Filsuvez (birch triterpenes)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Epidermolysis bullosa (EB) is a group of rare genetic skin disorders characterized by fragile skin that blisters, erodes, tears, and scars in response to minor friction or trauma. There are four main types of EB: EB simplex, dystrophic EB (DEB), junctional EB (JEB), and Kindler syndrome. Symptoms range from mild to severe and can include painful open wounds, scarring, disfigurement, and internal complications. The severity and presentation of symptoms, typically starting at birth or during infancy, differ significantly across types and subtypes. The US sees an estimated birth of 200 children per year with EB. There is no cure for EB and management focuses on wound care and preventing complications. The only other available therapy for EB is Vyjuvek (beremagene geperpavec-svdt), which is an approved gene therapy for the treatment of recessive or dominant DEB only.

Filsuvez (birch triterpenes) gel is a topical medication approved in December 2023for the treatment of wounds associated with DEB and JEB in those 6 months and older. It contains birch bark extract (as 10% birch triterpenes) formulated in sunflower oil and is thought to promote wound healing through anti-inflammatory and keratinocyte stimulating effects. Filsuvez (birch triterpenes) can be either applied directly to the wound surface and covered with wound dressing, or can be applied directly to the dressing. Filsuvez (birch triterpenes) is applied topically until the wound is healed, and each tube is for a one-time use only. It should not be used for oral, intravaginal, intra-anal, or ophthalmic application.

Definitions

"Dominant DEB (DDEB)" is a less severe form of DEB, resulting from mutations in a single copy of the COL7A1 gene.

"Dystrophic epidermolysis bullosa (DEB)" is a type of EB caused by mutations in the COL7A1 gene encoding type VII collagen. It can be inherited in an autosomal dominant (DDEB) or autosomal recessive (RDEB) manner.

"Epidermolysis Bullosa (EB)" is a group of rare, inherited skin conditions that cause skin to become incredibly fragile, resulting in blisters and tears even from minor friction or trauma.

"Junctional epidermolysis bullosa (JEB)" is a type of EB caused by mutations in genes encoding components of the hemidesmosomes and dermal-epidermal junction. It is inherited in an autosomal recessive manner.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"Recessive DEB (RDEB)" is a more severe form of DEB, caused by mutations in both copies of the COL7A1 gene.

"Wound thickness" is classified into partial or full thickness wounds based on the depth of skin layers involved. Partial thickness wounds affect the epidermis and may extend into the dermis. Full thickness wounds extend through the dermis and into the adipose tissue. Partial thickness wounds normally heal within 1 to 3 weeks. An EB partial thickness wound aged ≥21 days is considered to be delayed in wound healing.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers Filsuvez (birch triterpenes) medically necessary when ALL of the following criteria are met:

1. The medication is prescribed by or in consultation with a geneticist, dermatologist, or pathologist who is experienced in the diagnosis and treatment of epidermolysis bullosa (EB); *AND*
2. The member will not use Filsuvez (birch triterpenes) concurrently with Vyjuvek (beremagene geperpavec-svdt) or Zevaskyn (prademagene zamikerace); *AND*
3. The member will not use Filsuvez (birch triterpenes) on wounds that have been or will be treated with Zevaskyn (prademagene zamikeracel); *AND*
4. Filsuvez (birch triterpenes) is being prescribed at a dose and frequency that is within FDA approved labeling; *AND*
   The requested medication is being used within the quantity limit of: 1 tube per target wound per day, unless there is clinical rationale provided for exceeding this limit.
5. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Recessive Dystrophic Epidermolysis Bullosa (RDEB)

The Plan considers Filsuvez (birch triterpenes) medically necessary when ALL of the following criteria are met:

5. The member meets the above General Medical Necessity Criteria; *AND*
6. The member has a diagnosis of recessive dystrophic epidermolysis bullosa (RDEB); *AND*
7. The diagnosis is supported by genetic testing techniques, such as targeted gene sequencing, multigene panel testing, exome sequencing, or other genomic methods that document the following:

a. recessive DEB (RDEB), confirmed by two copies of pathogenic variants (biallelic) in the collagen type VII alpha 1 chain (COL7A1) gene. The type of mutations (e.g., nonsense, missense, splice-site mutations, or small insertions/deletions) should be specified; *AND*

