HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
19 MAY 2021

The legally binding text is the original French opinion version

guselkumab
TREMFYA 100 mg solution for injection in pre-filled syringe and in pre-filled pen

New indication

Key points

Favourable opinion for reimbursement, in the treatment, alone or in combination with methotrexate (MTX), of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

The objectives of treatment 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.

Nonsteroidal anti-inflammatories (NSAIDs) (up to the maximum authorised dose) are the reference first-line treatment. Analgesics can be used for residual pain, in conjunction with the other therapies. Local corticosteroid injections may be considered for joint pain and enthesitis.

As first-line therapy, conventional synthetic disease-modifying anti-rheumatic drugs or csDMARDs (methotrexate, leflunomide, sulfasalazine) should be considered in the event of peripheral arthritis refractory to symptomatic treatment. Conventional DMARDs have not demonstrated efficacy on isolated axial or enthesitic manifestations.

As second-line therapy, in the event of inadequate response, contraindication or intolerance to conventional disease-modifying anti-rheumatic drugs, biologic disease-modifying anti-rheumatic drugs (bDMARDs) or targeted synthetic therapies (tsDMARDs) may be considered.

The biologic therapies currently available include TNF inhibitors (adalimumab, etanercept, infliximab and certolizumab pegol) and interleukin inhibitors (an IL12/23 inhibitor, ustekinumab and two IL17 inhibitors, secukinumab and ixekizumab). These treatments have identical MAs from the second line of treatment, but the Committee recommends that they be used preferentially in the event of failure of TNF inhibitors (i.e., as third and later-line treatment).

In addition, two JAK inhibitors (tsDMARD) are available - tofacitinib (XELJANZ) and since recently upadacitinib (RINVOQ) - that also have an MA in the event of failure of at least one conventional DMARD (i.e., from the second line). Given the absence of clinical studies having directly compared tofacitinib with TNFα antagonists, the absence of superiority of upadacitinib compared to adalimumab and the greater experience with TNFα antagonists, the latter should be favoured as second-line disease-modifying therapy. In the absence of data versus interleukin inhibitors, the role of JAK inhibitors cannot be specified compared to these medicinal products.

In patients with non-severe, not very active forms, having responded inadequately to at least one csDMARD and in whom neither bDMARDs nor JAK inhibitors are appropriate, apremilast (OTEZLA), a PDE4 inhibitor, may be considered.

Role of the medicinal product in the care pathway

TREMFYA (guselkumab), IL23 inhibitor, is a second or third-line disease-modifying treatment for active psoriatic arthritis in adults following the failure of first-line treatment with a conventional disease-modifying treatment.
As with the other interleukin inhibitors, considering:
- **the absence of direct comparative data versus TNF inhibitors,**
- **experience of around 15 years with these medicinal products (marketing authorisation for etanercept dating back to 2003),**
- **demonstration of their efficacy on joint destruction,**

the Committee considers that anti-TNF inhibitors should be favoured first. TREMFYA (guselkumab) primarily has a role following the failure of at least one TNF inhibitor (i.e., as third and later-line therapy).

Special recommendations

Given the rare but serious potential risk of systemic reactions following injection, including anaphylactic reactions with subcutaneous guselkumab but also with other biologic disease-modifying drugs, the Transparency Committee recommends that the first subcutaneous injection of this drug be given in an appropriate care structure.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Psoriatic arthritis is a chronic disease, which can be serious and disabling in certain cases.

◗ The medicinal product TREMFYA 100 mg solution for injection in pre-filled syringe and pen (guselkumab) is a symptomatic disease-modifying antirheumatic drug.

◗ Considering:
- the demonstrated superiority of guselkumab compared to placebo on the ACR 20 response (primary endpoint), and the ACR 50 and ACR 70 responses (ranked secondary endpoints) with a moderate or modest effect size,
- a structural effect demonstrated *versus* placebo as a ranked secondary endpoint, only in patients with no prior biologic therapy and only for the four-weekly dosing regimen,
- the absence of comparison with an active treatment, in particular a TNF inhibitor, despite this being feasible,
- a safety profile consistent with the known profile in plaque psoriasis, marked primarily by infections, but also given a specific risk of frequent increases in transaminases in patients treated for psoriatic arthritis, and long-term immunogenic and carcinogenic risks that have not been evaluated,

the efficacy/adverse effects ratio of TREMFYA 100 mg (guselkumab) is moderate.
Additional efficacy data *versus* an active comparator, in particular a TNF inhibitor, and long-term safety data are required to assess the benefit of TREMFYA 100 mg (guselkumab) in the indication extension to psoriatic arthritis.

◗ There are numerous therapeutic alternatives, in particular TNF inhibitors, which have demonstrated an efficacy on joint destruction, in some cases with 15 years of experience of their use (see section 05 of this opinion).

◗ The Committee considers that in the event of failure of a conventional disease-modifying drug, TNF inhibitors should be favoured first considering experience with these medicinal products in terms of efficacy and safety. As is the case with other interleukin inhibitors, the role of TREMFYA 100 mg (guselkumab) is primarily following the failure of at least one TNF inhibitor (see section 08 of this opinion).

Public health impact

Considering:
- the seriousness of the disease and its disabling nature in severe forms,
- the low prevalence of forms with previous failure (inadequate response, intolerance or contraindication) to one or more disease-modifying treatments,
- the partially met medical need due to failures and intolerance to available treatments and resistance phenomena,
- the partial response to the partially met identified need due to a moderate or modest impact on morbidity and quality of life (demonstration based on the HAQ-DI functional disability score),
- the lack of additional demonstrated impact compared to the available medicinal products in the absence of direct comparative data *versus* these medicinal products, particularly TNF inhibitors,
- the lack of expected additional impact on the patient's care and/or life pathway,

TREMFYA 100 mg (guselkumab) is unlikely to have an additional impact on public health in the treatment of psoriatic arthritis in adults.

Considering all these elements, the Committee deems that the clinical benefit of TREMFYA 100 mg (guselkumab) solution for injection in pre-filled syringe and pen is moderate in the new MA indication.

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 new indication and at the MA dosages.

- **Recommended reimbursement rate: 65%**

Clinical Added Value

Considering:
- **the demonstrated superiority of guselkumab compared to placebo on the ACR 20 response (primary endpoint), and the ACR 50 and ACR 70 responses (ranked secondary endpoints) with a moderate or modest effect size,**
- **a structural effect demonstrated *versus* placebo as a ranked secondary endpoint, only in patients with no prior biologic therapy and only for the four-weekly dosing regimen,**
- **a safety profile consistent with the known profile in plaque psoriasis, marked primarily by infections, but also given a specific risk of frequent increases in transaminases in patients treated for psoriatic arthritis, and long-term immunogenic and carcinogenic risks that have not been evaluated,**
- **the absence of comparison with an active treatment, in particular a TNF inhibitor, despite this being feasible,**

the Transparency Committee considers that TREMFYA 100 mg (guselkumab) solution for injection in pre-filled syringe and pen provides no clinical added value (CAV V) in the care pathway for the treatment of active psoriatic arthritis in adults who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs).