HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
7 JULY 2021

The legally binding text is the original French opinion version

risankizumab
SKYRIZI 75 mg solution for injection in pre-filled syringe

Re-evaluation

Key points

Favourable opinion for reimbursement in the treatment of plaque psoriasis in adults, in severe chronic forms only, defined by:
- failure (insufficient response, contraindication or intolerance) of at least two treatments including non-biological systemic treatments and light therapy
- and an extensive form and/or significant psychosocial impact.

Unfavourable opinion for reimbursement in other forms of plaque psoriasis in adults.

The Committee will re-evaluate the reimbursement scope and the role in the care pathway for interleukin inhibitors, including SKYRIZI (risankizumab) in plaque psoriasis in adults and children.

What therapeutic improvement?

Therapeutic improvement compared to COSENTYX (secukinumab).

Role in the care pathway?

Current psoriasis treatments do not result in the definitive cure of the condition, but allow for transient and more or less complete disappearance of the lesions. The therapeutic arsenal includes local and general treatments. Local treatments can be used alone or combined either with each other or with general treatments.

In the most severe forms, systemic treatments can be used: methotrexate (reference treatment), ciclosporin as an alternative to methotrexate, retinoids (acitretin) in certain clinical forms or in combination with light therapy.

If these first-line systemic treatments fail or are not tolerated, systemic biological treatments are recommended: TNFα inhibitors (adalimumab, etanercept, infliximab, certolizumab pegol), IL12 and 23 interleukin inhibitors (ustekinumab), IL17 inhibitors (secukinumab, ixekizumab), IL17 receptor inhibitors (brodalumab) and IL23 inhibitors (risankizumab, guselkumab and tildrakizumab). According to the guidelines of the French society for Dermatology (2019), adalimumab (TNFα inhibitor) and ustekinumab (IL12 and 23 inhibitor) are the first-line systemic biological treatments. The role of apremilast (phosphodiesterase inhibitor 4) remains poorly defined with results significantly inferior to biological treatments.

The current treatment strategy is "rotational" between the different alternatives, the choice of treatment being guided by patient and disease characteristics (concomitant disease, extent of lesions, previous treatment history) and those of the proprietary medicinal product (adverse effects, cumulative dose).

Until its recent opinions of 2021, the Committee recommended that biological treatments be reserved for severe forms of plaque psoriasis in adults, defined by:
- failure (insufficient response, contraindication or intolerance) of at least two treatments including non-biological systemic treatments and light therapy
- and an extensive form and/or significant psychosocial impact.

However, considering:
- the results of the PSOBIOTEQ observational study, with follow-up for 3 years, demonstrating the establishment in clinical practice of the medicinal products ENBREL (etanercept), REMICADE (infliximab), HUMIRA (adalimumab) or STELARA (ustekinumab):

- in patients meeting the MA indication for these medicines, i.e.:

o predominantly having a moderate to severe form of plaque psoriasis based on PGA score and PASI score, along with,

o extensive lesions and a moderate to high impact on quality of life for a high proportion of patients,

o in whom conventional systemic treatments (methotrexate, ciclosporin) or phototherapy have failed for the great majority of patients,

- without challenging the known safety profile for these medicinal products, in particular without demonstrating an increased risk of tumours and serious infections after 3 years of follow-up,

- pharmacovigilance data demonstrating a globally unchanged safety profile,

the Committee now considers that ENBREL (etanercept), REMICADE (infliximab), HUMIRA (adalimumab) and STELARA (ustekinumab), are second-line systemic treatments in moderate to severe forms of plaque psoriasis in adults in the event of failure (insufficient response, contraindication or intolerance) of a first-line non-biological systemic treatment (methotrexate, ciclosporin or acitretin) and possibly phototherapy. The Committee reiterates that methotrexate remains the reference non-biological treatment, in accordance with the guidelines of the French society for Dermatology (2019). The decision to initiate treatment should take into account the disease history, patients' characteristics, their treatment history and the severity of their disease, the latter being assessed on the basis of the appearance of the lesions, as well as how extensive they are, the impact of the disease on quality of life and its psychosocial impact.

The Committee has undertaken to reassess the reimbursement scope and the role in the care pathway of all the other biological therapies in plaque psoriasis in adults and children.

Role of the medicinal product in the care pathway

Pending re-evaluation of all the biological medicines not included in the PSOBIOTEQ 1 observational study, including SKYRIZI 75 mg (risankizumab, IL23 inhibitor), this medicinal product remains a treatment reserved for severe chronic forms of plaque psoriasis in adults, defined by:
- failure (insufficient response, contraindication or intolerance) of at least two treatments including non-biological systemic treatments and light therapy
- and an extensive form and/or significant psychosocial impact.

Special recommendations

Given the risk of hypersensitivity reaction to subcutaneous risankizumab (see paragraph 4.4 of the SPC), the Transparency Committee recommends that the first subcutaneous injection of this drug be performed in an appropriate care structure.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Psoriasis is a chronic inflammatory skin condition, usually benign, that can, in its moderate to severe forms, have a significant impact on quality of life.

◗ SKYRIZI 75 mg (risankizumab) solution for injection in pre-filled syringe has a suspensive effect on symptoms.

