birch triterpenes topical gel (Filsuvez®)

Policy # 00882
Original Effective Date: 07/08/2024
Current Effective Date: 07/08/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider birch triterpenes topical gel (Filsuvez®)‡ for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for birch triterpenes topical gel (Filsuvez) will be considered when the following criteria are met:

- Initial
    - Patient has a diagnosis of dystrophic or junctional epidermolysis bullosa (EB) confirmed by genetic testing. Note that dystrophic EB is caused by pathogenic variants in the *COL7A1* gene and junctional EB is caused by pathogenic variants in one of the following genes: *LAMA3, LAMB3, LAMC2, COL17A1, ITGA6, ITGB4*, or *ITGA3*; AND
    - Patient is greater than or equal to 6 months of age; AND
    - Patient has one or more open wounds that will be treated; AND
    - Target wound(s) meet the following, according to the prescriber:
        - Target wound(s) is clean in appearance and does not appear to be infected; AND
        - Target wound(s) is $\geq$ 21 days old and < 9 months old; AND
          *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Target wound(s) is considered to be partial thickness; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Squamous cell and/or basal cell carcinoma has been ruled out for the target wound(s); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Patient has at least one clinical feature of EB (e.g., blistering, wounds, scarring); AND
- Filsuvez will not be used in combination with Vyjuvek™‡; AND
- Patient has NOT undergone stem cell transplant or curative gene therapy for the treatment of inherited EB.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Continuation
  - Patient has received an initial authorization for Filsuvez; AND
  - Previously treated wounds have responded to treatment with Filsuvez according to the treating provider.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the initial use of birch triterpenes topical gel (Filsuvez) on wounds that do NOT meet the following criteria to be **not medically necessary:****

- Target wound(s) is ≥ 21 days old and < 9 months old; AND
- Target wound(s) is considered to be partial thickness; AND
- Squamous cell and/or basal cell carcinoma has been ruled out for the target wound(s)

Based on review of available data, the Company considers the use of birch triterpenes topical gel (Filsuvez) when the patient has undergone stem cell transplant or curative gene therapy for the treatment of inherited EB to be **not medically necessary.****

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Based on review of available data, the Company considers the continued use of birch triterpenes topical gel (Filsuvez) when previously treated wounds have not responded to treatment to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of birch triterpenes topical gel (Filsuvez) when the patient selection criteria are not met (except those noted above to be **not medically necessary****) to be **investigational.***

Background/Overview

Filsuvez is a sterile botanical drug product for topical use that is approved for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older. The mechanism of action is unknown, but it is thought to work by promoting general wound healing. The recommended dose of Filsuvez is a 1 mm layer of gel applied to the affected wound surface and covered with a sterile non-adhesive wound dressing. Alternatively, Filsuvez can be applied directly to the dressing so that the topical gel is in direct contact with the wound. Filsuvez should be applied to cleansed wounds with wound dressing changes until the wound is healed.

EB is a group of skin fragility disorders characterized by blistering from minimal trauma with disruption at the dermoepidermal junction. Dystrophic EB (DEB) and junctional EB (JEB) are two subtypes of EB with DEB being more common than JEB. DEB is caused by mutations in the *COL7A1* gene leading to reduced or absent production of a protein that helps to attach the epidermis to the dermis. DEB can be further divided into two subtypes based on the inheritance pattern Dominant DEB (DDEB) is typically less severe than recessive DEB (RDEB), but there is considerable overlap in characteristics. The hallmark symptom of DEB is scarring of blisters on the skin and on other mucosal surfaces. Secondary extracutaneous complications are common in more severe forms of RDEB. Pain and itching can be common and reduce quality of life. Skin and oral mucosal scarring or nail loss can be irreversible and progressive, becoming more pronounced with age. Mitten deformities and joint contractures can result from scarring and constant wounds.

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Anemia, reduced bone mineral density, renal impairment, and the development of squamous cell carcinoma (SCC) are also potential complications of severe DEB. Early onset and aggressive SCC at chronic wound sites is typical of the condition and is the leading cause of death in patients with DEB. JEB is an autosomal recessive disorder characterized by skin blistering through the lamina lucida of the cutaneous basement membrane zone. It is caused by biallelic mutations in *LAMA3, LAMB3, LAMC2* or *COL17A1*. Wounds in JEB are characterized as having excessive granulation tissue, and frequently affect the face and occipital area, diaper area, and extremities. JEB can present in forms of varying severity with the most severe form causing death within the first 2 years of life.

Filsuvez is the first treatment to be approved specifically for JEB. Another treatment, Vyjuvek, has been approved for the treatment of DEB. Vyjuvek is a topically administered gene therapy that delivers the missing *COL17A1* gene to the cells in a wound. Neither Vyjuvek nor Filsuvez have been addressed in available guidelines and neither product could be considered curative. The mainstay of management of these conditions is supportive wound care as well and early recognition and treatment of complications.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Filsuvez was approved in December 2023 for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

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 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. 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.

The primary endpoint was the proportion of subjects with first complete closure of the target wound by Day 45 of the 90-day double-blind phase of the study, based on clinical assessment by the investigator. In the Filsuvez group, 41.3% of patients met this primary endpoint compared to 28.9% in the placebo group (95% CI 0.8, 25.6).

References

1. Filsuvez [package insert]. Chiesi USA, Inc. Wahlstedt, Germany. Updated May 2024.
2. Filsuvez Drug Evaluation. Express Scripts. Updated January 2024.

Policy History

Original Effective Date: 07/08/2024
Current Effective Date: 07/08/2024
06/06/2024 Medical Policy Committee review
06/12/2024 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 06/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.