DEB, characterized by blistering, wounds, and scarring and confirmed by genetic testing including COL7A1. The appearance of the wounds was to be clean with adequate granulation tissue, excellent vascularization, and to not appear infected. Patients receiving immunotherapy, chemotherapy, or other investigational products were not included. In addition, wound sites with current evidence or a history of squamous-cell carcinoma or active infection were excluded as sites for Vyjuvek (or placebo) application. Vyjuvek or placebo was applied only to open wounds. Wounds were evaluated weekly to determine continued application of Vyjuvek or placebo. If a healed wound reopened, application was resumed; if the wound remained closed, application was omitted. All but one patient had the recessive DEB genotype. At Month 6, significantly more Vyjuvek- vs. placebo-treated wounds were completely healed (67% vs. 22%, respectively; P = 0.002) [primary endpoint]. Similar results were observed at Month 3 favoring Vyjuvek vs. placebo for complete wound healing (71% vs. 20%, respectively; P < 0.001). Durability (complete wound healing at both Months 3 and 6) was seen in 50% vs. 7% of Vyjuvek- vs. placebo-treated wounds, respectively (difference 43%; 95% confidence interval: 23%, 63%). One patient had a chronic secondary wound of the back measuring > 100 cm^2 that had been open for > 10 years. Following Vyjuvek treatment, the patient was able to resume activities of daily living, including showering, which had not previously been possible due to the open nature of the wound.

Guidelines

Vyjuvek is not addressed in available guidelines. According to a position statement by the **European Reference Network for Rare Skin Diseases** (2021), wound care is the cornerstone of treatment for patients with DEB.[5] Careful and complete skin and wound assessment should be undertaken regularly, at least every 6 months. The healing rate of chronic wounds should be closely monitored, by checking wound edges.

The diagnosis of DEB is based on a combination of clinical features, family , and laboratory findings.[5] Laboratory techniques include immunofluorescence mapping, transmission electron microscopy, and molecular genetic testing. Whenever possible, laboratory diagnosis should be performed in a specialized DEB center. Genetic testing is the gold standard for the diagnosis of DEB, since it provides a definitive diagnosis and classification of the major DEB type and in many cases the subtype.

An **international consensus best practice guideline** on skin and wound care in epidermolysis bullosa (EB) [2017] notes that EB is a lifelong disease that requires specialist intervention and consideration to minimize complications and improve quality of life.[6] Management should take place in a specialized center by a multi-disciplinary team, ideally. Definitive diagnosis is most commonly made from analysis of a skin biopsy using positive immunofluorescence, antigenic mapping, and transmission electron microscopy. These key diagnostic tools help confirm diagnosis and indicate the particular subtype of EB. Due to the rarity of expertise and facilities, diagnosis is generally made using immunofluorescence and antigen mapping. Some laboratories are moving towards molecular diagnosis from exome sequencing of a panel of known skin fragility genes. Experienced clinicians can often make a provisional diagnosis on clinical observations, but a definitive diagnosis will always be required.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Vyjuvek. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Vyjuvek as well as the monitoring required for adverse events and long-term efficacy, approval requires Vyjuvek to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of Vyjuvek as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Vyjuvek is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Dystrophic Epidermolysis Bullosa.** Approve for the duration outlined below if the patient meets ONE of the following (A or B):
   Note: For new wound(s) the patient is directed to Initial Therapy criteria. If the patient is continuing to treat the same wound(s) the patient is directed to criteria for Patient Currently Receiving Vyjuvek on Previously Treated Wound(s).

A) Initial Therapy: Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient is ≥ 6 months of age; AND
- **ii.** The diagnosis is confirmed by genetic testing showing a pathogenic mutation in the collagen type VII alpha 1 chain (COL7A1) gene **[documentation required]**; AND
- **iii.** Patient meets ALL of the following (a, b, and c):
  - **a)** Patient has at least one clinical feature of dystrophic epidermolysis bullosa **[documentation required]**; AND
    Note: Examples of clinical features of dystrophic epidermolysis bullosa include but are not limited to blistering, wounds, and scarring.
  - **b)** Patient has one or more open wound(s) that will be treated (i.e., "target wound[s]); AND
  - **c)** Target wound(s) meet ALL of the following, according to the prescriber [(1), (2), and (3)]:
    - **(1)** Target wound(s) is clean in appearance and does not appear to be infected; AND
    - **(2)** Target wound(s) has adequate granulation tissue and vascularization; AND
    - **(3)** Squamous cell carcinoma has been ruled out for the target wound(s); AND
- **iv.** The medication is prescribed by or in consultation with a dermatologist or wound care specialist.

B) Patient is Currently Receiving Vyjuvek on **Previously Treated Wound(s)**: Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
Note: If the patient is treating a new wound(s) not previously treated with Vyjuvek or a reopened recurrent wound(s), then refer to Initial Therapy criteria above.
- **i.** According to the prescriber, the target wound(s) remains open; AND
- **ii.** According to the prescriber, the target wound(s) has decreased in size from baseline; AND
- **iii.** The medication is prescribed by or in consultation with a dermatologist or wound care specialist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Vyjuvek is not recommended in the following situations:

1. **Combination use with Filsuvez (birch triterpenes topical gel).** Combination use of Vyjuvek and Filsuvez have not been studied.[7]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Vyjuvek™ topical gel [prescribing information]. Pittsburgh, PA: Krystal Biotech; May 2023.
2. Guide SV, Gonzalez ME, Bagci IS, et al. Trial of beremagene geperavec (B-VEC) for dystrophic epidermolysis bullosa. *N Engl J Med.* 2022;387(24):2211-2219.
3. Payne AS. Topical gene therapy for epidermolysis bullosa. *N Engl J Med.* 2022;387(24):2281-2284.
4. Has C, Bauer JW, Bolling MC et al. Consensus and reclassification of inherited epidermolysis bullosa and other disorders with skin fragility. *Br J Dermatol.* 2020;183:614-627.
5. Has C, El Hachem M, Buckova H, et al. Practical management of epidermolysis bullosa: consensus clinical position statement from the European Reference Network for Rare Skin Diseases. *J Eur Acad Derm Venereol.* 2021;35:2349-2360.
6. Denyer J, Pillay E, Clapham J. Best practice guidelines for skin and wound care in epidermolysis bullosa. An International Consensus. *Wounds International.* 2017. Available at: https://af13d689-15eb-4199-8733-e91a7bb8ae3f.usrfiles.com/ugd/af13d6_01ed147ab87e49c584c20a917c47f19f.pdf. Accessed on: June 20, 2024.
7. Kern JS, Sprecher E, Fernandez MF, et al. Efficacy and safety of Olegel-S10 (birch triterpenes) for epidermolysis bullosa: results from the phase III randomized double-blind phase of the EASE study. *Br J Dermatol*. 2023;188:12-21.