PRIOR AUTHORIZATION POLICY

POLICY: Dermatology – Filsuvez Prior Authorization Policy
- Filsuvez® (birch triterpenes topical gel – Lichtenheldt GmbH/Chiesi)

REVIEW DATE: 01/21/2024

OVERVIEW

Filsuvez is indicated for the treatment of wounds associated with **dystrophic epidermolysis bullosa (DEB) and junctional epidermolysis bullosa (JEB) in patients ≥ 6 months of age**.[1]

Filsuvez is a sterile botanical drug product for topical use and contains birch triterpenes in an oil base. Birch triterpenes is a botanical drug substance composed of a mixture of pentacyclic triterpenes. Filsuvez should be applied to cleansed wounds with wound dressing changes until the wound is healed. If a Filsuvez-treated wound becomes infected, treatment should be discontinued until the infection has resolved.

Disease Overview

DEB usually presents at birth and is divided into two major types depending on the pattern of inheritance: recessive DEB (RDEB) and dominant DEB (DDEB).[6] All subtypes of DEB are caused by mutations in the gene coding COL7A1 leading to extreme skin fragility.[4,6] The hallmark of DEB is scarring of blisters, both on the skin and on other mucosal surfaces.[4]

JEB is an autosomal recessive disorder characterized by skin blistering through the lamina lucida of the cutaneous basement membrane zone.[4] The severity varies across the two major JEB subtypes, intermediate and severe, with severe disease causing death in the first 6 to 24 months of life. JEB is less common than DEB. Biallelic mutations in one of the three genes encoding the subunit chains of laminin 332 (LAMA3, LAMB3, LAMC2) can cause either JEB subtype, biallelic mutations of COL17A1 can also cause intermediate JEB and rarely severe JEB. Rare JEB subtypes are clinically and genetically heterogeneous and include several syndromic disorders. Wounds in JEB are characterized as having excessive granulation tissue, and frequently affect the face and occipital area, diaper area, and extremities.[6] Wounds may heal with pigment changes or with scarring. Other features of JEB include extensive skin and mucous membrane involvement, failure to thrive and sepsis in severe subtypes, nail dystrophy and loss, and hair loss in intermediate and localized subtypes.

Clinical Efficacy

The efficacy of Filsuvez was evaluated in EASE, a Phase III, randomized, double-blind, placebo-controlled, multicenter, pivotal study in patients ≥ 21 days of age with inherited DEB or JEB (n = 223).[2,3] Patients who had undergone stem cell transplant or gene therapy for the treatment of inherited epidermolysis bullosa (EB) were excluded. Additionally, patients with current and/or former malignancy including basal cell carcinomas and squamous cell carcinomas were ineligible to enroll.

The study consisted of a 90-day, double-blind, randomized, placebo-controlled treatment phase (published), followed by a 24-month, open-label, single-arm, follow-up phase (data unavailable).[3] In the double-blind phase, patients were randomized 1:1 to Filsuvez or placebo vehicle gel, both with standard of care wound dressing applied at least once every 4 days (treatment with Filsuvez or placebo was applied at the same time as the wound dressing change). One EB target wound was assigned for each patient. The target wound involved loss of the epidermis; extension into the dermis was allowable. The target wound size was 10 cm^2 to 50 cm^2 in surface area and the age of the target wound was ≥ 21 days but < 9 months according to the patient's report. For the assessment of wound closure and re-epithelization, the investigator photographed

the target wound and all other wounds that matched target wound criteria with a system that measures accurately, precisely, and reliably to provide high quality imaging and standardized documentation. Post-treatment assessments were made within 1 week of wound closure to determine the durability of healing.

The median patient age was 12 years.[2] The median wound size was 15.6 cm^2 and the median wound age was 35.5 days. Most patients had RDEB (78.5%); 9.0% of patients had DDEB and 11.0% of patients had JEB. In the DDEB subgroup, there was an imbalance between patients receiving Filsuvez (n = 6) and placebo (n = 14). Among patients with RDEB, more than 55% had generalized-severe RDEB.

At Day 45 (± 7 days) 41.3% vs. 28.9% of patients receiving Filsuvez vs. placebo, respectively, had complete wound closure (P = 0.013). However, a subgroup analysis by EB subtype demonstrated that patients with RDEB (Filsuvez n = 91 and placebo n = 84) were the only subgroup to have a statistically significant benefit from Filsuvez; complete target wound closure by Day 45 was achieved in 44.0% of wounds treated with Filsuvez vs. 26.2% of placebo-treated wounds (relative risk 1.72; 95% CI: 1.14, 2.59; P = 0.008). In patients with JEB (n = 26) and DDEB (n = 20), differences between Filsuvez and placebo groups did not reach statistical significance (18.6% vs. 26.7%, respectively, in JEB and 50% vs. 50%, respectively, in DDEB), although numbers were small. At Day 90, the difference in time to first target wound closure over was not significantly different between the Filsuvez and placebo arms (50.5% vs. 43.9%, respectively). Differences in total wound burden were not statistically different between Filsuvez and placebo. There were improvements in the Itch Man Scale (patients ≥ 4 years of age) with both Filsuvez and placebo (a significant difference with Filsuvez was only observed at Day 60).[2] There was a statistically significant reduction in procedural pain with Filsuvez vs. placebo at Days 14 and 90 only, not at other timepoints (Day 30, Day 45, and Day 60). In an analysis of dressing change frequency, patients treated with Filsuvez had a reduced requirement for daily dressing changes vs. placebo; at Day 90 this equated to one less dressing change every 2 weeks with Filsuvez vs. no change with placebo.

