Filsuvez (birch triterpenes)

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.

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

Policy Statement on Filsuvez (birch triterpenes) Efficacy Information

The Plan considers Filsuvez (birch triterpenes) unproven and not medically necessary for all indications, including in the treatment of wounds associated with dystrophic epidermolysis bullosa (DEB) and junctional epidermolysis bullosa (JEB) at this time. The evidence is currently insufficient to conclude that Filsuvez (birch triterpenes) provides a clinically meaningful benefit:

- While 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.

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

Medical Necessity Criteria for Filsuvez (birch triterpenes)

The Plan considers Filsuvez (birch triterpenes) to be not medically necessary for any indication, including in the treatment of wounds associated with dystrophic epidermolysis bullosa (DEB) and junctional epidermolysis bullosa (JEB) at this time. Therefore, there are no medical necessity criteria for coverage of this product.

Experimental or Investigational / Not Medically Necessary

Filsuvez (birch triterpenes) for any indication or use is considered not medically necessary by the Plan. Non-covered indications include, but are not limited to, the following:

1. Actinic Keratosis (AK).
2. Breast Cancer.
3. Burns.
4. Epidermolysis Bullosa (EB).

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Clinical Guideline Revision / History Information

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