BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

STELARA (ustekinumab), immunosuppressive interleukin inhibitor

In the treatment of Crohn’s disease:
Insufficient clinical benefit in patients naive to TNF inhibitors
Minor clinical added value in patients who have failed a conventional therapy (corticosteroids or immunosuppressants) and at least one TNF inhibitor.

Main points

- STELARA now has marketing authorisation in the treatment of adult patients with moderately to severely active Crohn’s disease (CD) who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNFα antagonist or have medical contraindications to such therapies.

- It should be restricted to patients who have failed a conventional therapy (corticosteroids or immunosuppressants) and at least one TNF inhibitor, taking into consideration its demonstrated efficacy and the identified medical need in this population.

- In patients who are naive to TNF inhibitors, its role in relation to TNF inhibitors cannot be determined because there was no direct comparison between ustekinumab and this class of medicines, although this was feasible.

- A new presentation in the form of 130 mg concentrate for solution for intravenous infusion is available only for induction treatment of CD.

Pre-existing indications*

STELARA already has marketing authorisation in the treatment of psoriasis in adults and adolescents and in psoriatic arthritis.

Therapeutic use

There is no curative medical treatment, but the current treatments are increasingly able to suspend symptoms, obtaining lasting disease control and a satisfactory quality of life. Management involves aminosalicylates such as mesalazine or sulfasalazine, corticosteroids, and immunosuppressants including azathioprine, 6-mercaptopurine and methotrexate (MTX). Two TNF inhibitors (infliximab and adalimumab) have marketing authorisation in the moderate to severe form of CD and are reserved for cases where treatment with corticosteroids and immunosuppressants has failed or is not tolerated. If there is no primary response, insufficient primary response, loss of response (breakthrough) or intolerance to treatment with TNF inhibitors, various therapeutic approaches can be taken to optimise treatment, such as:

- increasing the doses or frequency of administration of the TNF inhibitor, or adding in immunosuppressants;
- using a second TNF inhibitor;
- switching back to the 1st TNF inhibitor administered if the 2nd TNF inhibitor fails;
- using a biologic with a target other than TNF, such as vedolizumab (ENTYVIO), an α4β7 integrin inhibitor.

Surgery is necessary as a last resort in some patients but does not cure the disease.

* This summary does not cover these indications.

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Role of the medicinal product in the therapeutic strategy

STELARA and ENTYVIO (vedolizumab) have the same role in the 3rd-line management of Crohn’s disease, after failure of a conventional therapy including an immunosuppressant (such as azathioprine or 6-mercaptopurine) or a corticosteroid and at least one TNF inhibitor (adalimumab or infliximab).

In patients who are naive to TNF inhibitors, bearing in mind the relatively long experience with TNF inhibitors in this indication (about 20 years) and their proven efficacy in terms of inducing and maintaining clinical remission, the Committee considers that when treatment with a biologic drug is envisaged, TNF inhibitors should be preferred. In the absence of any direct comparison between ustekinumab and this class of medicines, its role in relation to TNF inhibitors in TNF inhibitor-naive patients cannot be determined.

Clinical data

In two studies (one in patients who had failed at least one TNF inhibitor and one in patients who had failed a standard treatment including corticosteroids or immunosuppressants), the superiority of induction treatment with ustekinumab to placebo was demonstrated in terms of clinical response at 6 weeks (the primary endpoint). This was defined as a reduction ≥ 100 points in CDAI score from inclusion or a CDAI score < 150 for patients whose initial CDAI score was ≥ 220 and ≤ 248. In a 3rd study evaluating maintenance treatment, ustekinumab was shown to be superior to placebo in terms of maintaining clinical remission at 44 weeks (the primary endpoint): there was a 17.2% improvement over placebo with treatment every 8 weeks and 13% with treatment every 12 weeks.

The comparison with mere placebo is regrettable in light of the current management strategy, particularly as adalimumab and infliximab had marketing authorisation when these studies were conducted. A comparison with a TNF inhibitor is needed for the role of ustekinumab to be determined in relation to these medicines.

No specific safety signals were detected from analysis of the available safety data, with respect to the main risks already identified since STELARA was marketed in other indications.

Special prescribing conditions

STELARA 45 mg and 90 mg solution for injection
- Medicine for initial hospital prescription.
- Prescription restricted to specialists in dermatology, rheumatology, internal medicine or gastroenterology and hepatology.
- Exception drug status

STELARA 130 mg
- Medicinal product reserved for hospital use
- Prescription restricted to specialists in gastroenterology, hepatology or internal medicine.

Benefit of the medicinal product

- The actual clinical benefit* of STELARA is insufficient in patients who are naive to TNF inhibitors and substantial in patients who have failed a conventional treatment (corticosteroids or immunosuppressants) (insufficient response, loss of response or intolerance) and at least one TNF inhibitor or who have contraindications to these treatments.
- STELARA provides minor clinical added value** (CAV IV) in the patients defined above with a substantial actual clinical benefit.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

This document was created on the basis of the Transparency Committee Opinion of 08 March 2017 (CT-15850) and is available at www.has-sante.fr

* The actual clinical benefit (ACB) 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 ACB, 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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