Guidelines

Filsuvez is not addressed in available guidelines. According to a position statement by the **European Reference Network for Rare Skin Diseases** (2021), wound care is the cornerstone of treatment for patients with EB.[5] Careful and complete skin and wound assessment should be undertaken regularly, at least every 6 months. The healing rate of chronic wounds should be closely monitored, by checking wound edges.

The diagnosis of EB is based on a combination of clinical features, family , and laboratory findings.[5] Laboratory techniques include immunofluorescence mapping, transmission electron microscopy, and molecular genetic testing. Whenever possible, laboratory diagnosis should be performed in a specialized EB center. Genetic testing is the gold standard for the diagnosis of EB, since it provides a definitive diagnosis and classification of the major EB type and in many cases the subtype.

An **international consensus best practice guideline** on skin and wound care in EB [2017] notes that EB is a lifelong disease that requires specialist intervention and consideration to minimize complications and improve quality of life.[6] Management should take place in a specialized center by a multi-disciplinary team, ideally. Definitive diagnosis is most commonly made from analysis of a skin biopsy using positive immunofluorescence, antigenic mapping, and transmission electron microscopy. These key diagnostic tools help confirm diagnosis and indicate the particular subtype of EB. Due to the rarity of expertise and facilities, diagnosis is generally made using immunofluorescence and antigen mapping. Some laboratories are moving towards molecular diagnosis from exome sequencing of a panel of known skin fragility genes. Experienced clinicians can often make a provisional diagnosis on clinical observations, but a definitive diagnosis will always be required.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Filsuvez. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Filsuvez as well as the monitoring required for adverse events and long-term efficacy, approval requires Filsuvez to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of Filsuvez as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Filsuvez is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Dystrophic Epidermolysis Bullosa.** Approve for the duration outlined below if the patient meets ONE of the following (A or B):
   Note: For new wound(s) the patient is directed to Initial Therapy criteria. If the patient is continuing to treat the same wound(s) the patient is directed to criteria for Patient Currently Receiving Filsuvez on Previously Treated Wound(s).
   - **A)** Initial Therapy: Approve for 3 months if the patient meets the following (i, ii, and iii):
     - **i.** Patient is ≥ 6 months of age; AND
     - **ii.** Patient meets ALL of the following (a, b, and c):
       - **a)** Patient has at least one clinical feature of dystrophic epidermolysis bullosa **[documentation required]**; AND
         Note: Examples of clinical features of dystrophic epidermolysis bullosa include but are not limited to blistering, wounds, and scarring.
       - **b)** Patient has one or more open wound(s) that will be treated (i.e., "target wound[s]); AND
       - **c)** Target wound(s) meet the following, according to the prescriber [(1), (2), (3), and (4)]:
         - **(1)** Target wound(s) is clean in appearance and does not appear to be infected; AND
         - **(2)** Target wound(s) is 10 cm^2 to 50 cm^2; AND
         - **(3)** Target wound(s) is ≥ 21 days and < 9 months old; AND
         - **(4)** Squamous cell and/or basal cell carcinoma has been ruled out for the target wound(s).
     - **iii.** The medication is prescribed by or in consultation with a dermatologist or wound care specialist.
   - **B)** Patient is Currently Receiving Filsuvez on **Previously Treated Wound(s)**: Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
     Note: If the patient is treating a new wound(s) not previously treated with Filsuvez or a reopened recurrent wound(s), then refer to Initial Therapy criteria above.
     - **i.** According to the prescriber, the target wound(s) remains open; AND
     - **ii.** According to the prescriber, the target wound(s) has decreased in size from baseline; AND
     - **iii.** The medication is prescribed by or in consultation with a dermatologist or wound care specialist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Filsuvez is not recommended in the following situations:

1. **Combination use with Vyjuvek (beremagene geperpavec-svdt topical gel).** Combination use of Vyjuvek and Filsuvez have not been studied. Patients who had undergone gene therapy for the treatment of inherited EB were excluded from the pivotal EASE trial with Filsuvez.[2]

2. **Junctional Epidermolysis Bullosa (JEB).** Efficacy has not proven to be better than placebo. In the pivotal EASE trial, patients with JEB comprised 11% of the total population (n = 26).[2] At Day 45 (± 7 days) complete wound closure In patients with JEB was greater in patients who received placebo vs. Filsuvez (26.7% vs. 18.6%).

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Filsuvez® topical gel [prescribing information]. Wahlstedt, Germany: Lichtenheldt GmbH/Chiesi; December 2023.
2. Kern JS, Sprecher E, Fernandez MF, et al. Efficacy and safety of Olegel-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.
3. Kern JS, Schwieger-Briel A, Lowe S, et al. Olegel-S10 phase 3 study "EASE" for epidermolysis bullosa: Study design and rationale. *Trials*. 2019;20:350.
4. Has C, Bauer JW, Bolling MC et al. Consensus and reclassification of inherited epidermolysis bullosa and other disorders with skin fragility. *Br J Dermatol.* 2020;183:614-627.
5. Has C, El Hachem M, Buckova H, et al. Practical management of epidermolysis bullosa: consensus clinical position statement from the European Reference Network for Rare Skin Diseases. *J Eur Acad Derm Venereol.* 2021;35:2349-2360.
6. Denyer J, Pillay E, Clapham J. Best practice guidelines for skin and wound care in epidermolysis bullosa. An International Consensus. *Wounds International.* 2017. Available at: https://af13d689-15eb-4199-8733-e91a7bb8ae3f.usrfiles.com/ugd/af13d6_01ed147ab87e49c584c20a917c47f19f.pdf. Accessed on January 22, 2024.