HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

16 SEPTEMBER 2020

The legally binding text is the original French opinion version

ixekizumab

TALTZ 80 mg solution for injection in pre-filled syringe and pen

New indications

Key points

Favourable opinion for reimbursement in the treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation and active ankylosing spondylitis in adults who have responded inadequately to non-steroidal anti-inflammatory drugs (NSAIDs).

What therapeutic improvement ?

No therapeutic improvement compared to TNF inhibitors.

Role in the care pathway ?

The joint objectives of treatment in patients with axial spondyloarthritis (axSpA) are to control symptoms (inflammation, pain and spinal stiffness) and prevent structural damage in order to preserve or improve the functional capacities, autonomy, social participation and quality of life of patients and obtain clinical remission or, failing this, a low level of disease activity.

The first-line medicinal treatment of axSpA is based on the use of NSAIDs (prescription on demand, adapted to the patient and the evolution of symptoms, up to the maximum dose) as a symptomatic treatment. In the event of failure or an inadequate effect of an NSAID used at the maximum tolerated dose, a switch of NSAID can be performed.

Adjuvant therapies such as analgesics can be combined with the NSAIDs for residual pain but systemic or local corticosteroid therapy is not justified in axial forms. Conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) (e.g., methotrexate, leflunomide, sulfasalazine) only appear to be effective in forms with peripheral joint involvement refractory to symptomatic treatment. Their efficacy in purely axial forms has not been demonstrated.

As second-line treatment, biologic therapies (bDMARDs) should be considered in patients with active disease despite NSAIDs. However, in the absence of inflammation demonstrated by laboratory tests or MRI, these biologic therapies are not indicated in nr-axSpA. A total of five TNF inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab3) and two IL-17A inhibitors (ixekizumab, secukinumab) have an MA in active nr-axSpA in the event of failure, inadequate response, intolerance or contraindication to NSAIDs.

According to the guidelines published by the French Radiology Society (SFR), TNF inhibitors are preferred as first-line treatment given current experience; however the lack of direct comparative data between them means that it is not possible to determine a hierarchy. In the event of loss of response, primary inefficacy or intolerance to a first TNF inhibitor, a rotation to a second TNF inhibitor or a switch to an IL-17A inhibitor are alternatives deemed to be beneficial.

Role of the medicinal product in the care pathway

The role of TALTZ (ixekizumab) in the treatment of active non-radiographic axial spondyloarthritis and ankylosing spondylitis in patients who have responded inadequately to NSAIDs is as second-line therapy, following the failure of TNF inhibitors, given the absence of direct comparison of ixekizumab with TNF inhibitors enabling its role to be specified compared to the latter in first-line therapy (patients never having received a TNF inhibitor) and the need at this stage in the strategy.

The Committee highlights the fact that robust data are available for TALTZ (ixekizumab) specifically in patients with ankylosing spondylitis not having responded to TNF inhibitors (COAST-W study), in contrast with COSENTYX (secukinumab). In patients with non-radiographic axial spondyloarthritis, the available data do not enable a hierarchy between TALTZ (ixekizumab) and COSENTYX (secukinumab) to be determined.

Special recommendations

The Committee reiterates :

- that it is recommended to administer the first subcutaneous injection of this medicinal product in an appropriate healthcare setting given the rare but serious potential risk of systemic reactions to the injection, including anaphylactic reactions with subcutaneous ixekizumab, as with other bDMARDs,
- and that it is important to manage cardiovascular risk factors given the increased cardiovascular risk in chronic inflammatory arthritis.

COMMITTEE'S CONCLUSIONS

Clinical benefit

Non-radiographic axial spondyloarthritis

◗ Axial spondyloarthritis without radiographic signs is a chronic disease which, in its severe form with an inadequate response or intolerance to NSAIDs, is painful and affects spinal mobility and functional capacities.
◗ These medicinal products are symptomatic disease-modifying treatments.
◗ Considering a size effect versus placebo deemed to be modest, the efficacy/adverse effects ratio of TALTZ (ixekizumab) is modest.
◗ There are therapeutic alternatives, represented, in particular, by TNF inhibitors (adalimumab, certolizumab pegol, etanercept and golimumab).
◗ In the treatment of patients with active non-radiographic axial spondyloarthritis who have responded inadequately to NSAIDs, TALTZ (ixekizumab) is a second-line treatment to be used following the failure of TNF inhibitors (see paragraph 09 of this opinion).

