HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
29 JUNE 2022

The legally binding text is the original French opinion version

ozanimod
ZEPOSIA 0.23 mg + 0.46 mg hard capsules
ZEPOSIA 0.92 mg hard capsules

New indication

Key points

Unfavourable opinion for reimbursement in the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.

Role in the care pathway?

The objectives of medicinal treatment are first to induce remission and then to maintain corticosteroid-free remission and improve quality of life.

The choice of treatment is governed, in particular, by the severity of the disease and the extent of colon damage. As second-line treatment of moderately to severely active UC in adult patients who have had an inadequate response to the conventional treatment, or for whom this treatment is contraindicated or poorly tolerated, TNF inhibitors (infliximab, adalimumab and golimumab) are the reference treatment. As second-line treatment, ENTYVIO (vedolizumab) represents an alternative to TNF inhibitors. However, a TNF inhibitor should be preferred to vedolizumab in two specific clinical situations:

- in the event of extra-intestinal manifestations (rheumatic, cutaneous and ocular manifestations, in particular), given the local action mechanism of vedolizumab;

- with infliximab being the recommended biologic therapy in the event of severe acute colitis (expert opinion).

As third-line treatment, in addition to the above treatments not yet used, the alternatives are a JAK inhibitor, tofacitinib (XELJANZ) and an IL-12/23 inhibitor, ustekinumab (STELARA). However, in patients over 65 years of age, smokers or former smokers, patients with other cardiovascular risk factors and patients with other cancer risk factors, tofacitinib should only be used if no other appropriate therapeutic alternative is available. “In the completed clinical trial (A3921133) in patients with rheumatoid arthritis (RA) aged 50 years or over and with at least one additional cardiovascular risk factor, an increase in the incidence of myocardial infarction was observed in comparison with TNF-alpha inhibitors. The trial also demonstrated an increase in the incidence of malignant tumours, excluding non-melanoma skin malignancies (NMSM), in particular lung cancer and lymphoma, with tofacitinib compared to TNF-alpha inhibitors. Prescribers should discuss the risks associated with the use of XELJANZ with their patients, in particular myocardial infarction, lung cancer and lymphoma.” (See Letter to healthcare professionals, 07/07/2021). The SPC, which was updated at the end of 2021, specifies that in ulcerative colitis (UC) “in the UC ongoing extension trial, cases of PE and DVT have been observed in patients using tofacitinib 10 mg twice daily and with underlying VTE risk factor(s).”

Role of the medicinal product in the care pathway

In moderately to severely active UC in adult patients who have had an inadequate response, lost response, or were intolerant to conventional therapy, considering the absence of clinical data enabling the therapeutic benefit of ozanimod (ZEPOSIA) to be determined compared to:

- firstly, TNFα inhibitors (infliximab, adalimumab and golimumab) and vedolizumab (ENTYVIO),

- and secondly ustekinumab (STELARA) and tofacitinib (XELJANZ),

and, taking into account the modest effect size determined in comparison with placebo in patients with a globally moderate form of UC, and the safety profile of ozanimod,

the Committee deems that the role of ozanimod (ZEPOSIA) in the care pathway has not been determined.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

In ulcerative colitis:

◗ Ulcerative colitis is a chronic inflammatory bowel disease (IBD) that results in severe chronic bloody diarrhoea, progressing in flare-ups. It leads to a marked deterioration in quality of life and exposes patients to serious complications: acute colitis, dysplasia and colon cancer.

◗ The proprietary medicinal product ZEPOSIA (ozanimod) is a symptomatic treatment of UC and a preventive treatment of recurrences.

◗ The efficacy/adverse effects ratio of ozanimod 1 mg/d in the treatment of moderately to severely active ulcerative colitis is inadequately established in the population of patients in whom conventional treatments and TNF inhibitors have failed, based on an exploratory subgroup analysis. In the population in the pivotal TRUENORTH study including both biologic treatment-naive and non-naive patients, ozanimod was more effective than placebo but with a modest effect size and in patients with a globally moderate form of UC.

◗ There are alternatives (see paragraph 05.)

◗ Considering the clinical data available, ozanimod has not demonstrated its role as either second-line therapy (following the failure of conventional treatments) or third-line therapy (following the failure of TNF inhibitors and vedolizumab).

Public health benefit

Considering:

- the seriousness and prevalence of ulcerative colitis, a serious and incapacitating chronic disease with high morbidity due to the frequency of acute flare-ups, its complications and recourse to surgery. It also causes a marked impairment in quality of life;
- the already partially met medical need, particularly in the third-line treatment of UC,
- the lack of response to the identified need in second and third-line treatment:
    - no expected additional impact on morbidity in comparison with placebo based on the results of the TRUENORTH study;
    - absence of demonstrated additional impact on morbidity in comparison with clinically relevant comparators;
    - the absence of elements capable of supporting an expected impact on the care and life pathway of patients in the absence of robust data on quality of life, colectomy and the absence of additional benefit in terms of corticosteroid-free remission and lasting remission in third-line treatment,

ZEPOSIA (ozanimod) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of ZEPOSIA (ozanimod) is insufficient in the MA indication.

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and at the MA dosages.