HAUTE AUTORITÉ DE SANTÉ

RHEUMATOLOGY
New indication
April 2018

SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

TALTZ (ixekizumab), anti-interleukin 17A immunosuppressant

Moderate clinical benefit for psoriatic arthritis but no proven clinical added value in the therapeutic strategy

Main points

- TALTZ has been granted a marketing authorisation, alone or in combination with methotrexate (MTX), for the treatment of active psoriatic arthritis in adults with an inadequate response or intolerance to one or more DMARD (Disease Modifying Anti Rheumatic Drug).
- Its efficacy has been demonstrated versus placebo on a composite criterion (ACR 20) in TNF inhibitor (TNFi) naive patients in one study, and in patients having previously received one or more TNFi in another study.
- The effect on structural damage progression has only been assessed and demonstrated in TNFi naive patients.
- As with ustekinumab (anti-IL 12 and 23, STELARA) and secukinumab (anti-IL 17 A, COSENTYX), it is not possible to specify the place of ixekizumab (anti-IL 17 A, TALTZ) compared to TNFi in the first-line treatment of psoriatic arthritis (i.e. in the event of failure of conventional DMARD) due to the absence of comparative data.

Pre-existing indication*

TALTZ has a marketing authorisation for the treatment of moderate to severe plaque psoriasis in adults.

Treatment strategy

- Psoriatic arthritis (PsA) therapeutic management combines symptomatic treatment (NSAIDs with or without analgesics) with DMARDs.
  Among DMARD, a distinction is made between conventional agents such as methotrexate, leflunomide and sulfasalazine (off-label), and biological agents (used in case of failure, contraindication or intolerance to conventional DMARD), such as TNFis and interleukin inhibitors.
  Five TNF inhibitors are currently available: adalimumab, etanercept, infliximab, golimumab and certolizumab pegol. All have been granted a marketing authorisation for the treatment of PsA. Due to the absence of direct comparative data, ranking these medications is not possible. In case of failure of one TNFi therapy, the use of another TNFi may be considered.

  Among interleukin inhibitors, ustekinumab (anti-IL-12/23) has been granted a marketing authorisation only after failure of conventional DMARD, and two anti-IL-17A, secukinumab and ixekizumab, have been granted a marketing authorisation after failure of DMARD (conventional and biologic).
- If biological treatments are unsuitable, apremilast (OTELZA), an oral phosphodiesterase 4 (PDE4) inhibitor, may be used.
- **Role of the proprietary medicinal product in the therapeutic strategy**
  As with STELARA and COSENTYX, it is difficult to specify the place of TALTZ compared to TNFi as first-line biotherapy treatments for psoriatic arthritis, i.e. in the event of failure of conventional DMARD, given the absence of comparative data.

* This summary does not concern this indication.

Nevertheless, given approximately 15 years of post-marketing data with TNFis, with evidence of efficacy on joint structural damage, this medicinal product class should be preferred as a first-line treatment if biological DMARD (bDMARD) are considered.

Considering the rare but serious risk of systemic injection reactions, including anaphylactic reactions, with TALTZ as well as with other bDMARD, the first subcutaneous injection of this medicinal product should be made in a suitable healthcare facility.

Clinical data

- Ixekizumab was assessed in two randomised double-blind studies, one versus placebo (with an adalimumab group for comparison with placebo, but not used to show equivalence or noninferiority with ixekizumab.) on bDMARD naive patients, the other versus placebo on patients having previously received one or more TNFi. The superiority of ixekizumab over placebo was demonstrated in these two studies with an absolute difference in terms of ACR 20 response at 24 weeks (primary endpoint) of 27.7 to 28.5%. The superiority of ixekizumab was also demonstrated in terms of structural damage progression inhibition (gated secondary endpoint) in bDMARD naive patients only.
- No studies have compared TALTZ to a TNFi, even though this comparison was feasible. However, comparison to secukinumab, another anti-IL 17A substance, was not feasible given concomitant development in this indication.
- No new safety signals have been identified in this indication compared to the psoriasis treatment indication. Long-term safety data remains limited.

Special prescribing conditions

- Medicinal product subject to initial annual hospital prescription.
- Initial prescription and renewal restricted to specialists in dermatology, internal medicine and rheumatology.

Benefit of the medicinal product

- For the treatment of psoriatic arthritis, the actual clinical benefit* of TALTZ is moderate.
- TALTZ does not provide any clinical added value** (CAV V) in the treatment strategy of active psoriatic arthritis in adult patients having had an insufficient response or intolerance to one or more DMARD.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee opinion of 4 April 2018 (CT-16854) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.
** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.