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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ROACTEMRA (tocilizumab), interleukin 6 receptor inhibitor

Insufficient actual benefit in the treatment of rheumatoid arthritis in adults not previously treated with methotrexate.

Main points

- ROACTEMRA, in combination with methotrexate (MTX), now has Marketing Authorisation in the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with MTX. In addition, it can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.
- In combination with MTX, it reduces the rate of progression of joint damage as measured by X-ray and improves physical function.
- It is preferable to give patients MTX as first-line therapy, with a treatment adjustment strategy that includes introducing a biopharmaceutical where applicable (after failure of MTX).
- ROACTEMRA has no role in the treatment strategy for patients who have not been previously treated with a conventional disease-modifying drug, in particular MTX.

Pre-existing indications

- ROACTEMRA already had Marketing Authorisation, in combination, in the treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists.
  It also has Marketing Authorisation in the treatment of systemic (or polyarticular) juvenile idiopathic arthritis.
- This summary does not cover these indications.

Therapeutic use

- As first-line treatment, MTX is the standard disease-modifying drug for RA. If there are contraindications or intolerance to MTX, leflunomide or sulfasalazine may be considered.
- For second and subsequent lines of treatments, in patients who have responded insufficiently or are intolerant to methotrexate:
  - If there are no poor prognostic factors, a combination of synthetic DMARDs (methotrexate/sulfasalazine/hydroxychloroquine) or indeed changing to a different synthetic DMARD (leflunomide, sulfasalazine) may be offered. If these fail (or are contraindicated), a biopharmaceutical should be considered.
  - If there are poor prognostic factors (especially if there is structural damage), adding a biopharmaceutical may be offered (a TNF antagonist, abatacept or tocilizumab and in some circumstances rituximab).
    Unlike tocilizumab, TNF antagonists, rituximab and abatacept as monotherapy have not been shown to be superior to methotrexate alone.
- **Role of the medicinal product in the therapeutic strategy**
  ROACTEMRA has no role in the treatment strategy for patients who have not been previously treated with MTX. The only exceptional situation in which prescribing a biopharmaceutical such as tocilizumab as monotherapy may be considered for first-line treatment would be a contraindication to all conventional DMARDs.

Clinical data

- A study evaluated tocilizumab (TCZ) 8 mg/kg in combination with methotrexate or as monotherapy versus MTX alone in 1,162 patients with moderate to severe, active and progressive RA with a mean duration of between 0.4 and 0.5 years. About 80% of patients had not had MTX before inclusion.
  The primary efficacy endpoint was the proportion of patients in remission (DAS28 < 2.6) at 24 weeks. The combination of tocilizumab 8 mg/kg + MTX was shown to be superior to MTX alone (TCZ 8 mg/kg + MTX: 44.8% versus MTX: 15.0%, p < 0.0001) as was tocilizumab 8 mg/kg as monotherapy (TCZ 8 mg/kg: 38.7% versus MTX: 15.0% (p < 0.0001).
- The safety profile of ROACTEMRA, used as monotherapy or in combination with MTX, appeared comparable with the existing known safety profile of the product.

Special prescribing conditions

- Medicinal product reserved for hospital use
- Prescription restricted to specialists in rheumatology or internal medicine
- Medicinal product requiring special monitoring during treatment.

Benefit of the medicinal product

- The actual benefit* of ROACTEMRA is insufficient to justify reimbursement by National Health Insurance.
- Does not recommend 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 16 December 2015 (CT-14490) and is available at **www.has-sante.fr**

[i] * 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".