Public health impact

Considering :

- the impact of active non-radiographic axial spondyloarthritis on the quality of life and functional capacities of patients, in particular in those in whom NSAIDs have failed,
- its prevalence,
- the medical need partially met by TNF inhibitors,
- demonstration of the superiority of ixekizumab compared to placebo in terms of disease activity, functional capacities and quality of life in a randomised, double-blind, placebo-controlled study conducted in 303 biological treatment-naive adult patients with active non-radiographic axial spondyloarthritis who have responded inadequately to NSAIDs, but with a modest effect size,
- the lack of elements supporting the absence of a deterioration in the care and/or life pathway in the absence of comparative data versus TNF inhibitors,
- the lack of any demonstrated impact on the organisation of care (hospitalisation, AE, etc.),
- the partial response to the identified medical need,

TALTZ (ixekizumab) is unlikely to have an additional impact on public health in the treatment of non-radiographic axial spondyloarthritis.

Considering all these elements, the Committee deems that the clinical benefit of TALTZ (ixekizumab) is moderate in the treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation in adults who have responded inadequately to NSAIDs.

Ankylosing spondylitis (radiographic axial spondyloarthritis)

◗ Ankylosing spondylitis is a chronic disease which, in its severe form with an inadequate response or intolerance to NSAIDs, is painful and affects spinal mobility and functional capacities.
◗ These medicinal products are symptomatic disease-modifying treatments.
◗ Based on available data, the efficacy/adverse effects ratio of TALTZ (ixekizumab) is high.
◗ There are therapeutic alternatives in this indication represented, in particular, by TNF inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab) and another IL 17 inhibitor, COSENTYX (secukinumab).
◗ In the treatment of patients with active radiographic axial spondyloarthritis who have responded inadequately to NSAIDs,TALTZ (ixekizumab) is a second-line treatment to be used following the failure of TNF inhibitors and preferentially to COSENTYX (secukinumab) (see paragraph 09 of this opinion).

Public health impact

Considering :

- the impact of active ankylosing spondylitis on the quality of life and functional capacities of patients, in particular in those in whom NSAIDs have failed,
- its prevalence,
- the medical need partially met by TNF inhibitors and COSENTYX (secukinumab),
- demonstration of the superiority of secukinumab compared to placebo in terms of disease activity, functional capacities and quality of life in two randomised, double-blind, placebo-controlled studies conducted in 341 biological treatment-naive adult patients with active ankylosing spondylitis having responded inadequately to NSAIDs, and in 316 adult patients with active ankylosing spondylitis having responded inadequately to NSAIDs and at least one TNF,
- the lack of elements supporting the absence of a deterioration in the care and/or life pathway in the absence of comparative data versus clinically relevant comparators, represented by TNF inhibitors,
- the lack of any demonstrated impact on the organisation of care (hospitalisation, AE, etc.),
- the partial response to the identified medical need,

TALTZ (ixekizumab) is unlikely to have an additional impact on public health in the treatment of ankylosing spondylitis.

Considering all these elements, the Committee deems that the clinical benefit of TALTZ (ixekizumab) is substantial in the treatment of active ankylosing spondylitis in adults who have responded inadequately to NSAIDs.

The Committee issues a 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 two new indications (active non-radiographic axial spondyloarthritis and active ankylosing spondylitis) and at the MA dosages.

Clinical Added Value

Considering :

- **the clinical benefit demonstrated versus placebo in the COAST-X, COAST-V and COAST-W studies in terms of ASAS40 responders (primary endpoint) and all the ranked secondary endpoints, in particular quality of life,**

but,

- **the modest extent of this benefit in patients with non-radiographic axial spondyloarthritis and**
- **the absence of comparison with TNF inhibitors in both indications, despite this being feasible,**

the Transparency Committee considers that TALTZ (ixekizumab) provides no clinical added value (CAV V) compared to TNF inhibitors in the treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation in adults who have responded inadequately to non-steroidal anti-inflammatory drugs (NSAIDs) and in active ankylosing spondylitis in adults who have responded inadequately to NSAIDs, in the same way as COSENTYX (secukinumab).