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PHARMACY / MEDICAL POLICY – 5.01.635

Pharmacologic Treatment of Epidermolysis Bullosa

BCBSA Ref. Policy: 5.01.47

Effective Date:	Mar. 1, 2025	RELATED MEDICAL POLICIES:
Last Revised:	Feb. 24, 2025	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
Filsuvez (birch triterpenes) Topical	**Filsuvez (birch triterpenes) may be considered medically necessary for the treatment of dystrophic epidermolysis bullosa (DEB) or junctional epidermolysis bullosa (JEB) when all the following criteria are met:** • The individual is aged 6 months or older **AND** • Has been diagnosed with DEB or JEB confirmed by genetic testing **AND** • Has had at least one open wound associated with DEB or JEB for ≥ 21 days that will be treated with Filsuvez (birch triterpenes) **AND** • Filsuvez (birch triterpenes) will not be used concurrently with Vyjuvek (beremagene geperpavec-svdt) **AND** • Filsuvez (birch triterpenes) is prescribed by or in consultation with a dermatologist or medical geneticist **AND** • Filsuvez (birch triterpenes) will be limited to one application per wound per day
Vyjuvek (beremagene geperpavec-svdt) Topical	**Vyjuvek (beremagene geperpavec-svdt) may be considered medically necessary in individuals with dystrophic epidermolysis bullosa when all the following criteria are met:** • The individual is aged 6 months or older **AND** • Has a confirmed diagnosis of dystrophic epidermolysis bullosa **AND** • Has documentation showing mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene **AND** • Confirmed negative pregnancy status **AND** • Does not have a current or history of squamous cell carcinoma in the wound **AND**

Drug	Medical Necessity
	• Vyjuvek (beremagene geperpavec-svdt) will be applied by a healthcare provider **AND** • Vyjuvek (beremagene geperpavec-svdt) will not be used concurrently with Filsuvez (birch triterpenes) **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 x 10^9 PFU (0.8 mL) for individuals 6 months to< 3 years old ○ 3.2 X 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
• **Filsuvez (birch triterpenes)** • **Vyjuvek (beremagene geperpavec-svdt)**	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.** **All other uses of Filsuvez (birch triterpenes) and Vyjuvek (beremagene geperpavec-svdt) for conditions not outlined in this policy are considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Non-formulary exception reviews for Filsuvez (birch triterpenes) and Vyjuvek (beremagene geperpavec-svdt) may be approved for up to 12 months.**

Length of Approval	
Approval	**Criteria**
	All other reviews for Filsuvez (birch triterpenes) and Vyjuvek (beremagene geperpavec-svdt) may be approved for up to 6 months.
Re-authorization criteria	**Non-formulary exception reviews for Filsuvez (birch triterpenes) and Vyjuvek (beremagene geperpavec-svdt) may be approved for up to 12 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.** **All other reviews for Filsuvez (birch triterpenes) and Vyjuvek (beremagene geperpavec-svdt) may be approved for 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 (Vyjuvek), per 0.1 ml
J3490	Unclassified drugs (use to report: Filsuvez)

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

Filsuvez (birch triterpenes) is managed under the pharmacy and medical benefit. Vyjuvek (beremagene geperpavec-svdt) is managed under the 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 individual.

Vyjuvek (beremagene geperpavec-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 1.6×10^9 plaque-forming units (PFU). For individuals aged three years and older, the maximum weekly recommended dose is 3.2×10^9 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.

Filsuvez (birch triterpenes)

The Phase 3 EASE trial, which enrolled 223 individuals with epidermolysis bullosa (EB). Of those individuals treated with Filsuvez, 41.3% achieved complete target wound closure within 45 days compared with 28.9% in the placebo control group (P = 0.013). However, key secondary endpoints were not met, including complete wound closure at 90 days compared to placebo. During the trial, about 80% of individuals changed their wound dressings every 1 to 2 days, with every 2 days being somewhat more common than daily at Days 30, 60, and 90 of the double-blind phase among individuals treated with Filsuvez. During the entire 90-day double-blind treatment period, separation in target wound closure occurred around Day 30 with the difference narrowing around Day 90. None of the secondary endpoints in the trial were met, except for a greater reduction in pain associated with dressing changes using the Wong Baker Faces scale in participants ≥4 years of age at Day 14 (P = 0.022). The difference between Filsuvez and vehicle were not statistically different for all other time points for which this outcome was measured, including at Day 90. Adverse events (AEs) occurred with similar frequency for Filsuvez (81.7%) compared with control gel (80.7%). AEs were predominantly of mild to moderate intensity (4.6% were severe). Any AEs leading to study withdrawal occurred in three individuals in the Filsuvez group and two individuals in the control group. One individual in the Filsuvez group and no individuals in the control group withdrew from the trial due to a serious AE that was deemed related to study treatment.

Practice Guidelines and Position Statements

European Reference Network for Rare Skin Diseases

The European Reference Network for Rare and Undiagnosed Skin Diseases published expert consensus clinical position statements in 2021 regarding practical recommendations for the management of patients suspected or diagnosed with epidermolysis bullosa covering diagnosis, wound management, oral care and treatment of pain and itch. They also published consensus clinical position recommendations in 2020 to aid decision-making and optimize clinical care by non-epidermolysis bullosa expert health professionals encountering emergency situations in babies, children and adults with epidermolysis bullosa. Both consensus statements were published prior to the Food and Drug Administration (FDA) approval beremagene geperpavec-svdt.

Dystrophic Epidermolysis Bullosa Research Association

International consensus best practice guidelines skin and wound care in epidermolysis bullosa were published in 2017. These guidelines were also published prior to the FDA approval beremagene geperpavec-svdt.

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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.
07/01/24	Annual Review, approved June 11, 2024. Added coverage criteria for Filsuvez (birch triterpenes). Updated Vyjuvek (beremagene geperpavec-svdt) coverage criteria to indicate that the product is not used concurrently with Filsuvez (birch triterpenes).
03/01/25	Annual Review, approved February 24, 2025. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA).

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member 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.