

DRUG POLICY

Filsuvez® (birch triterpenes)

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Filsuvez is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adults and pediatric patients 6 months of age and older.

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

1. Medical Records documenting clinical manifestations of disease.
2. Genetic test results supporting diagnosis of recessive dystrophic epidermolysis bullosa (RDEB)

Prescriber Specialties

The requested medication must be prescribed by or in consultation with a dermatologist or wound care specialist with expertise in the treatment of epidermolysis bullosa (EB).

Criteria for Initial Approval

Recessive Dystrophic Epidermolysis Bullosa (RDEB)

Authorization of 3 months may be granted for treatment of wounds in patients with recessive dystrophic epidermolysis bullosa (RDEB) and when all of the following criteria are met:

1. Member is 6 months of age or older.

2. Member has a diagnosis of recessive dystrophic epidermolysis bullosa (RDEB) confirmed by genetic testing AND is not an autosomal dominant subtype.
3. Member has clinical manifestations of disease (e.g., extensive skin blistering, skin erosions, scarring).
4. Member has open partial-thickness wounds associated with DEB for ≥ 21 days.
5. Filsuvez will not be administered to wound(s) that are currently healed.
6. Filsuvez will not be used in combination with Vyjuvek (beremagene geperpavec-svdt) or Zevaskyn (prademagene zamikeracel).
7. Dosing does not exceed one 23.4-gram tube per day.

Dominant Dystrophic Epidermolysis Bullosa (DDEB)

Filsuvez is considered not medically necessary for Dominant Dystrophic Epidermolysis Bullosa due to no clinical benefit demonstrated in clinical trials.

Junctional Epidermolysis Bullosa (JEB)

Filsuvez is considered not medically necessary for Junction Epidermolysis Bullosa due to insufficient clinical efficacy.

Continuation of Therapy

Recessive Dystrophic Epidermolysis Bullosa (RDEB)

Authorization of 6 months may be granted to all patients (including new members) requesting authorization for continuation of therapy when member meets all initial criteria and achieves or maintains a positive clinical response to Filsuvez therapy (e.g., decrease in wound size, decrease in pain or itch severity at dressing changes).

Other

Filsuvez (birch triterpenes) is considered **not medically necessary** for patients who do not meet the criteria set forth above.

Non-Formulary Exception Criteria

Non-Formulary Exception criteria applies to formularies which do not include the requested product(s) on the formulary drug list. Meeting the criteria above may satisfy some, or all, portions of the Non-Formulary Exception Criteria. A medication that is non-formulary may be covered when the Criteria for Approval AND the following criteria are met:

1. The requested drug must be used for an FDA-approved indication, or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines). Diagnostic testing/lab results required when applicable.
2. The prescribed dose/quantity must fall within the FDA-approved labeling or dosing guidelines found in the compendia of current literature.
3. All covered formulary alternative drugs on any tier will be ineffective, have been ineffective, would not be as effective as the non-formulary drug, or would have adverse effects. Documentation is required and must include chart note(s) or other documentation indicating prior treatment failure, severity of the adverse event (if any), and dosage and duration of the prior treatment, or contraindication to formulary alternatives.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits Apply

Medication	Standard Limit	FDA Recommended Dosing
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Filsuvez (birch triterpenes) 10% gel	One 23.4 gram tube per day	Apply a 1-mm layer to the affected wound surface with dressing changes until wound is healed
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CLINICAL RATIONALE

Background

Epidermolysis bullosa (EB) is a rare genetic skin disorder that causes fragility and blistering of the skin. There are four types of EB: epidermolysis bullosa simplex (EBS), dystrophic epidermolysis bullosa (DEB), junctional epidermolysis bullosa (JEB), and Kindler epidermolysis bullosa (KEB). These 4 types are further broken down into 30 different sub-types which are inherited as either autosomal dominant or recessive and with varying clinical presentations. DEB and JEB are two of the main types of EB. DEB is caused by mutations in collagen type VII alpha 1 chain (COL7A1 gene); blisters at the level of lamina densa and upper dermis and contributes to 25% to 50% of cases. JEB is caused by mutations in Laminin 332, plectin, and $\alpha 6\beta 4$ integrin; blisters in the epidermal-dermal junction and contributed to 5% to 20% of cases.

