HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
20 APRIL 2022

The legally binding text is the original French opinion version

tofacitinib
XELJANZ 5 mg tablets
XELJANZ 1 mg/ml solution for injection in vial

Inclusion (oral solution) and new indication (tablet)

Key points

Favourable opinion for reimbursement in the treatment of active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis (PsA) in patients 2 years of age and older, who have responded inadequately to previous therapy with disease modifying antirheumatic drugs (DMARDs).

Tofacitinib can be given in combination with methotrexate (MTX) or as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

The aim of JIA treatment is to combat inflammation, relieve pain and stiffness and to prevent or slow joint damage. Management is within a specialised setting and involves immediate-acting symptomatic treatments (NSAIDs, corticosteroids) as well as disease modifying antirheumatic drugs, which may be conventional (csDMARDs), such as methotrexate, which is the most widely used, or leflunomide (off-label), or biologic (bDMARDs), particularly TNF alpha inhibitors, depending on the form of JIA.

Polyarticular juvenile idiopathic arthritis with or without rheumatoid factor
The biologic therapies with an MA in pJIA following the failure of these csDMARDs are as follows:
- two TNF inhibitors, in IV form: ENBREL (etanercept) and HUMIRA (adalimumab)
- an IL-6 inhibitor: ROACTEMRA (tocilizumab), SC and IV form.
- a T lymphocyte co-stimulation inhibitor, ORENCIA (abatacept), IV and SC form.

It should be noted that SIMPONI (golimumab) also has an MA but is not funded in France in this indication.

Juvenile oligoarthritis
Two biologic therapies have an MA in juvenile extended oligoarthritis from the age of 2 years in patients who have had an inadequate response to, or who have proved intolerant of, methotrexate: ENBREL (etanercept), TNF inhibitor, and ROACTEMRA (tocilizumab), an IL-6 inhibitor.

Juvenile psoriatic arthritis
ENBREL (etanercept) is the only biologic therapy with an MA in this indication when the response to a csDMARD has been inadequate, from the age of 12 years.

Role of XELJANZ (tofacitinib) in the therapeutic strategy:
XELJANZ (tofacitinib), a JAK 1 and 3 inhibitor, is a disease-modifying anti-rheumatic drug for polyarticular juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) in patients 2 years of age and older, who have responded inadequately to previous therapy with DMARDs.
However, considering the lack of direct comparative data versus biologic therapy (in particular TNF inhibitors), despite this being feasible, and the greater experience with this class of medicinal products, the Committee considers that the role of XELJANZ (tofacitinib) is primarily following the failure of at least one biologic therapy, in particular a TNF inhibitor (i.e. in third and later-line treatment).

Special recommendations

Due to the risk of infections as a result of this treatment, the Committee recommends that patients ensure their vaccinations are up to date before the initiation of treatment, including human papillomavirus (HPV) vaccination where this is recommended.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Juvenile idiopathic arthritis (JIA) is a serious and debilitating chronic disease.

◗ The proprietary medicinal product XELJANZ (tofactinib) is a symptomatic medicinal product.

◗ Considering:
- The superiority of continuation of treatment with tofacitinib compared to discontinuation of tofacitinib (placebo group), demonstrated in the A3921104 study in patients who had already achieved a JIA ACR30 response after an 18-week run-in phase with tofacitinib in terms of occurrence of disease flare (primary endpoint), as well as their JIA ACR 30, 50 and 70 responses, and quality of life with the CHAQ-DI response (ranked endpoints).
- the absence of direct comparison with an active treatment, in particular a TNF inhibitor, despite this being feasible;
- a safety profile consistent with the known profile in adults,

the efficacy/adverse effects ratio of XELJANZ (tofacitinib) is high.

◗ There are therapeutic alternatives, in particular TNF inhibitors, which have demonstrated an efficacy, with greater experience of their use (see section 05 of this opinion)

◗ the Committee considers that the role of XELJANZ (tofacitinib) is primarily following the failure of at least one biologic therapy, in particular a TNF inhibitor (i.e. in third and later-line treatment) (cf. section 09 of this opinion)

Public health benefit

Considering:
- the seriousness of the disease and its disabling nature in severe forms, and its low prevalence, the partially met medical need due to failures and intolerance to available treatments and resistance phenomena,
- the absence of any demonstrated additional impact on morbidity or on quality of life compared to the available medicinal products due to a lack of direct comparative data versus these medicinal products, in particular TNF inhibitors, but also the partial response to the identified partially met need treatment due to resistance phenomena and/or the safety associated with these medicinal products,
- the lack of expected additional impact on the patient's care and/or life pathway,

XELJANZ (tofacitinib) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of XELJANZ (tofacitinib) is substantial 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 indication and at the marketing authorisation dosages.

◗ **Recommended reimbursement rate: 65%**

Clinical Added Value

In the absence of direct comparative data versus the other biologic medicinal products available, the Transparency Committee considers that XELJANZ (tofacitinib) provides no clinical added value (CAV V) in the care pathway for the treatment of active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis (PsA) in patients 2 years of age and older, who have responded inadequately to previous therapy with DMARDs.