HAUTE AUTORITÉ DE SANTÉ

RHEUMATOLOGY – GASTROENTEROLOGY – DERMATOLOGY
New medicinal product
July 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

INFLECTRA, REMSIMA, FLIXABI biosimilars of infliximab, TNF inhibitor

No clinical benefit demonstrated relative to REMICADE (reference biotherapy).

Main points

- INFLECTRA, REMSIMA and FLIXABI are biosimilars of REMICADE. They have the same indications as REMICADE in rheumatology (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis), gastroenterology (ulcerative colitis and Crohn's disease) and dermatology (psoriasis). The have the same strenght, the same pharmaceutical form, the same administration route and the same composition of excipients as REMICADE.
- The bioequivalence of these biosimilars to REMICADE has been demonstrated in a pharmacokinetic study performed in patients with ankylosing spondylitis (INFLECTRA and REMSIMA) and in healthy volunteers for FLIXABI. Their clinical equivalence was assessed in patients with rheumatoid arthritis.

Therapeutic use

- FLIXABI, INFLECTRA and REMSIMA, as biosimilar medicinal products of REMICADE, have the same role as REMICADE in the therapeutic strategy in each of its indications.
- In order to improve traceability of biologics, the brand name and batch number of the product administered must be clearly recorded in the patient record.

Clinical data

- In a phase I study, the pharmacokinetic equivalence of the infliximab biosimilar versus to the standard infliximab biotherapy (REMICADE) was demonstrated in 250 patients with ankylosing spondylitis for INFLECTRA and REMSIMA, and in 159 healthy volunteers for FLIXABI to REMICADE.
- In a phase III study, controlled, randomised, double-blind study conducted in 606 patients with active rheumatoid arthritis despite methotrexate treatment for INFLECTRA and REMSIMA and 584 patients for FLIXABI, the therapeutic equivalence was demonstrated by measuring the difference observed between the biosimilar and REMICADE in terms of ACR20 responders at week 30. This is included in the predefined equivalence margin [-15; +15]. The data at 54 weeks suggest a maintained efficacy. Overall, the nature of the reported adverse event was comparable between biosimilars and REMICADE and met expected type according to the REMICADE SPC.
- A clinical study is in progress in the indication in Crohn's disease for INFLECTRA and REMSIMA, and an observation study is planned for FLIXABI in Crohn's disease and spondylitis. Patient monitoring registries are planned as part of the risk management plan for these three medicinal products.

Special prescribing conditions

- Reserved for hospital use.

Benefit of the medicinal product

- The actual benefit* of these biosimilars (INFLECTRA, REMSIMA and FLIXABI) is substantial in all of the particulars of the Marketing Authorisation in the following indications:
  - rheumatoid arthritis
  - psoriatic arthritis
  - ankylosing spondylitis
  - Crohn's disease in adults and children
  - ulcerative colitis in adults and children

In the psoriasis indication:
As for REMICADE, and the other biologics, the actual clinical benefit of INFLECTRA, REMSIMA and FLIXABI is substantial in the treatment of severe chronic plaque psoriasis in adults, defined by:
- failure (i.e., non-responder patients, patients with contraindication or intolerance) with at least two treatments including nonbiologic systemic treatments and (MTX, cyclosporine and acitretin) and phototherapy; and
- an extensive body area affected and/or substantial psychosocial impact.
For other patients who do not meet these treatment criteria, the actual benefit is insufficient.

- As a biosimilar medicines, INFLECTRA, REMSIMA and FLIXABI do not provide any clinical added value ** relative to the standard biotherapy, REMICADE (IACB V, non-existent).

- 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 21 January 2015 (CT-13697, CT - 13741 and of 29 June 2016 (CT 15264) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. 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".