SUMMARY

lebrikizumab

EBGLYSS 125 mg/ml

solution for injection

First listing

Original French opinion adopted by the Transparency Committee on 29 May 2024

The legally binding text is the original French opinion version

Summary of opinion

➔ **In adults**

Favourable opinion for reimbursement only in "the treatment of moderate to severe atopic dermatitis in adults who are candidates for systemic therapy, in the event of inadequate response, intolerance or contraindication to ciclosporin".

Unfavourable opinion for reimbursement in in adults with inadequate response to topical therapies and who are ciclosporin-naïve, in the absence of comparative data.

Transparency Committee's conclusions

Clinical Benefit

Pending the reassessment of systemic therapies in atopic dermatitis in the light of the next French recommendations on the management of atopic dermatitis, the Committee considers that:

In adults

- Atopic dermatitis is not usually a serious disease but in its moderate to severe forms, it has a significant impact on the quality of life of patients and marked psychosocial repercussions.
- This is a medicinal product intended to have a suspensive effect on symptoms.
- In the absence of direct comparison with ciclosporin, the efficacy/adverse effects ratio of EBGLYSS (lebrikizumab) has not been established in adults with moderate to severe atopic dermatitis with inadequate response to topical treatments and who are ciclosporin-naive. In patients with inadequate response, intolerance or contraindication to ciclosporin, its efficacy/ adverse effects ratio is high.

➔ This medicinal product is a second-line systemic therapy to be reserved for adults with moderate to severe atopic dermatitis, in the event of inadequate response, intolerance or contraindication to ciclosporin.

➔ Public health benefit

Considering:

- the seriousness of the disease in its severe forms requiring systemic therapy and its significant impact on patients' quality of life;
- the prevalence of the disease (between 2 and 5% of the population);
- the medical need that is partially met in adults and adolescents with moderate to severe atopic dermatitis who are candidates for systemic therapy;
- the partial response to the identified need given:
  - a demonstrated impact versus placebo at week 16 in adults and adolescents aged ≥ 12 years (body weight ≥ 40 kg):
    - in terms of morbidity (in particular, for IGA 0 or 1, EASI-75 and EASI-90 responses and pruritus), as monotherapy or in combination with topical corticosteroids, in patients with inadequate response, intolerance or contraindication to ciclosporin,
    - in terms of quality of life, with a clinically relevant difference in terms of variation in mean DLQI score, observed in monotherapy only, in one out of two studies,
    - but with no evidence of an additional impact in terms of morbidity or quality of life versus ciclosporin and other systemic therapies,
  - the absence of an expected or demonstrated additional impact on the organisation of care and the patient's life and care pathway,

EBGLYSS (lebrikizumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of EBGLYSS 125 mg/ml (lebrikizumab) solution for injection in pre-filled syringe or pen is:

- **substantial only in the treatment of moderate to severe atopic dermatitis in adults who are candidates for systemic therapy, in the event of inadequate response, intolerance or contraindication to ciclosporin,**
- **insufficient to justify public funding cover in view of the available alternatives in the other situations covered by the MA in adults.**

The Committee issues:

- **a favourable opinion for inclusion of EBGLYSS 125 mg/ml (lebrikizumab) solution for injection in pre-filled syringe or pen in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use only in the treatment of moderate to severe atopic dermatitis in adults who are candidates for systemic therapy, in the event of inadequate response, intolerance or contraindication to ciclosporin and at the MA dosages,**
- **an unfavourable opinion for inclusion in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the treatment of moderate to severe atopic dermatitis in adults with inadequate response to topical treatments and who are ciclosporin-naive, in the absence of comparative data.**

➔ Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%

In adolescents ≥ 12 years

- Atopic dermatitis is not usually a serious disease but in its moderate to severe forms, it has a significant impact on the quality of life of patients and marked psychosocial repercussions.
- This is a medicinal product intended to have a suspensive effect on symptoms.
- The efficacy/adverse effects ratio is high.
- It is a first-line systemic therapy to be reserved for adolescents (12 years or older) with moderate to severe atopic dermatitis, in the event of inadequate response to topical treatments.

Public health benefit

Considering:

- the seriousness of the disease in its severe forms requiring systemic therapy and its significant impact on patients' quality of life;
- the high prevalence of the disease in adolescents (14.3%);
- the medical need that is partially met in adolescents with moderate to severe atopic dermatitis who are candidates for systemic therapy;
- the partial response to the identified need given:
  - a demonstrated impact versus placebo at week 16 in adults and adolescents aged ≥ 12 years (body weight ≥ 40 kg) with moderate to severe atopic dermatitis who are candidates for systemic therapy:
    - in terms of morbidity (in particular, for IGA 0 or 1, EASI-75 and EASI-90 responses and pruritus), as monotherapy or in combination with topical corticosteroids, in patients with inadequate response, intolerance or contraindication to ciclosporin,
    - in terms of quality of life, with a clinically relevant difference in terms of variation in mean DLQI score, observed in monotherapy only, in one out of two studies,
    - but with no evidence of an additional impact in terms of morbidity or quality of life versus ciclosporin and other systemic therapies,
  - the absence of clinical data specific to adolescents, who represented 11 to 22% of the study populations,
  - the absence of an expected or demonstrated additional impact on the organisation of care and the patient's life pathway,

EBGLYSS (lebrikizumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of EBGLYSS 125 mg/ml (lebrikizumab) solution for injection in pre-filled syringe or pen is substantial in the MA indication in adolescents 12 years and older (body weight ≥ 40 kg).

