# Clinical Policy: Birch Triterpenes (Filsuvez)

Reference Number: CP.PHAR.669
Effective Date: 03.01.24
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

## Description

Birch triterpenes (Filsuvez®) is a botanical drug product containing birch triterpenes from birch bark in an oil base.

## FDA Approved Indication(s)

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

## Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® that Filsuvez is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Epidermolysis Bullosa** (must meet all)**:**

1. Diagnosis of DEB or JEB confirmed by genetic testing (*see Appendix D*);
2. Prescribed by or in consultation with a geneticist, dermatologist, or histopathologist;
3. Age ≥ 6 months;
4. Target wounds are partial-thickness and have been present for ≥ 21 days and < 9 months (see *Appendix E)*;
5. Documentation of size of target wounds at baseline;
6. Provider attestation that member is concomitantly receiving standard of care preventative or treatment therapies for wound care (e.g., polymeric membrane, superabsorbent dressings, soft-silicone foam, enzyme alginogel, protease; *see Appendix F*);
7. For DEB, Filsuvez is not prescribed concurrently with Vyjuvek™;
8. Dose does not exceed 1 tube per target wound per day.

**Approval duration: 3 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

**A. Epidermolysis Bullosa** (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Filsuvez is not applied on target wounds that have completely healed;
3. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters (a or b):
   a. Decrease in wound size;
   b. Decrease in pain or itch severity for target wound sites associated with dressing changes;
4. For DEB, Filsuvez is not prescribed concurrently with Vyjuvek;
5. If request is for a dose increase, new dose does not exceed 1 tube per target wound per day.

**Approval duration: 6 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

DEB: dystrophic epidermolysis bullosa
EB: epidermolysis bullosa
FDA: Food and Drug Administration
IFM: immunofluorescence mapping
JEB: junctional epidermolysis bullosa
TEM: transmission electron microscopy

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

None reported

*Appendix D: Diagnosis Information*

- DEB is a rare epidermolysis bullosa (EB) subtype caused by mutation in the COL7A1 gene or PLOD3 gene.
- JEB is a rare EB subtype caused by mutation in the LAMA3, LAMB3, LAMC2, COL17A1, ITGA3, ITGA6, or ITGB4 gene.
- Per 2017 Best Practice Guidelines for Skin and Wound Care in EB, the most recent classification for EB names four categories of the condition defined by the level of cleavage at the dermal and epidermal junction:
  - EB simplex (EBS)
  - Junctional EB (JEB)
  - Dystrophic EB (DEB)
  - Kindler syndrome
- Per 2020 Clinical Practice Guidelines for Laboratory Diagnosis of EB, genetic testing is always recommended for the diagnosis of EB. Methods for clinical diagnosis in EB include immunofluorescence mapping (IFM), transmission electron microscopy (TEM), or genetic testing (e.g., next-generation sequencing, whole-exome sequencing, and Sanger sequencing).
  - IFM is recommended to obtain a rapid diagnosis and prognosis and to prioritize genetic testing and facilitate interpretation of genetic results.
  - TEM is useful in a limited number of cases and should be performed when IFM and genetic testing do not deliver conclusive results.
- Per 2017 Best Practice Guidelines for Skin and Wound Care in EB, definitive diagnosis is most commonly made from analysis of a skin biopsy using positive immunofluorescence, antigenic mapping, and TEM. Due to rarity of expertise and facilities, diagnosis is generally made using immunofluorescence and antigen mapping.

- Invitae Epidermolysis Bullosa and Palmoplantar Keratoderma Panel analyzes genes associated with EB. More information can be found on the Invitae website: https://www.invitae.com/en/providers/test-catalog/test-434344.

*Appendix E: General Information*

- Wounds of the skin are 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.
- Filsuvez accelerates the re-epithelialization of wounds due to an enhancement of keratinocyte differentiation and migration. Hence, its mechanism of action targets wounds that are delayed in wound healing which are prone to become chronic wounds. These wounds are of high clinical relevance and a major source of complications in patients with EB.

