SUMMARY

refined dry extract of birch bark
FILSUVEZ 10%,
gel
First assessment

Original French opinion adopted by the Transparency Committee on 23 November 2022

The legally binding text is the original French opinion version

Key points

Favourable opinion for reimbursement only in the treatment of partial thickness wounds associated with recessive dystrophic epidermolysis bullosa (EB) in patients 6 months and older.

Unfavourable opinion for reimbursement in the other clinical situations of the MA.

What therapeutic improvement?

No clinical added value in the therapeutic strategy for partial thickness wounds associated with recessive dystrophic epidermolysis bullosa in patients 6 months and older.

Role in the care pathway?

In the absence of curative treatment, the management of hereditary EB relies solely on symptomatic treatment, and involves preventing bullous detachment (protecting areas from injury, daily hygiene), promoting wound healing, managing pain and pruritus, preventing complications and monitoring for the development of cancer.

Management must be adapted to the type of EB and the characteristics of each wound. Nursing care plays an essential role in the management of these wounds (desloughing, management of blisters, application of dressings and interfaces).

The choice of dressing, with or without an interface, depends on the type of wound:

- Alginates (desloughing)
- Hydrocellular dressings (exuding wounds) and thin hydrocellular dressings (low exuding wounds)
- Interfaces (fragile skin with blisters)
- Silver dressings (infected wounds). However, it has not been established that these products can prevent infection or improve healing rates of infected wounds.
- Hydrofibre dressings (exuding wounds or in the event of redness/discharge)

Role of FILSUVEZ in the care pathway

Considering:

- evidence of the superiority of FILSUVEZ gel (refined dry extract of birch bark) compared to a placebo gel, in terms of achievement of first complete closure at D45, in patients (children and adults) with inherited EB (dystrophic EB, junctional EB and Kindler syndrome) receiving the standard treatment, including the application of non-adherent dressings and interfaces,
- the absence of evidence of a benefit in terms of maintenance of healing,
- the lack of long-term comparative efficacy and safety data, beyond 90 days, in a chronic disease context,
- limitations in terms of the transposability of the efficacy results to subpopulations of patients with dominant dystrophic EB and junctional EB (MA indication), representing only 9% (n = 20) and 11.7% (n = 26) of patients included in the primary analysis population,
- the safety profile marked by a risk of wound complications (increase in wound size, reopening of the wound and wound pain: 61.5% in the FILSUVEZ group versus 53.5% in the placebo gel group),

➔ **Within the reimbursement scope:**

the Committee considers that FILSUVEZ (refined dry extract of birch bark) only has a role in the treatment of partial thickness wounds associated with recessive dystrophic epidermolysis bullosa (EB) in patients 6 months and older.

➔ **Within the scope included in the MA but not retained for reimbursement:**

FILSUVEZ has no role in the treatment of partial thickness wounds associated with dominant dystrophic EB and junctional EB in patients 6 months and older, in the absence of robust data in these subpopulations.

Committee's conclusions

Clinical Benefit

- Inherited EB is a rare hereditary skin disease that is serious in its severe forms, potentially fatal, painful, itchy, and has a significant impact on the quality of life of patients and caregivers.
- FILSUVEZ (refined dry extract of birch bark) gel is a symptomatic medicinal product.
- The efficacy/adverse effects ratio of FILSUVEZ (refined dry extract of birch bark) in the treatment of partial thickness wounds associated with epidermolysis bullosa (EB) is:
  - low only for the recessive dystrophic type, in view of the available data and the population included in the EASE study (BEB-13),
  - inadequately established in the other clinical situations of the MA, given the limitations in terms of transposability of the results.
- There are no medicinal alternatives. Treatment is based solely on nursing care, with, in particular, wound dressing.
- Combined with standard wound care, FILSUVEZ is a first-line treatment in patients 6 months and older with partial thickness wounds associated with recessive dystrophic epidermolysis bullosa (EB).

  FILSUVEZ has no role in the treatment of the other clinical situations of the MA.

Public health benefit

Considering:

- the seriousness of the disease in its severe forms, which are potentially life-threatening,
- the low prevalence of the disease (in particular the junctional EB subtype),
- the very partially met medical need,
- the lack of response to the identified need considering:
  - the modest efficacy of FILSUVEZ and the safety risks (in particular wound complications and infection, pain, pruritus),
  - the lack of evidence of an impact on the quality of life of patients and caregivers,
  - the lack of evidence of a favourable impact on the care and/or life pathway of patients (no evidence of an impact on healing time or maintenance of healing and the need for nursing care),

FILSUVEZ is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of FILSUVEZ is:

- **low, only in the treatment of partial thickness wounds associated with recessive dystrophic epidermolysis bullosa (EB) in patients 6 months and older.**
- **insufficient in the other clinical situations of the MA (dominant dystrophic EB and junctional EB).**

The Committee issues the following opinions:

- **favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the treatment of partial thickness wounds associated with recessive dystrophic epidermolysis bullosa (EB) in patients 6 months and older, and at the MA dosages.**

- **unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the other clinical situations of the MA, and at the MA dosages.**

Clinical Added Value

Treatment of partial thickness wounds associated with recessive dystrophic epidermolysis bullosa (EB) in patients 6 months and older

Considering:

- evidence in a study of good methodological quality of the superiority of FILSUVEZ (refined dry extract of birch bark) gel compared to a placebo gel, in terms of achievement of first complete closure at D45, in 223 patients (children and adults) with inherited EB receiving the standard treatment, including the application of non-adherent dressings and interfaces, but a modest difference in favour of FILSUVEZ,
- the predominance of patients with recessive dystrophic EB in the study, representing 78.5% of the sample size, and results in this subpopulation suggesting a greater clinical benefit in terms of complete closure of the wound at D45 (44.0% vs. 26.2%),
- uncertainties in terms of the efficacy in patients with dominant dystrophic EB and junctional EB, representing only 9% (n = 20) and 11.7% (n = 26) of patients included in the primary analysis population,
- the absence of:
  - evidence of the superiority of FILSUVEZ compared to placebo gel on the first of the ranked secondary endpoints (time to complete closure of the target wound until the end of the treatment period at D90) and, consequently, on none of the other ranked secondary endpoints,
  - evidence of efficacy on maintenance of healing, which is the real challenge of treatment, although this was initially scheduled in the protocol, limiting the clinical relevance of the primary endpoint,
  - robust data on the quality of life of patients or caregivers,
- the safety profile marked, in particular, by a risk of wound complications (increase in wound size, reopening of the wound and wound pain: 61.5% in the FILSUVEZ group versus 53.5 % in the placebo gel group),
- the medical need currently partially met by symptomatic non-medicinal management including skincare delivered by nurses, dressings and interfaces (medical devices) and monitoring for complications,

the Committee considers that FILSUVEZ provides no clinical added value (CAV V) in the current care pathway for partial thickness wounds associated with recessive dystrophic bullosa epidermolysis bullosa (EB) in patients 6 months and older.