PREMERA | BLUE CROSS

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PHARMACY / MEDICAL POLICY – 5.01.635

Pharmacologic Treatment of Epidermolysis Bullosa

Effective Date:	Sept. 1, 2023	RELATED MEDICAL POLICIES:
Last Revised:	Jan. 1, 2024	None
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Epidermolysis Bullosa (EB) is a collection of rare genetic disorders that affect the fragility of the skin. These disorders are characterized by abnormal structures that disrupt either the junction between the dermis and epidermis or the basal layer of the epidermis itself. As a result, the skin becomes more susceptible to damage from physical pressure. Common signs of EB include the formation of blisters, erosion of the skin, the presence of nonhealing ulcers, and the development of scars after minor injuries. EB is classified into four major categories, such as, epidermolysis bullosa simplex (EBS), junctional epidermolysis bullosa (JEB), dystrophic epidermolysis bullosa (DEB) and kindler epidermolysis bullosa (KEB).

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
Vyjuvek (beremagene geoerpavec-svdt) Topical	**Vyjuvek (beremagene geoerpavec-svdt) may be considered medically necessary in individuals with dystrophic epidermolysis bullosa when the following criteria are met:** • Individual is 6 months of age and older **AND** • Individual has a confirmed diagnosis of dystrophic epidermolysis bullosa **AND** • Individual has documentation showing mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene **AND** • Confirmed negative pregnancy status **AND** • Individual does not have a current or history of squamous cell carcinoma in the wound **AND** • Must be applied by the healthcare provider **AND** • Use is prescribed by or in consultation with a dermatologist or medical geneticist **AND** • The maximum weekly dose prescribed is based on the age of the individual: ○ 1.6×10^9 PFU (0.8 mL) for individuals 6 months to< 3 years old ○ 3.2×10^9 PFU (1.6 mL) for individuals 3 years and older ***Note:** PFU = Plaque forming units. Maximum weekly volume is the volume after mixing Vyjuvek suspension with excipient gel

Drug	Investigational
Vyjuvek (beremagene geoerpavec-svdt)	**All other uses of Vyjuvek (beremagene geoerpavec-svdt) for conditions not outlined in this policy are considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Vyjuvek (beremagene geoerpavec-svdt) may be approved up to 6 months.**
Re-authorization criteria	**Future re-authorization of Vyjuvek (beremagene geoerpavec-svdt) may be approved up to 6 months as long as the drug-specific coverage criteria are met, and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation, and medication history.

Coding

Code	Description
HCPCS	
J3401	Beremagene geperpavec-svdt for topical administration, containing nominal 5 x 109 PFU/ml vector genomes, per 0.1 ml (Vyjuvek) (new code effective 1/1/2024)
J3590	Unclassified drugs

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Consideration of Age

Age limits specified in this policy are determined according to FDA-approved indications where applicable.

Benefit Application

Vyjuvek is managed under the pharmacy and medical benefit.

Evidence Review

Dystrophic Epidermolysis Bullosa Background

Dystrophic Epidermolysis Bullosa (DEB) is a prominent subgroup within the category of conditions known as epidermolysis bullosa (EB). DEB is characterized by formation of blisters on the skin and mucosal membranes, which subsequently heal but leave behind scar tissue. The underlying cause of DEB is attributed to mutations occurring in the COL7A1 gene. This gene encodes the alpha-1 chain of type VII collagen. Collagen VII is the primary component of the anchoring fibrils situated beneath the lamina densa of the epidermal basement membrane zone. DEB manifests in four major subtypes, along with several rare, dominant, or recessive variations. The clinical features commonly observed in DEB include skin fragility, blister formation, scarring, nail abnormalities, and the development of milia in areas where blisters have healed. The therapeutic approach for DEB includes supportive care. These includes the wound care to promote healing, effective infection control measures to prevent and manage infections, strategies to address and treat complications that may arise, and provision of nutritional support to ensure optimal nourishment for the patient.

Vyjuvek (beremagene geoerpavec-svdt)

Vyjuvek is a non-integrating gene therapy that employs a genetically modified, replication-deficient, herpes-simplex virus type 1 vector. It is indicated for the treatment of wounds in individuals 6 months of age and older with dystrophic epidermolysis bullosa with mutation in the collagen type VII alpha 1 chain (COL7A1) gene. Vyjuvek has the ability to transduce both keratinocytes and fibroblasts. Upon cellular entry, the vector genome is delivered to the nucleus,

initiating the transcription of the human COL7A1 gene. The resulting transcripts enable the production and secretion of mature COL7 protein by cell. These COL7 molecules self-assemble into elongated, slender bundles known as anchoring fibrils. Anchoring fibrils play a vital role in maintaining the cohesion between the epidermis and dermis, thereby ensuring the integrity of the skin.

Vyjuvek is formulated as a biological suspension combined with an excipient gel for topical application. The recommended dose of Vyjuvek is determined based on the individual's age. For individuals aged between six months and less than three years old, the maximum weekly recommended dose is 1.6 X 10^9 plaque-forming units (PFU). For individuals aged three years and older, the maximum weekly recommended dose is 3.2 X 10^9 PFU. The most common adverse reactions associated with Vyjuvek treatment include itching, chills, redness, rash, cough, and runny nose. There is currently no available data regarding the use of Vyjuvek in the pregnant women.

