BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

FILSUVEZ® (birch triterpenes) topical gel Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Filsuvez (birch triterpenes) topical gel and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Dermatologist

  2. Individual is 6 months of age or older

  3. Individual has a confirmed diagnosis of wounds associated with dystrophic epidermolysis bullosa (DEB) and junctional epidermolysis bullosa (JED)

  4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:

a. Skin biopsy for immunofluorescence mapping (IFM) of a recently made blister
b. Genetic testing to confirm the exact EB type (see Definitions section)

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)
6. Wounds are described as partial thickness and are outside of the anogenital area
7. Individual does not have epidermolysis bullosa simplex (EBS)
8. Individual has wounds that are 10 cm^2 to 50 cm^2 in size and are between 21 days to less than 9 months in age
9. Individual does not have wounds that are older than 9 months or more
10. Individual does not have wounds that show clinical signs of infection
11. Individual does not have a history of or current squamous cell carcinoma
12. Individual has not undergone stem cell transplant or gene therapy for the treatment of inherited EB

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Filsuvez (birch triterpenes) topical gel and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Dermatologist
2. Individual's condition has responded while on therapy with response defined as achieved and maintains some degree of wound closure but has not yet attained complete wound closure (i.e., re-epithelialization without drainage) of all wounds from EB
3. Individual has been adherent with the medication
4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)
5. Wounds are described as partial thickness and are outside of the anogenital area
6. Individual does not have epidermolysis bullosa simplex (EBS)
7. Individual has wounds that are 10 cm^2 to 50 cm^2 in size and are between 21 days to less than 9 months in age

8. Individual does not have wounds that are older than 9 months or more
9. Individual does not have wounds that show clinical signs of infection
10. Individual does not have a history of or current squamous cell carcinoma
11. Individual has not undergone stem cell transplant or gene therapy for the treatment of inherited EB

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Filsuvez (birch triterpenes) topical gel is indicated for the treatment of wounds associated with dystrophic epidermolysis bullosa (DEB) and junctional epidermolysis bullosa (JEB) in adult and pediatric patients 6 months of age and older.

Filsuvez (birch triterpenes) topical gel is a sterile botanical drug product for topical use and contains birch triterpenes in an oil base. Birch triterpenes is composed of a mixture of pentacyclic triterpenes. The mechanism of action of Filsuvez (birch triterpenes) in the treatment of wounds associated with epidermolysis bullosa (EB) is unknown.

In addition to Filsuvez (birch triterpenes) topical gel, Vyjuvek (beremagene geperpavec-svdt) topical gel is a herpes-simplex virus type 1 (HSV-1) vector-based gene therapy indicated for the treatment of wounds in patients 6 months of age and older with DEB with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene. Collagen VII is the main component of the anchoring fibrils located below the lamina densa of the epidermal basement membrane zone.

EB is a rare group of genetic skin fragility disorders characterized by blistering of the skin in response to minor injury. Onset of EB is usually at birth or shortly thereafter. Individuals repeatedly develop painful wounds that take days to months to heal. Current treatment of EB involves is primarily preventative and supportive measures including protection from mechanical forces by avoiding rubbing, early treatment of wounds to prevent infections, and protection of the wound with adequate non-adhesive dressings to enable healing.

EB should be suspected in individuals with a history of recurrent blistering or erosions following mild trauma and in neonates presenting with blisters and erosions without another obvious etiology. The accurate identification of the EB subtype is performed only in specialized laboratories and requires immunofluorescence mapping (IFM) with specific monoclonal antibodies targeting EB-specific proteins, transmission electron microscopy (TEM), or mutational analysis. Skin biopsy for immunofluorescence mapping (IFM) of a freshly induced blister is the first-line

approach for the diagnosis of EB in most cases. Genetic testing is strongly recommended in all patients to confirm the exact EB diagnosis.

There are four major types of EB with more than 30 subtypes. Classification is based upon the ultrastructural level of blister formation within the epidermal basement membrane zone. Major types of EB include dystrophic epidermolysis bullosa (DEB; sublamina densa), junctional epidermolysis bullosa (JEB; intralaminar lucida), epidermolysis bullosa simplex (EBS; intraepidermal), and Kindler epidermolysis bullosa (KEB; intraepidermal, intralaminar lucida, and sublamina densa).

Extracutaneous manifestations are common to all severe subtypes of EB and include hair and nail abnormalities, intraoral blistering and scarring, dental abnormalities, esophageal strictures, and genitourinary abnormalities. Skin infections, sepsis, malnutrition, anemia, and squamous cell carcinoma are frequent complications and are associated with significant morbidity and mortality.

DEB is characterized by blistering of the skin and mucosae that heal with scarring and milia (whiteheads). It is caused by autosomal dominant or recessive mutations in the *COL7A1* gene, encoding the alpha-1 chain of type VII collagen, resulting in tissue cleavage below the lamina densa of the basement membrane zone. In severe recessive dystrophic epidermolysis bullosa (RDEB), blistering starts at birth.

