Medical Policy

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

Title: Filsuvez (birch triterpenes) Medical Drug Criteria

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

CLINICAL RATIONALE

Epidermolysis bullosa (EB)	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.(2) EB types are divided into four main groups according to the depth below the skin surface at which the blisters occur. Approximately 20% of EB cases are dystrophic (DEB), 10% junctional (JEB), and 70% simplex (EBS); Kindler syndrome is very rare. The genetic errors in EB result in defects in the proteins that make the outer skin layer (epidermis) adhere to the deeper layer (dermis). Some types of EB are inherited dominantly, others are inherited recessively. There are more than 30 clinical

	subtypes. 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.(2,4) 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)
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Efficacy	The efficacy of Filsuvez for the treatment of partial-thickness wounds associated with inherited EB was evaluated in a randomized, double-blind, placebo-controlled trial in adults and pediatric subjects 6 months of age and older (EASE; NCT03068780) with dystrophic EB (DEB) and junctional EB (JEB). Subjects were randomized 1:1 to receive FILSUVEZ (n=109) or

	placebo topical gel (n=114) and instructed to apply approximately 1 mm (0.04 inch) of the investigational product to all their wounds at each dressing change (every 1 to 4 days) for 90 days (+/- 7 days). If a treated wound became infected, it was advised to discontinue treatment to that wound until the infection had resolved. At randomization, 1 wound was selected by the investigator as the target wound for the evaluation of the primary efficacy endpoint. The target wound was defined as a partial-thickness wound of 10-50 cm^2 in surface area and present for 21 days to 9 months prior to screening. Of the 223 subjects randomized, the median age was 12 years (range: 6 months to 81 years), 70% were under 18 years of age, and 60% were male and 40% were female. Eighty three (83)% of subjects were White, 5% were Asian, 1% were Black or African American, and 10% were other races or did not have race recorded. For ethnicity, 35% identified as Hispanic or Latino and 65% identified as not Hispanic or Latino. Of these 223 subjects, 195 had DEB, of which 175 subjects had recessive DEB (RDEB) and 20 had dominant DEB (DDEB); in addition, there were 26 subjects with JEB and 2 subjects with EB simplex. Squamous cell carcinoma of the skin (SCC) was reported as an adverse event in the double-blind and open-label periods of EASE. Four subjects with recessive dystrophic EB each reported one SCC.(1) EASE's top-line findings showed that the trial met its main goal, with a significantly greater proportion of Filsuvez-treated patients exhibiting wound closure within 45 days, compared with those using a placebo gel (41.3% vs. 28.9%). This benefit was exclusive to participants with recessive DEB, who showed a 72% higher likelihood of wound closure within 45 days with Filsuvez relative to a placebo gel. No significant differences in wound closure were detected between Filsuvez and a placebo among participants with dominant DEB or JEB. Recessive DEB is commonly more severe than dominant DEB. While a greater proportion of patients using Filsuvez showed wound closure within three months, faster than those on the placebo gel, these differences failed to reach statistical significance. All participants who completed the three-month period entered the study's extension phase, in which all are using Filsuvez for two years to heal their wounds. The goal is to evaluate the therapy's safety over the long-term.(3)
Safety	Filsuvez has no FDA labeled contraindications for use.(1)
Efficacy	The efficacy of Filsuvez for the treatment of partial-thickness wounds associated with inherited EB was evaluated in a randomized, double-blind, placebo-controlled trial in adults and pediatric subjects 6 months of age and older (EASE; NCT03068780) with dystrophic EB (DEB) and junctional EB (JEB). Subjects were randomized 1:1 to receive FILSUVEZ (n=109) or placebo topical gel (n=114) and instructed to apply approximately 1 mm (0.04 inch) of the investigational product to all their wounds at each dressing change (every 1 to 4 days) for 90 days (+/- 7 days). If a treated wound became infected, it was advised to discontinue treatment to that wound until the infection had resolved. At randomization, 1 wound was selected by the investigator as the target wound for the evaluation of the primary efficacy endpoint. The target wound was defined as a partial-thickness wound of 10-50 cm^2 in surface area and present for 21 days to 9 months prior to screening. Of the 223 subjects randomized, the median age was 12 years (range: 6 months to 81 years), 70% were under 18 years of age, and 60% were male and 40% were female. Eighty three (83)% of subjects were White, 5% were Asian, 1% were Black or African American, and 10% were other races or did not have race recorded. For ethnicity, 35% identified as Hispanic or Latino and 65% identified as not Hispanic or Latino. Of these 223 subjects, 195 had DEB, of which 175 subjects had recessive DEB (RDEB) and 20 had dominant DEB (DDEB); in addition, there were 26

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Safety	Filsuvez has no FDA labeled contraindications for use.(1)

See package insert for FDA preshttps://dailymed.nlm.nih.gov/dailymed/index.cfm

REFERENCES

Number	Reference
1	Filsuvez prescribing information. Lichtenheldt GmbH. December 2023.
2	Fine JD. Inherited epidermolysis bullosa. Orphanet J Rare Dis. 2010 May 28;5:12. doi: 10.1186/1750-1172-5-12
3	Figueiredo, M. Filsuvez gel becomes 1st therapy approved in EU for EB wounds. Epidermolysis Bullosa News. June 2022. https://epidermolysisbullosanews.com/news/filsuvez-gel-becomes-1st-therapy-approved-eu-eb-wounds.
4	EB Research Network. EB research network: understanding EB & its classification. 2022. https://www.eb-researchnetwork.org/research/what-is-eb/.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. 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.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Filsuvez	birch triterpenes gel	10 %	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Filsuvez	birch triterpenes gel	10 %	

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. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All agents are eligible for continuation of therapy 1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. The patient has a diagnosis of dystrophic or junctional epidermolysis bullosa as confirmed by ONE of the following: (medical records required) 1. Immunofluorescence mapping (IFM) **OR** 2. Transmission electron microscopy (TEM) **OR** 3. Genetic testing **OR** C. The patient has another FDA labeled indication for the requested agent **AND**

Module	Clinical Criteria for Approval
	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. There is support for 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 **Length of Approval:** 4 months **Renewal Evaluation** **Target Agent(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 [Note: patients not previously approved for the requested agent will require initial evaluation review] **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** 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 **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 07-01-2024 Effective 08-01-2024	New medical policy added to the bcbsks.com web site. Policy Maintained by Prime Therapeutics LLC.