The Committee issues a favourable opinion for inclusion of EBGLYSS 125 mg/ml (lebrikizumab) solution for injection in pre-filled syringe or pen in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in adolescents 12 years and older (body weight ≥ 40 kg) in the MA indication and at the MA dosages.

Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%

Clinical Added Value

Pending the reassessment of systemic therapies in atopic dermatitis in the light of the next French recommendations on the management of atopic dermatitis, the Committee considers that:

In adults

➔ **Within the reimbursement scope retained by the Committee (in the event of inadequate response, intolerance or contraindication to ciclosporin)**

Considering:

- demonstration in phase 3 studies of good methodological quality having included adults and adolescents 12 years and older (body weight ≥ 40 kg, 11 to 22% of the study populations) with moderate to severe atopic dermatitis who are candidates for systemic therapy:
  - the superiority of lebrikizumab compared to placebo, with a substantial effect size, in terms of IGA 0 or 1, EASI-75 and EASI-90 responses, and pruritus after 16 weeks of treatment (ranked endpoints), as monotherapy (ADvocate 1 and 2 studies) or in combination with topical corticosteroids (ADhere study),
  - the superiority of lebrikizumab compared to placebo for the EASI-75 response after 16 weeks of treatment, in combination with topical corticosteroids, in patients with inadequate response or contraindications to ciclosporin (ADvantage study),
  - demonstration of a clinically relevant improvement in quality of life (Δ DLQI ≥ 4 points) after 16 weeks of treatment compared to placebo in the ADvocate 1 study,
- exploratory results suggesting maintenance of clinical responses (IGA 0 or 1 and EASI-75) up to 104 weeks of follow-up,
- the medium-term safety profile of lebrikizumab primarily marked by conjunctivitis and injection site reactions;

but:

- the absence of comparison with ciclosporin and the other systemic interleukin inhibitors, in particular dupilumab, and JAK inhibitors currently available;
- the absence of long-term data beyond 104 weeks given the safety risks associated with immunosuppression (serious infections, cancer);

the Committee deems that EBGLYSS (lebrikizumab) 125 mg/ml solution for injection provides no clinical added value (CAV V) in the care pathway for the treatment of moderate to severe atopic dermatitis in adults who are candidates for systemic therapy, in the event of inadequate response, intolerance or contraindication to ciclosporin, which includes other interleukin inhibitors (dupilumab, tralokinumab) and JAK inhibitors (baricitinib, upadacitinib and abrocitinib).

In adolescents ≥ 12 years

Considering:

- demonstration in phase 3 studies of good methodological quality having included patients with moderate to severe atopic dermatitis who are candidates for systemic therapy:

- the superiority of lebrikizumab compared to placebo, with a substantial effect size, in terms of IGA 0 or 1, EASI-75 and EASI-90 responses, and pruritus after 16 weeks of treatment (ranked endpoints), as monotherapy (ADvocate 1 and 2 studies) or in combination with topical corticosteroids (ADhere study) in adults or adolescents (11 to 22% of the study populations, body weight ≥ 40 kg),
- the superiority of lebrikizumab compared to placebo for the EASI-75 response after 16 weeks of treatment, in combination with topical corticosteroids, in adults or adolescents (12% of the study population, body weight ≥ 40 kg) with inadequate response or contraindications to ciclosporin (ADvantage study),
- demonstration of a clinically relevant improvement in quality of life (Δ DLQI ≥ 4 points) after 16 weeks of treatment compared to placebo in the ADvocate 1 study,

– exploratory results suggesting maintenance of clinical responses (IGA 0 or 1 and EASI-75) up to 104 weeks of follow-up;
– the medium-term safety profile of lebrikizumab in studies in atopic dermatitis primarily marked by conjunctivitis and injection site reactions;

but:

– the absence of a direct comparison between lebrikizumab and dupilumab although this would have been possible, in particular in a specific study in adolescents;
– the absence of long-term data beyond 104 weeks given the safety risks associated with µimmunosuppression (serious infections, cancer);

the Committee deems that EBGLYSS (lebrikizumab) 125 mg/ml solution for injection provides no clinical added value (CAV V) in the care pathway for the treatment of moderate to severe atopic dermatitis in adolescents 12 years and older (body weight ≥ 40 kg) who are candidates for systemic therapy, which includes two interleukin inhibitors (dupilumab and tralokinumab) and one JAK inhibitor (upadacitinib).