JEB is characterized by blistering of the skin and mucosae that heal with scarring. Most cases of severe JEB are caused by autosomal recessive mutations in the *LAMA3*, *LAMB3*, and *LAMC2* genes, encoding laminin 332, resulting in tissue cleavage in the lamina lucida of the basement membrane zone. A severe form of JEB presents with extensive, mucocutaneous blistering at birth and is associated with early mortality. An intermediate form of JEB is caused by mutations predominantly affecting *COL17A1*, encoding type XVII collagen, and shows a generally milder course.

EBS is the most common type of EB and is characterized by localized or generalized, trauma-induced skin blistering that heals without scarring. In most cases, it is caused by autosomal dominant mutations in the *KRT5* and *KRT14* genes encoding keratins, resulting in tissue cleavage at the level of the basal keratinocytes.

KEB is a distinct type of EB characterized by skin blistering, photosensitivity, progressive poikiloderma, and extensive skin atrophy. It is caused by biallelic loss-of-function variants in the *FERMT1* gene, encoding the focal adhesion protein fermitin family homolog 1 (FFH1).

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Classification of classical epidermolysis bullosa (EB):

EB type	Level of skin cleavage	Inheritance	Mutated gene(s)	Targeted protein(s)
Dystrophic epidermolysis bullosa (DEB)	Dermal below the lamina densa, within the upper papillary dermis at level of anchoring fibrils	Autosomal dominant	*COL7A1*	Type VII collagen
		Autosomal recessive	*COL7A1*	Type VII collagen

Junctional epidermolysis bullosa (JEB)	Junctional within the lamina lucida of the dermoepidermal junction	Autosomal recessive	*LAMA3*, *LAMB3*, *LAMC2*	Laminin 332
			COL17A1	Type XVII collagen
			ITGA6, *ITGB4*	Integrin alpha-6 beta-4
			ITGA3	Integrin alpha-3 subunit
Epidermolysis bullosa simplex (EBS)	Intraepidermal within the basal layer of keratinocytes	Autosomal dominant	*KRT5*, *KRT14*	Keratin 5, Keratin 14
			PLEC	Plectin
			KLH24	Kelch-like member 14
		Autosomal recessive	*KRT5*, *KRT14*	Keratin 5, Keratin 14
			DST	Bullous pemphigoid antigen 230 (BP230) (syn. BPAG1e, dystonin)
			EXPH5 (syn. *SLAC2B*)	Exophilin-5 (syn. synaptotagmin-like protein homolog lacking C2 domains b, Slac2-b)
			EXPH5 (syn. *SLAC2B*)	Exophilin-5 (syn. synaptotagmin-like protein homolog lacking C2 domains b, Slac2-b)
			PLEC	Plectin
			CD151 (syn. *TSPAN24*)	CD151 antigen (syn. tetraspanin 24)
Kindler epidermolysis bullosa (KEB)	Mixed/multiple (intraepidermal, intralaminar lucida, or sublamina densa	Autosomal recessive	*FERMT1* (syn. *KIND1*)	Fermitin family homolog 1 (syn. kindlin-1)

Resources:

Filsuvez (birch triterpenes) 10% topical gel product information, revised by Amryt Pharmaceuticals DAC. 12-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 01, 2024.

Laimer M, Bauer J, Murrell DF. Epidermolysis bullosa: Epidemiology, pathogenesis, classification, and clinical features. In: UpToDate, Hand JL, Corona R. Editor(s) (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2024. Topic last updated February 21, 2024. Accessed March 01, 2024.

Bruckner AL, Murrell DF. Diagnosis of epidermolysis bullosa. In: UpToDate, Hand JL, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2024. Topic last updated April 07, 2023. Accessed March 01, 2024.

Murrell DF. Overview of the management of epidermolysis bullosa. In: UpToDate, Hand JL, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2024. Topic last updated January 08, 2024. Accessed March 01, 2024.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03068780: Double-blind, Randomized, Vehicle-controlled, Phase III, Efficacy and Safety Study With 24-month Open-label Follow-up of Oleogel-S10 in Patients With Inherited Epidermolysis Bullosa. Available from: http://clinicaltrials.gov. Last update posted July 20, 2023. Last verified July 2023. Accessed March 01, 2024.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03068780: Study Protocol: Double-blind, Randomized, Vehicle-controlled, Phase III, Efficacy and Safety Study with 24-month Open-label Follow-up of Oleogel-S10 in Patients with Inherited Epidermolysis Bullosa EASE Study. Available from: http://clinicaltrials.gov. Last update posted July 20, 2023. Last verified July 2023. Accessed March 01, 2024.

Kern JS, Sprecher E, Fernandez MF, et al.: Efficacy and safety of Oleogel-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. Accessed March 07, 2024.