Clinical Policy: Birch Triterpenes (Filsuvez)

Reference Number: PA.CP.PHAR.669
Effective Date: 02/2024
Last Review Date: 01/2025

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 PA Health & Wellness® 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. Member does not have current evidence or history of squamous cell carcinoma in the area that will undergo treatment;
8. Filsuvez is not prescribed concurrently with Vyjuvek™;
9. Dose does not exceed 1 tube per target wound per day.

Approval duration: 3 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
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. 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. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53

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 • Chronic wounds	• Stimulates high levels of exudate • Distinct smell does not necessarily indicate infection • Can still be difficult to retain on vertical surfaces	• Change frequently until exudate reduces
Super-absorbent dressings	• Cutimed Siltec • Sorbion Sachet S • Filvasorb/ Vilwasorb Pro • 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 • Mepitel One • Adaptic Touch • Cuticell Contact	• Moist wound • Contact layer		
Lipido-colloid	• Urgo Tul	• Moist wound, drier wounds and protection of vulnerable healed areas • Used as an alternative to soft	• Where retention is difficult (e.g., vertical surfaces)	

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
		silicon (see above) in the presence of over-granulation		
Soft silicone foam	• Mepilex • Mepilex Lite • Mepilex Transfer	• Absorption of exudate • Protection • Lightly exuding wounds • To transfer exudate to absorbent dressing • Where conformability is required (e.g., digits, axillae)	• Over-heating • May need to apply over recommended atraumatic primary dressing	
Foam	• Allevyn • UrgoTul Absorb • 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 • Biatain Silicone Border/ Biatain Border Lite • Allevyn Gentle Border • Allevyn Border Lite • Kerrafoam	• Isolated wounds • DDEB and mild RDEB	• Bordered dressings may require removal with SMAR to avoid skin stripping • May require primary contact layer • Poor absorption of highly viscous exudate	• Up to 4 days depending on personal choice

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
	• UrgoTul Absorb Border			
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 • Neonates and infants	• Small neonates at risk of hypothermia as dressing is cooling • May be used with topical morphine only when pain is difficult to control	• Change daily or when dry • May need Urgotul as primary contact layer
Polymeric membrane	• PolyMem • PolyMem Max	• Chronic and acute wounds where cleansing is required	• Stimulates high levels of exudate — use barrier film to protect periwound skin if required • Distinct smell does not necessarily indicate infection • Can still be difficult to retain on vertical surfaces	• As determined by exudate level • Change frequently until exudate reduces
Lipido-colloid	• Urgo Tul	• Wound contact layer	• Can be combined with an absorbant layer for moderately to heavily exuding wounds	

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
Soft silicone mesh	• Mepitel One • Cuticell Contact • Adaptic Touch	• Soft silicone wound contact layer		
Hydrofiber	• Aquacel • 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 • Mepilex Lite • Mepilex Transfer	• Protection • Absorption • Excessive exudate	• May adhere if placed directly on wound bed, use an atraumatic contact layer	
Soft silicone foam with super-absorbers	• Cutimed Siltec	• BSN medical	• Protection • Absorption • 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 • PolyMem Max • PolyMem WIC (under a secondary dressing or further layer of PolyMem)	• Infected wounds • Recalitrant wounds	• Can provide initial increase in exudate resulting in further skin damage if not properly controlled • Distinct smell does not necessarily indicate infection • Protect periwound skin	• Change when wet to avoid hypotherm ia
Enzyme alginogel	• Flaminal Hydro • Flaminal Forte	• Low exudate • High exudate	• Debrides, de-sloughs and antimicrobial	• Re-apply at each dressing change at

Dressing Type	Brand	Indications	Contraindication/ Comments	Wear Time
			• Has some action in modulating excess proteases • Can be used on all wounds apart from third degree burns • Do not use if patient has sensitivity to alginates or polyethylene glycol	least 2 mm thick
Honey		• Sensitive wounds	• Can cause transient stinging or pain due to its acidity and high osmotic 'pull' • In turn this will contribute to high levels of exudate	
Protease modulator	• UrgoTul Start range • Promogran • Promogran Prisma (with silver)	• When excess protease may be present	• Promogran/ Promogran Prisma may cause initial transient stinging • Excess product cannot be saved once opened as it degrades on contact with air • 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.	See dosing regimen

Indication	Dosing Regimen	Maximum Dose
	Apply Filsuvez to cleansed wounds with wound dressing changes until the wound is healed.	

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; May 2024. Available at: https://resources.chiesiusa.com/Filsuvez/FILSUVEZ_PI.pdf. Accessed October 22, 2024. Accessed January 8, 2024.
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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
Policy created	01/2024
Added exclusion of concomitant use with Vyjuvek (Vyjuvek is not FDA-approved for use in junctional epidermolysis bullosa).	04/2024
1Q 2025 annual review: for initial approval criteria, added “member does not have current evidence or history of squamous cell carcinoma in the area that will undergo treatment” per competitor analysis and EASE study trial design; references reviewed and updated.	01/2025