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GASTROENTEROLOGY
New medicinal product
January 2015.

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ENTYVIO (vedolizumab), anti-α4β7 integrin

In patients who failed corticosteroids, immunomodulators and TNFα antagonist therapy: minor improvement in the treatment of ulcerative colitis and no clinical benefit demonstrated in the treatment of Crohn's disease.

In TNFα antagonist naïve patients, reimbursement is not recommended due to an insufficient actual benefit.

Main points

- ENTYVIO is a biologic treatment with a Marketing Authorisation for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) and Crohn's disease (CD) who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist .
- In TNFα antagonist naïve patients, due to lack of Head-to-Head comparison data betweenvedolizumab and TNFα antagonist , the role of ENTYVIO relative to TNFα antagonist cannot be determined.
- In patients with immunomodulators failure and TNFα antagonist failure, there is no treatment alternative with Marketing Authorisation.
- Its efficacy is well established in UC.
- In CD, at theinduction phase, the efficacy data are contrasted with negative results versus placebo.

Therapeutic use

In UC, treatment goal is to obtain a maintained corticosteroid-free clinical remission and with endoscopic and histological mucosal healing. Management relies on various lines of treatment with the combination of conventional topical or oral treatments: 5-aminosalicylates, corticosteroids and immunomodulators. After failure of or intolerance to these conventional treatments, TNFα antagonist agents are a drug treatment alternative to surgery. Cyclosporine is sometimes used (off-label) as a last resort before surgery.

In CD, treatment goal is to obtain clinical remission. There is no curative medical treatment. Management relies on 5-aminosalicylates, corticosteroids and immunomodulators. The use of TNF α antagonists (infliximab and adalimumab) is reserved for treatment failures or intolerance to immunomodulators. Surgery is necessary as a last resort in some patients but does not cure the disease.

In these two conditions, no medicinal product specifically has Marketing Authorisation in patients who failed TNF α antagonists. Various treatment options are implemented in clinical practice: increasing dose or frequency of administration of TNF α antagonists or combination with immunomodulators, switch to a second TNFα antagonist (three TNFα antagonists agents are available in the treatment of UC and two in CD), or resumption of the first TNFα antagonist administered in case of failure of the second TNFα antagonist. When these measures do not provide a treatment response satisfaction, patients have arrived at the end of their therapeutic options.

Role of the medicinal product in the therapeutic strategy

In patients who have never received a TNFα antagonist, due to lack of Head-to-Head comparison data between vedolizumab and TNFα antagonist, the role of ENTYVIO relative to TNFα antagonists cannot be determined.
In patients who failed TNFα antagonists in UC and CD, its role is positioned after the failure of current therapeutic strategies, including immunomodulators (such as azathioprine and 6-mercaptopurine), corticosteroids and TNFα antagonists.

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Clinical data

- Efficacy in UC

One study showed the superiority of vedolizumab over placebo in terms of induction of clinical response (absolute difference of 21.7%, p <0.0001) and clinical remission at week 6 (absolute difference of 11.5%, p = 0.0009), along with clinical remission (absolute difference of 26.1% with the every 8 weeks regimen, p<0.0001) and maintenance of clinical response at week 52 (absolute difference of 32.8% with the every 8 weeks regimen, p<0.0001). The results of the exploratory analyses pre specified in the protocol suggested a demonstration of superiority relative to placebo in the primary endpoints of clinical response at week 6 and clinical remission at week 52, in both naive patients and failure TNFα antagonist patients .
No head-to-head comparison data versusTNFα antagonist are available.

- Efficacy in Crohn's disease:

In one study, the superiority of vedolizumab relative to placebo was demonstrated in terms of clinical remission at week 6 (co-primary endpoint) with a modest absolute difference of 7.8% [1.2; 14.3] p = 0.02, and questionable clinical relevance which was lower than what was expected according to the study protocol (16%). Its superiority to placebo was not demonstrated in the second co-primary endpoint, clinical response CDAI-100. The exploratory analyses pre specified in the protocol did not show a difference versus placebo in treatment-naive patients or in TNFα antagonist failure patients w. The superiority of vedolizumab to placebo in terms of clinical remission at week 52 was demonstrated (absolute difference versus placebo of 17.4% with the every 8 weeks regimen, p = 0.0007).
In a complementary study of short duration (10 weeks), for induction treatment of patients who predominantly failed TNFα antagonists (76%), no difference was found between vedolizumab and placebo in the primary endpoint (clinical remission at week 6).

- Analysis of available safety data has not revealed any particular signal. No cases of PML were reported

Special prescribing conditions

Medicinal product reserved for hospital use
Prescription restricted to specialists in gastroenterology, hepatology or internal medicine.

Benefit of the medicinal product

- The actual benefit* of ENTYVIO is:
  - insufficient in TNFα antagonist -naive patients in both UC and CD.
  - in patients who have failed treatment (inadequate response with, lost response to or intolerance to corticosteroids, immunomodulators and TNFα antagonists, substantial in the treatment of UC and moderate in the treatment of CD.
- ENTYVIO provides a minor clinical added value** (CAV IV) in adult patients with moderately to severely active UC who failed treatment (inadequate response with, lost response to or intolerance to) corticosteroids, immunomodulators and TNFα antagonists.
- ENTYVIO does not provide a clinical added value** (CAV V) in adult patients with moderately to severely active CD who failed treatment (inadequate response with, lost response to or intolerance to) corticosteroids, immunomodulators and TNFα antagonists.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 07 January 2014 (CT-13782) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.
** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.

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