BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

KEVZARA (sarilumab), interleukin 6 receptor inhibitor

Substantial actual benefit but no clinical benefit demonstrated in the treatment of rheumatoid arthritis after failure of one or more disease-modifying treatments

Main points

- KEVZARA, administered subcutaneously, has Marketing Authorisation in the treatment of rheumatoid arthritis (RA) after failure of one or more disease-modifying treatments.
- It is a second-line treatment after failure of conventional disease-modifying treatments such as methotrexate (MTX) or a third-line treatment (failure of a biological medicinal product) or beyond (failure of multiple conventional disease-modifying and/or biological treatments).
- Its superiority has been demonstrated in monotherapy compared with adalimumab in second-line (inadequate response or intolerance to MTX) treatment.
- KEVZARA has not been compared to available third-line alternatives, in particular the other anti-IL6 (tocilizumab), abatacept or rituximab.

Therapeutic use

- Treatment of RA is based on the early prescription (earliness is a determining factor in the success of the treatment) of a disease-modifying treatment to induce clinical and laboratory remission. The standard conventional disease-modifying treatment remains MTX. Different disease-modifying treatments need to be available because of the phenomena of treatment failure or intolerance, as well as the need in terms of galenic optimisation.
- **Role of the medicinal product in the therapeutic strategy**

  KEVZARA can be used after failure (inadequate response or intolerance) of one or more disease-modifying treatments, in second-line treatment (after failure of conventional disease-modifying treatments such as MTX), in third-line treatment (failure of a biological medicinal product) or beyond (failure of multiple conventional disease-modifying treatments and/or biological medicinal products).

  It must preferably be used in combination with MTX. It can be used as monotherapy only in case of intolerance to MTX or when treatment with MTX is inappropriate.

  Considering the identified rare but serious risk of a systemic reaction to the injection, including anaphylactic reactions with subcutaneous sarilumab, but also with other biological disease-modifying treatments, it is recommended that the first subcutaneous injection of this medicinal product be performed at a suitable care facility.

Clinical data

- In one study conducted in 1,197 patients with RA who had an inadequate clinical response to MTX, the superiority of sarilumab at doses of 200 mg and 150 mg every 2 weeks in combination with MTX was demonstrated compared with placebo+MTX. The primary efficacy endpoints were ACR20 response rate at week 24, change in HAQ-DI (Health Assessment Questionnaire - Disability Index) from baseline to week 16 and change in mTSS (van der Heijde-modified Total Sharp Score) from baseline to week 52.
- In a second study conducted in 546 patients with RA who had an inadequate clinical response or intolerance to one or more anti-TNF agents, the superiority of sarilumab in combination with conventional disease-modifying treatments (MTX, sulfasalazine, leflunomide and hydroxychloroquine) was demonstrated compared with placebo + conventional disease-modifying treatments.

  The primary efficacy endpoints were ACR20 response rate at week 24 and change in HAQ-DI at week 12.

- In a third study conducted in 369 patients with moderate to severe active RA unable to receive treatment with MTX due to intolerance or inadequate response to MTX, the superiority of sarilumab 200 mg monotherapy compared with adalimumab 40 mg monotherapy was demonstrated in terms of reduced disease activity assessed by DAS 28 score.
- Sarilumab has primarily been associated with the occurrence of infections, neutropenia and thrombocytopenia, increased transaminases and lipids and injection site reactions. Some cases of gastrointestinal perforation have been reported.

Special prescribing conditions

- Medicinal product for initial hospital prescription
- Initial and repeat prescription restricted to specialists in rheumatology and internal medicine
- Medicinal product requiring special monitoring during treatment.

Benefit of the medicinal product

- The actual benefit* of KEVZARA is substantial.
- KEVZARA does not provide clinical added value** (CAV V) in the strategy for management of moderate to severe active rheumatoid arthritis in adult patients who have had an inadequate response, or intolerance, to one or more disease-modifying treatments.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinions of 22 November 2017 and 10 January 2018 (CT-16468) 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”.