8. The member is ≥6 months of age or older; *AND*
9. There is documentation of ALL of the following of the target wound(s):
    a. Partial-thickness (i.e., 10 cm^2 to 50 cm^2 in size)*; and*
    b. Present for ≥21 days but <9 months*; and*
    c. Clean in appearance*; and*
    d. Adequate granulation tissue*; and*
    e. Excellent vascularization*; and*
    f. No evidence it is infected; *AND*
10. There is documentation of size of target wound(s) at baseline; *AND*
11. Documentation the member is receiving standard-of-care preventive or treatment therapies for wound care, control of infection, and/or nutritional support as applicable; *AND*
12. The member is unable to use, or has tried and failed Vyjuvek (beremagene geperpavec-svdt)[s].

If the above prior authorization criteria are met, the requested medication will be approved for an initial approval duration of up to 6-months.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Medical Necessity Criteria

Recessive Dystrophic Epidermolysis Bullosa (RDEB)

The Plan considers Filsuvez (birch triterpenes) medically necessary when ALL of the following criteria are met:

1. The member meets the above applicable General Medical Necessity Criteria and/or Initial Clinical Review; *AND*
2. The member has experienced a documented improvement in wound healing while on Filsuvez (birch triterpenes). This improvement must be validated by clinical documentation showing ONE of the following:
    a. Decrease in wound size*; or*
    b. Decrease in number of partial-thickness wounds*; or*
    c. Increase in granulation tissue*; or*
    d. Partial or complete wound closure*; AND*
3. The member meets ONE of the following with documentation:
    a. The target wound remains open and meets ALL of the following:
        i. Clean in appearance*; and*
        ii. Adequate granulation tissue*; and*
        iii. Excellent vascularization*; and*

iv. No evidence it is infected; *or*

b. At least one (1) *new* target wound(s) meeting ALL of the following:
   i. Partial-thickness (i.e., 10 cm^2 to 50 cm^2 in size)*; and*
   ii. Present for ≥21 days but <9 months*; and*
   iii. Clean in appearance*; and*
   iv. Adequate granulation tissue*; and*
   v. Excellent vascularization*; and*
   vi. No evidence it is infected; *and*
   vii. When applicable [e.g., members without a history of trying Vyjuvek (beremagene geperpavec-svdt) on previous wounds], the member is unable to use, or has tried and failed Vyjuvek (beremagene geperpavec-svdt)[s]*; AND*

4. Filsuvez (birch triterpenes) will not be applied on target wound(s) that have completely healed; *AND*
5. The member is receiving standard-of-care preventive or treatment therapies for wound care, control of infection, and/or nutritional support as applicable*; AND*
6. There is no recorded evidence of unacceptable toxicity or adverse reactions to Filsuvez (birch triterpenes) that would necessitate discontinuation of treatment. Routine monitoring for common adverse events such as pruritus and skin squamous-cell carcinoma (SCC) should be reflected in the clinical chart; *AND*
7. There is clinical chart documentation (within the last 6 months) demonstrating all of the above.

<u>If the above reauthorization criteria are met, the requested product will be authorized for up to 6-months.</u>[s]

Experimental / Investigational, or unproven[s]

Filsuvez (birch triterpenes) for any other indication or use is considered experimental, investigational, or unprove. Non-covered indications include, but are not limited to, the following:

1. Actinic Keratosis (AK).
2. Breast Cancer.
3. Burns.
4. Epidermolysis Bullosa (EB) simplex (EBS)
5. Kindler syndrome.
6. Other types of EB that are not dystrophic or junctional.