Evidence of Efficacy

The efficacy and safety of Vyjuvek was assessed in a phase 3, randomized, double-blind, intra-subject placebo-controlled trial. This trial included 31 individuals aged 6 months of age and older with dystrophic epidermolysis bullosa (DEB) with mutations in the COL7A1 gene. Each participant had two comparable wounds selected based on the size, region, and appearance. These wounds were randomly assigned to receive either topical application of Vyjuvek or the placebo (excipient gel) once a week for 26 weeks.

In this trial the size of wounds treated with Vyjuvek gel ranged from 2 to 57 cm^2, with 74% of wounds measuring less than 20 cm^2. On the other hand, the size of the wound treated with placebo gel ranged from 2 to 52 cm^2, with 71% of wounds measuring less than 20 cm^2. The primary efficacy outcome was determined by the proportion of complete wound closure at 24 weeks, confirmed by two consecutive study visits spaced two weeks apart (at week 22 and 24 or at week 24 and 26). This outcome was compared between the wounds treated with Vyjuvek and the wounds treated with placebo gel. Complete wound closure was defined as the sustained closure of the wound observed at two consecutive visits two weeks apart. At the specified time points (week 22 and 24 or week 24 and 26), the proportion of wounds achieving complete closure in the Vyjuvek gel-treated group was 65%, whereas the proportion of complete closure in the placebo-treated group was 26%, resulting in a significant p-value of 0.012.

The secondary efficacy outcome assessed the proportion of complete wound closure at weeks 8 and 10, or at week 10 and 12, again comparing the treatment group and the placebo group. At

the specified time points (week 8 and 10 or week 10 and 12), the proportion of wounds achieving complete closure in the Vyjuvek gel-treated group was 68%, whereas the proportion of complete closure in the placebo-treated group was 23%, resulting in a significant p-value of 0.003.

References

1. Martin L, Johann B, et al. Epidermolysis bullosa: Epidemiology, pathogenesis, classification, and clinical features. Epidermolysis bullosa: Epidemiology, pathogenesis, classification, and clinical features - UpToDate. Accessed June 5, 2023.
2. Krystal Biotech, Inc. Ph 3 Efficacy and Safety of B-VEC for the Treatment of DEB (GEM-3). Available at: Ph 3 Efficacy and Safety of B-VEC for the Treatment of DEB - Full Text View - https://www.clinicaltrials.gov/ct2/show/NCT04491604. Accessed June 5, 2023.
3. VYJUVEK (beremagene geperpavec-svdt) [package insert]. Pittsburgh, PA. Krystal Biotech, Inc. Revised May 2023.

History

Date	Comments
07/01/23	New policy, approved June 13, 2023. Added coverage criteria for Vyjuvek™ for individuals 6 months of age and older with dystrophic epidermolysis bullosa with confirmed mutation in COL7A1 gene. Added HCPC code J3590 for Vyjuvek™.
09/01/23	Interim Review, approved August 7, 2023. Updated Vyjuvek initial authorization and re-authorization time duration to 6 months.
01/01/24	Coding update. Added new HCPCS code J3401.

benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.

Discrimination is Against the Law

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Washington residents: You can also file a civil rights complaint with the Washington State Office of the Insurance Commissioner, electronically through the Office of the Insurance Commissioner Complaint Portal available at https://www.insurance.wa.gov/file-complaint-or-check-your-complaint-status, or by phone at 800-562-6900, 360-586-0241 (TDD). Complaint forms are available at https://fortress.wa.gov/oic/onlineservices/cc/pub/complaintinformation.aspx.

Alaska residents: Contact the Alaska Division of Insurance via email at insurance@alaska.gov, or by phone at 907-269-7900 or 1-800-INSURAK (in-state, outside Anchorage).

Language Assistance

ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 800-722-1471 (TTY: 711).

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 800-722-1471 (TTY: 711).

注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 800-722-1471 (TTY：711）。

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 800-722-1471 (TTY: 711).

주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 800-722-1471 (TTY: 711) 번으로 전화해 주십시오.

ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 800-722-1471 (телетайп: 711).

LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 800-722-1471 (TTY: 711).

MO LOU SILAFIA: Afai e te tautala Gagana fa'a Sāmoa, o loo iai auaunaga fesoasoan, e fai fua e leai se totogi, mo oe, Telefoni mai: 800-722-1471 (TTY: 711).

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注意事項：日本語を話される場合、無料の言語支援をご利用いただけます。800-722-1471 （TTY:711）まで、お電話にてご連絡ください。

PAKDAAR: Nu saritaem ti Ilocano, ti serbisyo para ti baddang ti lengguahe nga awanan bayadna, ket sidadaan para kenyam. Awagan ti 800-722-1471 (TTY: 711).

УВАГА! Якщо ви розмовляєте українською мовою, ви можете звернутися до безкоштовної служби мовної підтримки. Телефонуйте за номером 800-722-1471 (телетайп: 711).

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ਧਿਆਨ ਦਿਓ: ਜੇ ਤੁਸੀਂ ਪੰਜਾਬੀ ਬੋਲਦੇ ਹੋ, ਤਾਂ ਭਾਸ਼ਾ ਵਿੱਚ ਸਹਾਇਤਾ ਸੇਵਾ ਤੁਹਾਡੇ ਲਈ ਮੁਫਤ ਉਪਲਬਧ ਹੈ। 800-722-1471 (TTY: 711) 'ਤੇ ਕਾਲ ਕਰੋ।

เรียน: ถ้าคุณพูดภาษาไทยคุณสามารถใช้บริการช่วยเหลือทางภาษาได้ฟรี โทร 800-722-1471 (TTY: 711).

ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 800-722-1471 (TTY: 711).

UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer 800-722-1471 (TTY: 711).

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