Medical Policy

BlueCross BlueShield Kansas
An Independent licensee of the
Blue Cross Blue Shield Association

Title: Vyjuvek (beremagene geperpavec- svdt) Medical Drug Criteria Program Summary

Professional / Institutional
Original Effective Date: January 1, 2024
Latest Review Date:
Current Effective Date: January 1, 2024

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Vyjuvek™ (beremagene geperpavec-svdt) Biological suspension mixed with excipient gel for topical application	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		1

See package insert for FDA prescribing information:
https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Epidermolysis Bullosa	Epidermolysis bullosa (EB) encompasses a number of disorders characterized by recurrent blister formation as the result of structural fragility within the skin and selected other tissues caused by mutations in CLO7A1, the gene encoding the anchoring fibril component, collagen VII. All types and subtypes of EB are rare; the overall incidence and prevalence of the disease within the United States is approximately 19 per one million live births and 8 per one million population, respectively. Clinical manifestations range widely, from localized blistering of the hands and feet to generalized blistering of the skin and oral cavity, and injury to many internal organs. Each EB subtype is known to arise from mutations within the genes encoding for several different proteins, each of which is intimately involved in the maintenance of keratinocyte structural stability or adhesion of the keratinocyte to the underlying dermis. EB is best diagnosed and subclassified by the collective findings obtained via detailed personal and family history, in concert with the results of immunofluorescence antigenic mapping, transmission electron microscopy, and in some cases, by DNA analysis. Optimal patient management requires a multidisciplinary approach and revolves around the protection of susceptible tissues against trauma, use of sophisticated wound care dressings, aggressive nutritional support, and early medical or surgical interventions to correct whenever possible the extracutaneous complications. Prognosis varies considerably and is based on both EB subtype and the overall health of the patient. Currently, there is no cure for EB. Supportive care includes daily wound care, bandaging, and pain management as needed.(2,3)
Efficacy	Vyjuvek (beremagene geperpavec) is a replication-defective and nonintegrating, modified herpes simplex virus 1 vector that is topically applied to deliver a functional version of the COL7A1 gene directly to skin cells. Treatment with Vyjuvek seeks to restore the production of type VII collagen in patients with EB. The GEM-1 trial evaluated the efficacy and safety of Vyjuvek in healing skin wounds in nine adult and pediatric patients. After 12 weeks, complete wound closure (reduction in wound area from baseline greater than or equal to 95 percent) was observed in 83 percent of the Vyjuvek treated wounds compared with 14 percent of the wounds treated with placebo. In many cases, the wound-healing duration was longer than 6 months. Adverse effects were mild and included fever, rash, and itching. Exclusion criteria included the presence of medical illness expected to complicate participation, presence of serum antibodies to type collagen VII, active infection in the area that will undergo treatment, evidence of systemic infection, and current evidence or a history of squamous cell carcinoma in the area that will undergo treatment.(3,4) The GEM-3 trial was a multi-center, randomized, double-blind placebo-controlled phase 3 trial that enrolled 31 people aged 6 months or older. Treatment response to Vyjuvek was not associated with anti-HSV-1 serostatus at baseline or with anti-COL7 seroconversion. The HSV-1 serology status of the study patients was as follows:(5,7) • At baseline, 14 of the 22 patients (63.6%) were anti-HSV-1

	seropositive and 8 were seronegative, in agreement with seropositivity rates of the general US population
	• 6 of 8 (75.0%) baseline seronegative patients seroconverted at 6 months
	  ○ For baseline seropositive patients, where quantitative differences at study completion could be calculated, antibody responses were not determined to be meaningful
	• At baseline, 1 of 22 patients (4.5%) was positive for anti-COL7 antibodies.
	  ○ 13 of 18 patients (72.2%) with matched serum samples seroconverted by 6 months; no clinically significant immunologic reactions or differences in treatment response were seen
	
	GEM-3 met the primary and secondary efficacy endpoints in complete wound healing relative to placebo. Complete wound healing at 3 and 6 months in patients with dystrophic epidermolysis bullosa was more likely with topical administration of Vyjuvek than with placebo. An open-label extension study is underway to assess the long-term safety and efficacy of Vyjuvek for patients greater than or equal to 6 months of age, regardless of prior enrollment in GEM-3.(5,6)

REFERENCES

Number	Reference
1	Vyjuvek prescribing information. Krystal Biotech, Inc. May 2023.
2	Fine JD. Inherited epidermolysis bullosa. Orphanet J Rare Dis. 2010 May 28;5:12. doi: 10.1186/1750-1172-5-12
3	ClinicalTrials.gov Identifier: NCT03536143. A phase I/II study of KB103, a topical HSV1-COL7, on DEB patients. Updated January 31, 2023. https://clinicaltrials.gov/ct2/show/NCT03536143?cond=NCT03536143&draw=2&rank=1.
4	Gurevich I, Agarwal P, Zhang P, et al. In vivo topical gene therapy for recessive dystrophic epidermolysis bullosa: a phase 1 and 2 trial. *Nat Med*. 2022;28(4):780-788. doi:10.1038/s41591- 022-01737-y
5	Marinovich, M. Peter, Gonzalez, Mercedes E., et. al. GEM-3: A Phase 3 Study of Beremagene Geperpavec (B-VEC), an Investigational, Topical Gene Therapy, for the Treatment of Dystrophic Epidermolysis Bullosa (DEB). https://ir.krystalbio.com/static-files/bb74b04e-7e3d-44f8-afda-5469a3cf16b4.
6	Guide, Sharon V, Gonzalez, Mercedes E., et al. Trial of Beremagene Geperpavec (B-VEC) for Dystrophic Epidermolysis Bullosa. N Engl J Med. 2022 Dec 15;387(24):2211-2219. doi: 10.1056/NEJMoa2206663.
7	Marinovich, M. Peter, Gonzalez, Mercedes E., et al. GEM-3: Phase 3 Safety and Immunogenicity Results of Beremagene Geperpavec (B-VEC), an Investigational, Topical Gene Therapy for Dystrophic Epidermolysis Bullosa (DEB). https://ir.krystalbio.com/static-files/52bf3182-9694-43c1- 9e6b-0af5d4952a91.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
	Vyjuvek	beremagene geperpavec- svdt gel	5000000000 PFU/2.5ML	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Vyjuvek	beremagene geperpavec-svdt gel	5000000000 PFU/2.5ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of epidermolysis bullosa as confirmed by ONE of the following: A. Immunofluorescence mapping (IFM) **OR** B. Transmission electron microscopy (TEM) **OR** C. Genetic testing **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The patient does NOT have current evidence or a history of squamous cell carcinoma in the area that will undergo treatment **AND** 4. The patient does NOT have an active infection in the area that will undergo treatment **AND** 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., dermatologist, geneticist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication **Length of Approval:** 6 months **Renewal Evaluation** **Target Agents(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization criteria **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The patient does NOT have current evidence or a history of squamous cell carcinoma in the area that will undergo treatment **AND**

Module	Clinical Criteria for Approval
	4. The patient does NOT have an active infection in the area that will undergo treatment **AND** 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., dermatologist, geneticist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication **Length of Approval: 12 months**

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

REVISIONS	
Posted 12-01-2023 Effective 01-01-2024	Policy added to the bcbsks.com web site.