Not Medically Necessary[s]

Filsuvez (birch triterpenes) for dominant dystrophic epidermolysis bullosa (DDEB) is considered not medically necessary. Efficacy with Filsuvez (birch triterpenes) has not been proven to be better than placebo. In the pivotal EASE trial (NCT03068780), the primary endpoint was the proportion of patients with first complete closure of the target wound within 45 days (N=223). In the subgroup analysis, at day 45 (±7 days), complete wound closure in patients with DDEB in the placebo group (50%) was equal to

the Filsuvez group (50%). In this subgroup with DDEB (n=20), Vyjuvek treatment failed to reach statistical significance [95% confidence interval (CI) for the treatment difference: -47.8, 47.8].

Filsuvez (birch triterpenes) for Junctional Epidermolysis Bullosa (JEB) is considered not medically necessary. Efficacy with Filsuvez (birch triterpenes) has not been proven to be better than placebo. In the pivotal EASE trial (NCT03068780), the primary endpoint was the proportion of patients with first complete closure of the target wound within 45 days (N=223). In the subgroup analysis, at day 45 (±7 days), complete wound closure in patients with JEB was higher in the placebo group (26.7%) vs. Filsuvez (18.6%). In this subgroup with JEB (n=26), Vyjuvek treatment failed to reach statistical significance (95% CI for the treatment difference: -40.4, 23.5).

In the open label extension (OLE) trial, 78% (n=160) had RDEB, 8.8% (n=18) had DDEB, 12.2% (n=25) had JEB, and 1.0% (n=2) had EBS in the total population (N=205). However, the OLE data did not provide subgroup analysis by epidermolysis bullosa type. See Appendix A for further OLE information.

The Plan will continue to monitor emerging evidence and will reassess its position as new data become available.

Appendix A

- The pivotal phase 3 EASE trial (ClinicalTrials.gov ID NCT03068780) met its primary endpoint, demonstrating a higher rate of complete target wound closure within 45 days with Filsuvez (birch triterpenes) compared to vehicle control (41.3% vs 28.9%, p=0.013), the treatment effect was modest and driven primarily by the recessive DEB (RDEB) subgroup.
    - There were no statistically significant differences in efficacy between Filsuvez (birch triterpenes) and control for the dominant DEB (DDEB) or JEB subgroups, though sample sizes were small.
    - The effect on complete wound closure was not durable, with no significant difference between Filsuvez (birch triterpenes) and control by the end of the 90-day double-blind period.
        - By day 90, the cumulative proportion of participants with first target wound closure was 50.5% for Filsuvez (birch triterpenes) vs. 43.9% for control gel (RR 1.16, 95% CI 0.88–1.52; P = 0.296).
    - The key secondary efficacy endpoints in the EASE trial showed mixed results, with some endpoints not demonstrating statistically significant differences between Filsuvez (birch triterpenes) and control gel - indicating a lack of robust, clinically meaningful benefit.
- A 24-month long-term single-arm open-label study assessed safety and efficacy of Filsuvez (birch triterpenes) in 205 participants. They found that 77.1% of participants experienced an adverse event (typically mild-to-moderate in nature), low risk of target wound infection (n=7), and statistically significant improvements in body surface area percentage (BSAP) of wounds, and EB Disease Activity and Scarring Index (EBDASI). Mean BSAP changes from baseline at 3, 12 and 24 months were -4.3% (8.1) (P < 0.001), -5.9% (8.6) (P < 0.001) and -3.7% (9.0) (P = 0.003),

respectively. Changes in EBDASI skin activity score from baseline were observed: -3.9 (P <0.001), -5.1 (P <0.001) and -3.0(P = 0.007) at 3, 12 and 24 months, respectively. However, this single-arm study was unable to assess the impact of FIlsuvez (birch triterpenes) against an active control or placebo product, thus it is unclear if these significant changes are clinically meaningful or robust compared to usual care.

- The NICE Guidelines, based in the United Kingdom, recommend the use of birch bark extract, within its marketing authorization, for the treatment of partial thickness wounds associated with dystrophic and junctional epidermolysis bullosa in people aged 6 months and over.

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Clinical Guideline Revision / History Information

Original Date: 06/27/2024

Reviewed/Revised: 11/01/2025, 08/03/2026