*Appendix F: Recommended Wound Care for EB*

Per 2017 Best Practice Guidelines for Skin and Wound Care in EB:

- Wounds should be dressed with nonadherent silicone dressings, foam dressings that absorb exudates, and nonadherent silicone-based tape. Diluted bleach baths or compresses, topical antiseptics, and topic antibiotics are used as preventative measures against bacterial infections.
- Standard of Care for general EB skin and wound care:
  - First choice of dressing for chronic EB wounds (when available): PolyMem, Flaminal Hydro/Forte
- Standard of Care for DEB skin and wound care:
  - First choice of dressing for general DEB wounds (when available): PolyMem, Cutimed Siltec (super-absorbent)
- Standard of Care for JEB skin and wound care:
  - First choice of dressing for general JEB wounds (when available): PolyMem with UrgoTul, IntraSite Conformable (Infants and eroded blister sites), Kytocel (if bleeding nailbeds), Mepitel One or Cuticell Contact with PolyMem as a secondary dressing if wet
- Recommended dressings for DEB skin and wound care:

| Dressing Type | Brand | Indication/ Function | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| Polymeric membrane | PolyMem | • Where cleansing is required<br>• Chronic wounds | • Stimulates high levels of exudate<br>• Distinct smell does not necessarily indicate infection<br>• Can still be difficult to retain | • Change frequently until exudate reduces |

| Dressing Type | Brand | Indication/ Function | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| | | | on vertical surfaces | |
| Super-absorbent dressings | • Cutimed Siltec<br>• Sorbion Sachet S<br>• Filvasorb/ Vilwasorb Pro<br>• Kerramax Care | • High exudate levels | • Can be cut between super-absorbent crystals, which appear in rows (as opposed to cutting across the crystal lattice) | |
| Soft silicone mesh | • Mepitel<br>• Mepitel One<br>• Adaptic Touch<br>• Cuticell Contact | • Moist wound<br>• Contact layer | | |
| Lipido-colloid | • Urgo Tul | • Moist wound, drier wounds, and protection of vulnerable healed areas<br>• Used as an alternative to soft silicon (see above) in the presence of over-granulation | • Where retention is difficult (e.g., vertical surfaces) | |
| Soft silicone foam | • Mepilex<br>• Mepilex Lite<br>• Mepilex Transfer | • Absorption of exudate<br>• Protection<br>• Lightly exuding wounds<br>• To transfer exudate to absorbent dressing | • Over-heating<br>• May need to apply over recommended atraumatic primary dressing | |

| Dressing Type | Brand | Indication/ Function | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| | | • Where conformability is required (e.g., digits, axillae) | | |
| Foam | • Allevyn<br>• UrgoTul Absorb<br>• Aquacel Foam | • Absorption and protection | • May adhere if placed directly on wound bed, use alternative contact layer | |
| Bordered foam dressings | • Mepilex Border/ Mepliex Border Lite<br>• Biatain Silicone Border/ Biatain Border Lite<br>• Allevyn Gentle Border<br>• Allevyn Border Lite<br>• Kerrafoam<br>• UrgoTul Absorb Border | • Isolated wounds<br>• DDEB and mild RDEB | • Bordered dressings may require removal with SMAR to avoid skin stripping<br>• May require primary contact layer<br>• Poor absorption of highly viscous exudate | • Up to 4 days depending on personal choice |
| Keratin | • Keragel | • Chronic wounds | • Dilute with blend emollient if stinging occurs | • Reapply with dressing changes |

- Recommended dressings for JEB skin and wound care:

| Dressing Type | Brand | Indication/ Function | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| Hydrogel impregnate gauze | Intrasite Conformable | • Eroded blister site<br>• Neonates and infants | • Small neonates at risk of hypothermia as dressing is cooling<br>• May be used with topical | • Change daily or when dry<br>• May need Urgotul as primary |

| Dressing Type | Brand | Indication/ Function | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| | | | morphine only when pain is difficult to control | contact layer |
| Polymeric membrane | • PolyMem<br>• PolyMem Max | • Chronic and acute wounds where cleansing is required | • Stimulates high levels of exudate — use barrier film to protect periwound skin if required<br>• Distinct smell does not necessarily indicate infection<br>• Can still be difficult to retain on vertical surfaces | • As determined by exudate level<br>• Change frequently until exudate reduces |
| Lipido-colloid | • Urgo Tul | • Wound contact layer | • Can be combined with an absorbent layer for moderately to heavily exuding wounds | |
| Soft silicone mesh | • Mepitel One<br>• Cuticell Contact<br>• Adaptic Touch | • Soft silicone wound contact layer | | |
| Hydrofiber | • Aquacel<br>• Durafiber | • Very moist wounds where it is difficult to keep dressing in place | • Lightly exuding or dry wounds | • Rehydrate with water or saline to remove, if necessary |
| Soft silicone foam | • Mepilex<br>• Mepilex Lite<br>• Mepilex Transfer | • Protection<br>• Absorption<br>• Excessive exudate | • May adhere if placed directly on wound bed, use an atraumatic contact layer | |

| Dressing Type | Brand | Indication/ Function | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| Soft silicone foam with super-absorbers | • Cutimed Siltec | • BSN medical | • Protection<br>• Absorption<br>• Excessive exudate | • Can be cut between super-absorbent crystals |