The prevalence of dystrophic epidermolysis bullosa is roughly 1 to 9 out of every million people and can be either dominant dystrophic epidermolysis bullosa (DDEB) or recessive dystrophic epidermolysis bullosa (RDEB). Symptoms typically show up at birth and the dominant form of DEB is usually milder. Blistering is typically localized on the hands, feet, elbows, and knees, although it can be more widespread. Common signs include scarring, tiny white bumps (milia), issues with the lining of moist body openings (mucous membranes), and problems with the nails, which may be missing or abnormal. In some cases, nail dystrophy might be the only noticeable symptom. Patients with dominant DEB typically have a normal lifespan. The prevalence of recessive dystrophic epidermolysis bullosa is roughly 1.35 cases per one million individuals. RDEB can be severe, represents one of the most debilitating subtypes of epidermolysis bullosa, and is usually more generalized. In RDEB, recurrent skin/mucosal blisters and erosions turn into chronic wounds, infections, cutaneous squamous cell carcinomas with high metastatic potential, which may lead to premature death. Common signs include malnutrition, anemia, esophageal strictures, growth retardation, pseudo-syndactyly, development of contractures, malformation of teeth, microstomia, and corneal abrasions. The prevalence of junctional epidermolysis bullosa is less than one case per one million individuals. Symptoms of JEB can be very severe including infection, malnutrition, dehydration, electrolyte imbalance, or obstructive airway complications leading to death during infancy.

Filsuvez is a topical sterile botanical drug product from birch bark that is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa in adult and pediatric patients more than or equal to 6 months of age. The exact mechanism of Filsuvez is unknown, but it has demonstrated antibacterial, antimycotic, antiviral, anti-inflammatory, antitumoral, and wound-healing properties.

Efficacy

EASE was a Phase 3, 90-day, randomized, double-blind, placebo-controlled study in patients with dystrophic, junctional, or Kindler epidermolysis bullosa. This was then followed by a 24-month open-label extension study. The study evaluated safety, efficacy, and tolerability of Filsuvez in patients 21 days and older. Filsuvez or control vehicle would be administered with standard of care wound dressing change at least once every four days. Patients enrolled in EASE had a median age of 12 years (ranging from 6 months to 81 years). Of the 233 participants, a majority had dystrophic epidermolysis bullosa (195: 175 RDEB, 20 DDEB), 26 has junctional epidermolysis bullosa, and 2 had epidermolysis bullosa simplex. The participants were 60% male, 40% female, 83% White, 5% Asian, 1% Black or African American, and 10% were of other races or chose not to report race. Baseline measures includes wound size documents via photographic data. Participants had to have an epidermolysis bullosa target wound (partial-thickness wound of 10–50 cm² in surface area present for 21 days to 9 months).

Primary endpoints for the study looked at the proportion of patients with first complete wound closure, defined as first appearance of complete re-epithelialization without drainage, of the target epidermolysis bullosa wound within 45 days $\pm$ 7 days of treatment. Secondary endpoints evaluated included time to complete wound closure, proportion of patients with first target wound closure within day 90 days $\pm$ 7 days, and pain reduction associated with dressing changes using the Wong Baker Faces scale at day 14

Filsuvez was superior to vehicle for the proportion of patients with first complete target wound closure within 45 days (41.3% vs. 28.9%; RR 1.44, 95% CI 1.01 to 2.05, $p = 0.013$), however it was only statistically significant for the recessive dystrophic epidermolysis bullosa subtype. In a subgroup analysis of the primary endpoint of the EASE trial. Filsuvez was no more efficacious than vehicle at healing wounds in patients with dominant dystrophic epidermolysis bullosa and junctional epidermolysis bullosa. The analysis showed that Filsuvez's efficacy in treating recessive dystrophic epidermolysis bullosa was what lead to the trial meeting the primary endpoint in the total population. The subtypes are as follows: recessive dystrophic epidermolysis bullosa: 44% vs. 26.2%; RR 1.72, 95% CI 1.14 to 2.59, $p = 0.008$, dominant dystrophic epidermolysis bullosa: 50% vs. 50%; 95% CI -47.8 to 47.8, $p =$ not significant, junctional epidermolysis bullosa: 18.2% vs. 26.7%; 95% CI -40.4 to 23.5, $p =$ not significant. None of the secondary endpoints were met, except in greater pain reduction associated with dressing changes using the Wong Baker Faces scale at day 14 ($p=0.022$).

Safety

Adverse events reported in clinical trials of Filsuvez were primarily related to application site reactions. The most common adverse reactions were local hypersensitivity and skin reactions, including urticaria and dermatitis. If signs and symptoms of local or systemic hypersensitivity reactions occur, Filsuvez should be discontinued immediately, and appropriate therapy should be initiated.

Conclusion

In summary, the clinical benefit of treatment for dominant dystrophic epidermolysis bullosa and junctional epidermolysis bullosa has not been demonstrated. The establishment of a clinical benefit is warranted in further clinical trials.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

REFERENCES

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POLICY HISTORY

Policy #: 05.05.38

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