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DERMATOLOGY
New medicinal product
October 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

TREMFYA (guselkumab), interleukin 23 inhibitor immunosuppressant

High clinical benefit for the treatment of severe chronic plaque psoriasis in adults defined by:
- **failure of at least two treatments including non-biological systemic treatments and light therapy**
- **and an extensive form and/or significant psychosocial impact**

but no demonstrated clinical improvement compared to other anti-interleukins.

Insufficient clinical benefit to justify reimbursement for other forms.

Main points

- TREMFYA has MA for the treatment of moderate to severe plaque psoriasis in adults, requiring systemic treatment.
- It has demonstrated its superiority over HUMIRA (adalimumab).
- TREMFYA is a second-line systemic treatment to be reserved for adults with severe chronic plaque psoriasis, 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 with significant psychosocial impact.

Therapeutic strategy

- Skin moisturising using emollients is frequently associated with topical treatments which are the first-line treatment of limited plaque psoriasis: dermocorticosteroids, vitamin D3 analogues, retinoids (vitamin A derivatives), and less frequently tars, anthralin and keratolytics.
  Systemic treatments target moderate to severe forms of psoriasis. These consist of methotrexate (conventional treatment), light therapy, retinoids (generally combined with light therapy), ciclosporin, apremilast and systemic biological treatments (TNFα and interleukin inhibitors). Although its efficacy is modest, due to its good safety profile, apremilast may be useful for delaying the initiation of biological treatments.
  Biological anti-TNF and interleukin inhibitor treatments (the anti-IL12/IL23 agent STELARA and the anti-IL17 agents COSENTYX, TALTZ and KYNTHEUM) should be reserved for severe chronic forms of plaque psoriasis in adults defined above.
  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).
- **Role of the medicinal product in the therapeutic strategy**
  TREMFYA, anti-IL23, is a systemic treatment to be reserved for severe chronic forms of plaque psoriasis in adults defined above.

Clinical data

- Guselkumab was assessed in the treatment of moderate to severe plaque psoriasis in two placebo- and active comparator (adalimumab)-controlled, double-blind, randomised studies in candidate patients for systemic treatment or light therapy (1 study of 48 weeks on 837 patients and 1 study of 24 weeks on 992 patients). The

dosage of guselkumab was one 100 mg dose administered subcutaneously (SC) at weeks 0 and 4, followed by one dose every 8 weeks and that of adalimumab was one 80 mg SC dose at week 0, followed by one 40 mg SC dose at week 1, and subsequently 40mg SC dose every 2 weeks. For blinding, the patients of each group received a placebo of the other treatment under study.

- The findings demonstrated the superiority of guselkumab over the placebo on the two co-primary endpoints ($p < 0.001$) with investigator-assessed responder rates with clear or almost clear lesions (IGA 0 or 1) of 85.1% and 84.1% in the guselkumab group versus 6.9% and 8.5% in the placebo and PASI 90 responder rates of 73.3% and 70.0% in the guselkumab group versus 2.9% and 2.4% in the placebo group.
- One double-blind, randomised study demonstrated the superiority of guselkumab over ustekinumab in terms of IGA response of 0 or 1 and a score improvement of at least 2 points between weeks 28 and 40 in patients having an insufficient response to ustekinumab after a 16-week treatment with ustekinumab. Nevertheless, this study is not relevant as, according to the therapeutic strategy, after the failure of ustekinumab, another biological treatment should have been initiated, with an anti-TNFα agent or another interleukin inhibitor.
- The most frequent adverse effects with guselkumab are: upper respiratory tract infections, gastro-enteritis, Herpes simplex infections, dermatophytosis, headache, diarrhoea, urticaria, arthralgia and erythema at the injection site. Severe hypersensitivity reactions require immediate discontinuation of the administration of Tremfya and the initiation of an appropriate treatment.

Special prescription requirements

- Medicinal product subject to initial annual hospital prescription.
- Initial prescription and renewal reserved for dermatology or internal medicine specialists.

Benefit of the medicinal product

- The actual clinical benefit* of TREMFYA is high for the treatment of plaque psoriasis in adults, for patients with severe, chronic plaque psoriasis defined above.
- In other forms, the actual clinical benefit is insufficient to justify reimbursement by public funding.
- TREMFYA does not provide an improvement in actual clinical benefit** (IACB V) compared to other anti-interleukins.
- Approval for non-hospital pharmacy reimbursement and for hospital treatment for patients with a high actual clinical benefit.

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This document was drafted on the basis of the Transparency Committee opinion dated 03/10/2018 (CT-16892) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The improvement in actual clinical benefit (IACB) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the IACB rating from I, major, to IV, minor. An IACB rating of V (equivalent to "no IACB") denotes a "lack of clinical improvement"