Policy Number	**RX501.164**
Policy Effective Date	**12/15/2024**

Beremagene geperpavec-svdt

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Related Policies (if applicable)
None

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current peer-reviewed scientific literature. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and acceptable standards of medical practice. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted

study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

Beremagene geperpavec-svdt (Vyjuvek™) **may be considered medically necessary** for the treatment of dystrophic epidermolysis bullosa (DEB) when **ALL** of the following criteria are met:

- Individual is aged 6 months or older; and
- Individual has documented genetic mutation(s) in the collagen type VII alpha 1 chain (*COL7A1*) gene; and
- Individual has clinical manifestation consistent with DEB.

Beremagene geperpavec-svdt (Vyjuvek™) **is considered experimental, investigational and/or unproven** for all other indications, including but not limited to:

- Current evidence or a history of squamous cell carcinoma in the area that will undergo treatment; or
- Individual is actively receiving chemotherapy or immunotherapy; or
- Individual has received a skin graft in the past three (3) months.

Policy Guidelines

None.

Description

Dystrophic epidermolysis bullosa (DEB), one of the major forms of a group of conditions called epidermolysis bullosa, is a rare condition that causes fragile, blistering skin. Blisters may appear in response to minor injury, or even from heat, rubbing, or scratching. The signs and symptoms of DEB usually appears in infancy and can vary widely among affected individuals. In mild cases, blistering may primarily affect the hands, feet, knees, and elbows. Severe cases of this condition involve widespread blistering that can lead to vision loss, scarring, and other serious medical problems.

Researchers classify dystrophic epidermolysis bullosa into major types based on the inheritance pattern and features of the condition. Although the types differ in severity, their features overlap significantly, and they are all caused by mutations in the collagen type VII alpha 1 chain (*COL7A1*) gene. *COL7A1* gene mutations alter the structure or disrupt the production of the type VII collagen subunit protein. These changes affect the production of type VII collagen. When type VII collagen is abnormal or missing, the formation of anchoring fibrils is impaired. A shortage of these fibrils disrupts the connection of the epidermis to the dermis, and friction or

other minor trauma can cause the two skin layers to separate. This separation leads to the formation of blisters, which can cause extensive scarring as they heal. (1)

Treatment for DEB may first include lifestyle changes and home care, with medications to help control pain and itching. Recently, the U.S. Food and Drug Administration (FDA) approved the first gene therapy treatment for DEB. Vyjuvek is a genetically modified herpes-simplex virus used to deliver normal copies of the *COL7A1* gene to the wounds. COL7 molecules arrange themselves into long, thin bundles that form anchoring fibrils that hold the epidermis (skin) and dermis together, which is essential for maintaining the integrity of the skin. Vyjuvek has also been modified to eliminate its ability to replicate in normal cells. Vyjuvek is mixed into an excipient (non-active ingredient) gel prior to topical application. A healthcare professional evenly applies Vyjuvek gel in droplets to a patient's wounds once a week. (2)

Regulatory Status
On May 19, 2023, the U.S. FDA approved beremagene geperpavec-svdt (Vyjuvek™) (Krystal Biotech, Inc.) for the 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. (3)

Rationale

This medical policy was developed in July 2023 and is based on the clinical study provided to the U.S. Food and Drug Administration for approval.

Beremagene geperpavec-svdt (Vyjuvek™) (3)
The efficacy of Vyjuvek gel in subjects one year of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (*COL7A1)* gene was evaluated in one randomized, double-blind, intra-subject placebo-controlled trial. All study subjects had clinical manifestations consistent with DEB and genetically confirmed mutation(s) in the *COL7A1* gene. Two comparable wounds in each subject were selected and randomized to receive either topical application of Vyjuvek gel or the placebo (excipient gel) weekly for 26 weeks.

The study enrolled 31 subjects (20 males and 11 females), including 30 subjects with autosomal recessive DEB and one subject with autosomal dominant DEB. The size of the Vyjuvek gel-treated wounds ranged from 2 to 57 cm^2 , with 74% of wounds <20 cm^2 and 19% from 20 to <40 cm^2 . The size of the placebo gel-treated wounds ranged from 2 to 52 cm^2 , with 71% of wounds <20 cm^2 and 26% from 20 to <40 cm^2 . The mean age of the subjects was 17 years (1 year to 44 years), including 61% pediatric subjects (n=19, age from 1 year to <17 years). Sixty-four percent of subjects were White; 19% were Asian, and the remainder were American Indian or Alaska Native.

Efficacy was established on the basis of improved wound healing defined as the difference in the proportion of complete (100%) wound closure at 24 Weeks confirmed at two consecutive study visits 2 weeks apart, assessed at Weeks 22 and 24 or at Weeks 24 and 26, between the Vyjuvek gel-treated and the placebo gel-treated wounds. Efficacy was supported by the difference in the proportion of complete wound closure assessed at Weeks 8 and 10 or at Weeks 10 and 12 between the Vyjuvek gel-treated and the placebo gel-treated wounds. Complete (100%) wound closure was defined as durable wound closure evaluated at two consecutive visits two weeks apart. The efficacy results are summarized in Table 1.

Table 1. Summary of the Efficacy Results for Vyjuvek gel (ITT Population)

Wound Closure Assessment Timepoints	Complete Wound Closure, n (%) Vyjuvek gel (N=31)	Complete Wound Closure, n (%) Placebo gel (N=31)	Treatment Difference (95% CI)	p value
Weeks 22 & 24 or Weeks 24 & 26	20 (65)	8 (26)	39% (14, 63)	0.012
Weeks 8 & 10 or Weeks 10 & 12	21(68)	7 (23)	45% (22, 69)	0.003

ITT: intention-to-treat.

Summary of Evidence

Based on the results of the clinical trial provided to the U.S. Food and Drug Administration for approval, beremagene geperpavec-svdt (Vyjuvek™) may be considered medically necessary for the treatment of wounds in individuals 6 months of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (*COL7A1*) gene. Beremagene geperpavec-svdt (Vyjuvek™) is considered experimental, investigational and/or unproven for all other indications.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J3401

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

References

1. MedlinePlus. Dystrophic epidermolysis bullosa. National Library of Medicine. Feb 01, 2020. Available at: <https://www.medlineplus.gov> (accessed July 17, 2023).
2. FDA New Release. FDA Approved First Topical Gene Therapy for Treatment of Wounds in Patients with Dystrophic Epidermolysis Bullosa. May 19, 2023. Available at: <https://www.fda.gov> (accessed July 17, 2023).
3. FDA. Highlights of Prescribing Information - Vyjuvek™ (beremagene geperpavec-svdt). Revised May 2023. Available at: <https://www.fda.gov> (accessed July 17, 2023).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
12/15/2024	Reviewed. No changes.
11/15/2023	New medical document. Beremagene geperpavec-svdt (Vyjuvek™) may be considered medically necessary for the treatment of dystrophic epidermolysis bullosa (DEB) when ALL of the following criteria are met: individual is aged 6 months or older; individual has documented genetic mutation(s) in the collagen type VII alpha 1 chain (*COL7A1*) gene; and individual has clinical manifestation consistent with DEB. Beremagene geperpavec-svdt (Vyjuvek™) is considered experimental, investigational and/or unproven for all other indications, including but not limited to: current evidence or a history of squamous cell carcinoma in the area that will undergo treatment; individual is actively receiving chemotherapy or immunotherapy; or individual has received a skin graft in the past three (3) months.