- Recommended dressings for chronic EB wounds based on consensus opinion:

| Dressing Type | Brand | Indications | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| Polymeric membrane | • PolyMem<br>• PolyMem Max<br>• PolyMem WIC (under a secondary dressing or further layer of PolyMem) | • Infected wounds<br>• Recalitrant wounds | • Can provide initial increase in exudate resulting in further skin damage if not properly controlled<br>• Distinct smell does not necessarily indicate infection<br>• Protect periwound skin | • Change when wet to avoid hypotherm ia |
| Enzyme alginogel | • Flaminal Hydro<br>• Flaminal Forte | • Low exudate<br>• High exudate | • Debrides, de-sloughs and antimicrobial<br>• Has some action in modulating excess proteases<br>• Can be used on all wounds apart from third degree burns<br>• Do not use if patient has sensitivity to alginates or polyethylene glycol | • Re-apply at each dressing change at least 2 mm thick |
| Honey | | • Sensitive wounds | • Can cause transient stinging or pain due to its acidity and high osmotic 'pull' | |

| Dressing Type | Brand | Indications | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| | | | • In turn this will contribute to high levels of exudate | |
| Protease modulator | • UrgoTul Start range<br>• Promogran<br>• Promogran Prisma (with silver) | • When excess protease may be present | • Promogran/ Promogran Prisma may cause initial transient stinging<br>• Excess product cannot be saved once opened as it degrades on contact with air<br>• A secondary dressing required and the product may provoke initial heavy exudate | • Frequent dressing changes may be required to avoid maceration |

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| DEB, JEB | Apply a 1 mm layer of Filsuvez to the affected wound surface only. Do not rub in the gel. Cover the wound with a sterile non-adhesive wound dressing. Alternatively, apply Filsuvez directly to the dressing so that the topical gel is in direct contact with the wound.<br><br>Apply Filsuvez to cleansed wounds with wound dressing changes until the wound is healed. | See dosing regimen |

## VI. Product Availability

Topical gel tube: 25 mL (10% w/w of birch triterpenes)

## VII. References

1. Filsuvez Prescribing Information. Wahlstedt, Germany: Lichtenheldt GmbH Pharmazeutische Fabrik; December 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215064s000lbl.pdf. Accessed January 8, 2024.
2. ClinicalTrials.gov. Phase III efficacy and safety study of Oleogel-s10 in epidermolysis bullosa (EASE). Available at: https://clinicaltrials.gov/study/NCT03068780. Accessed January 8, 2023.

3. Kern JS, Sprecher E, Fernandez MF, et al. Efficacy and safety of Oleogel-s10 (birch triterpenes) for epidermolysis bullosa: results from the phase III randomized double-blind phase of the EASE study. *Br J Dermatol*. 2023 Jan 23;188(1):12-21. doi: 10.1093/bjd/ljac001.
4. Denyer J, Pillay E, Clapham J, et al. Best practice guidelines for skin and wound care in epidermolysis bullosa. An International Consensus. Wounds International, 2017.
5. Has C, Liu L, Bolling MC, Charlesworth AV, et al. Clinical practice guidelines for laboratory diagnosis of epidermolysis bullosa. *Br J Dermatol*. 2020 Mar;182(3):574-592. doi: 10.1111/bjd.18128.
6. Mellerio JE, El Hachem M, Bellon N, et al. Emergency management in epidermolysis bullosa: consensus clinical recommendations from the European reference network for rare skin diseases. *Orphanet J Rare Dis*. 2020 Jun 6;15(1):142.
7. El Hachem M, Zambruno G, Bourdon-Lanoy E, et al. Multicentre consensus recommendations for skin care in inherited epidermolysis bullosa. *Orphanet J Rare Dis*. 2014 May 20;9:76.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 01.08.24 | 02.24 |
| Added exclusion of concomitant use with Vyjuvek in dystropic epidermolysis bullosa (Vyjuvek is not FDA-approved for use in junctional epidermolysis bullosa). | 03.05.24 | 05.24 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**
**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.