◗ Its efficacy/adverse effects ratio is high, though additional data is needed to assess its long-term efficacy and safety (beyond 104 weeks).

◗ Pending re-evaluation of all the biological medicines not included in the PSOBIOTEQ 1 observational study, SKYRIZI 75 mg (risankizumab) remains a treatment reserved for severe chronic forms of plaque psoriasis in adults, defined by:

- failure (insufficient response, contraindication or intolerance) of at least two treatments including non-biological systemic treatments and light therapy
- and an extensive form and/or significant psychosocial impact

◗ There are therapeutic alternatives.

◗ <u>Public health impact:</u>

Considering:

- the severe condition of patients in chronic forms of psoriasis resistant to non-biological systemic treatments, associated with a significant deterioration in quality of life, but its low prevalence;
- the partially met medical need, despite the existence of numerous alternatives, due to failures of available treatments and resistance phenomena;
- the partial response to the identified need given:
    - demonstration of an additional impact in terms of morbidity compared to secukinumab after 1 year of treatment without any new safety signals compared to the available data at week 16;
    - demonstration of an impact in terms of quality of life versus placebo and ustekinumab in the short term (16 weeks);

  but:
    - the absence of demonstration of an additional impact in terms of morbidity as induction therapy (week 16) versus secukinumab (demonstration of non-inferiority);
    - the absence of demonstration of a superiority compared to more recent interleukin inhibitors (IL17 inhibitor/IL17 and IL23 receptor inhibitor);
    - doubts with respect to the transposability of the results in terms of efficacy, quality of life and safety (immunogenic, carcinogenic and cardiovascular risks), in the absence of long-term data beyond one year for efficacy, 16 weeks for quality of life and 2 years for safety;
- the absence of demonstration of an additional impact in terms of the organisation of care, the patient's care and life pathway despite a simplified dosing regimen every 12 weeks;

SKYRIZI 75 mg (risankizumab) is unlikely to have an additional impact on public health.

Considering these elements, the Committee deems that, pending re-evaluation of all the biological medicines not included in the PSOBIOTEQ 1 observational study, the clinical benefit of SKYRIZI 75 mg (risankizumab) solution for injection in pre-filled syringe remains:

- **substantial in the treatment of plaque psoriasis in adults, in severe chronic forms only, defined by:**
  - **failure (insufficient response, contraindication or intolerance) of at least two treatments including non-biologic systemic treatments and light therapy**
  - **and an extensive form and/or significant psychosocial impact.**
- **insufficient in the other forms to justify public funding cover.**

The Committee issues a favourable opinion for maintenance of inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the treatment of plaque psoriasis in adults, in severe chronic forms only, defined by:

- **failure (insufficient response, contraindication or intolerance) of at least two treatments including non-biological systemic treatments and light therapy**
- **and an extensive form and/or significant psychosocial impact,**

and at the MA dosages.

The Committee maintains an unfavourable opinion for reimbursement in other forms of plaque psoriasis in adults.

The Committee will re-evaluate the reimbursement scope and the role in the care pathway for interleukin inhibitors, including SKYRIZI (risankizumab) in plaque psoriasis in adults and children.

- **Recommended reimbursement rate: 65%**

Clinical Added Value

Considering:

- **demonstration of the superiority of risankizumab compared to secukinumab (COSENTYX) at week 52 in terms of percentage of PASI 90 responders (second co-primary efficacy endpoint with management of α risk inflation related to the multiplicity of tests) with a particularly high and clinically relevant size effect (absolute difference of 30% of responders) in the phase III IMMerge study;**
- **demonstration, in this same study, of the superiority of risankizumab compared to secukinumab on the ranked secondary endpoints assessed at week 52 (PASI 75 and PASI 100 responses and sPGA score = 0 or 1) also with a marked difference between the treatments;**
- **the initially demonstrated superiority of risankizumab compared to adalimumab (HUMIRA) and ustekinumab (STELARA) with clinically relevant differences in terms of percentage of complete or almost complete disappearance of lesions (sPGA = 0 or 1) and percentage of PASI 90 responses after 16 weeks (co-primary endpoints), as well as maintenance of this superiority up to week 52;**
- **a safety profile comparable to that of other interleukin inhibitors;**

despite:

- **the absence of demonstration of superiority versus secukinumab at week 16 in the IMMerge study, with only non-inferiority having been demonstrated in terms of PASI 90 response (first co-primary endpoint);**
- **the absence of demonstration of an additional impact of risankizumab compared to secukinumab in terms of quality of life (the impact of quality of life was demonstrated versus placebo only at week 16);**
- **the performance of IMMerge as a single-blind study (assessor blinded);**
- **the lack of long-term efficacy and safety data (beyond 104 weeks) and quality of life data beyond 16 weeks;**

SKYRIZI 75 mg (risankizumab) solution for injection in pre-filled syringe provides no clinical added value (CAV IV) compared to COSENTYX (secukinumab) in adults with severe chronic plaque psoriasis, defined by:

- **failure (insufficient response, contraindication or intolerance) of at least two treatments including non-biologic systemic treatments and light therapy,**
- **and an extensive form and/or significant psychosocial impact.**