HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
19 MAY 2021

The legally binding text is the original French opinion version

adalimumab
HUMIRA 40 mg solution for injection in pre-filled syringe
HUMIRA 40 mg solution for injection in pre-filled pen
HUMIRA 80 mg solution for injection in pre-filled syringe
HUMIRA 80 mg solution for injection in pre-filled pen

New indication

Key points

Favourable opinion for reimbursement in the paediatric indication extension, i.e., the treatment of moderately to severely active ulcerative colitis in paediatric patients (from 6 years of age) who have had an inadequate response to conventional therapy including corticosteroids and/or 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

The objectives of the treatment of ulcerative colitis (UC) in children and adolescents are to induce and maintain clinical remission and improve quality of life (in particular to maintain schooling). As in adults, there is no curative treatment for ulcerative colitis (UC).

In paediatric patients from 6 years of age with severely active forms who have had an inadequate response to conventional therapy including corticosteroids and/or 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies, infliximab (REMICADE and its biosimilars) is the only TNF with an MA. It is administered by intravenous infusion. The alternatives in these patient are ciclosporin (off-label) and surgery for severe corticosteroid-resistant and corticosteroid-dependent forms. Ciclosporin is rapidly effective in corticosteroid-resistant patients, but its long-term safety is poor (nephrotoxicity, induced cancer risk), meaning that it cannot be considered as a long-term treatment. In practice, it is used for a short period (3 months) to induce remission pending the efficacy of another long-term treatment introduced simultaneously. Surgery is required in around 25 to 45% of patients due to an absence of improvement of symptoms or disease complications. The choice of surgery depends on age, how long the UC has been present, the degree of extension of the disease in the bowel, pregnancy plans, rectal status and risk factors for bowel cancer. In fact, total proctocolectomy and ileoanal anastomosis (IAA), with an ileal pouch, is a major surgical procedure that needs to be performed in 2 or 3 stages. Mortality is low (less than or equal to 1%) and morbidity high (30-40%: occlusions, pelvic sepsis, etc.). In addition, it significantly reduces female fertility.

Role of the medicinal product in the care pathway

HUMIRA (adalimumab) is a second-line option in the treatment of moderately to severely active ulcerative colitis in paediatric patients (from 6 years of age) who have had an inadequate response to conventional therapy including corticosteroids and/or 6-MP or AZA, or who are intolerant to or have medical contraindications for such therapies. It is an alternative to infliximab administered by the IV route, the other TNF inhibitor with an MA in this indication in paediatric patients. However, there is no comparative data available relative to the efficacy and safety of these two medicinal products.

The Committee highlights that treatment with HUMIRA (adalimumab) should be initiated and supervised by a qualified physician experienced in the diagnosis and treatment of UC. It reiterates that it is essential to ensure good treatment compliance.

Special recommendations

Given the risk of hypersensitivity reactions with adalimumab administered subcutaneously (see paragraph 4.4 of the SPC), 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

In UC in children from 6 years of age and in adolescents:

◗ Ulcerative colitis is an inflammatory bowel disease (IBD) affecting some or all of the mucosa of the colon, and generally that of the rectum, that progresses by flare-ups interspersed with remissions of variable duration. It leads to a marked deterioration in quality of life and exposes patients to a risk of serious complications: acute colitis, dysplasia and bowel cancer, in particular, with a risk that is two times higher in children than in adults. The treatment of UC in children is difficult due to its rarity, the difficulty of diagnosing it and manifestations that differ from those in adults, with potentially more aggressive forms.

◗ HUMIRA (adalimumab) is a symptomatic medicinal product.

◗ The efficacy/adverse effects ratio of adalimumab in UC in children is high.

◗ REMICADE and its biosimilars (infliximab) is an alternative to HUMIRA (adalimumab) in the treatment of severely active ulcerative colitis in children and adolescents (from 6 to 17 years of age) who have had an inadequate response to conventional therapy including corticosteroids and/or 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies. Ciclosporin may also be used off-label in severe forms. In moderately active forms of UC, there is no comparator with an MA in France.

◗ It is a second-line treatment, like REMICADR and its biosimilars (infliximab).

Public health impact

Considering:

- the seriousness of paediatric UC related to the fact that it can have a significant physical and psychological impact, and its low prevalence,
- the partially met medical need,
- the inadequately demonstrated response to the identified need given the methodological limitations of the available study (see 8.4 summary and discussion) and the absence of comparison with infliximab, meaning that the additional impact in terms of morbidity and quality of life cannot be assessed,
- an impact on the care and/or life pathway that remains to be established: it is possible that HUMIRA, due to its SC administration conditions, could be liable to reduce recourse to the healthcare system and hence improve the quality of life of treated patients compared to patients on REMICADE. However, no data is available that can confirm this,

HUMIRA (adalimumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of HUMIRA (adalimumab) is substantial in the MA indication extension in the treatment of UC in paediatric patients from 6 years of age.

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 low quality of research evidence for the clinical efficacy of adalimumab (HUMIRA) in this indication based on the results of a non-comparative study (following amendment of the protocol) and on comparison with an external placebo, the results of which cannot be interpreted,**
- **the absence of comparative data versus infliximab (REMICADE and its biosimilars), another TNF inhibitor with an MA, despite this comparison being possible,**

but taking into account:

- **the potential benefit of having access to a subcutaneous form in children and,**
- **the established efficacy and safety profile of adalimumab in adults and in other paediatric indications, particularly Crohn's disease,**

the Transparency Committee considers that HUMIRA (adalimumab) provides no clinical added value (CAV V) in the strategy for the treatment of moderately to severely active ulcerative colitis in paediatric patients (from 6 years of age) who have had an inadequate response to conventional therapy including corticosteroids and/or azathioprine (AZA) or 6-mercaptopurine (6-MP), or who are intolerant to or have medical contraindications for such therapies.