HAUTE AUTORITÉ DE SANTÉ

RHEUMATOLOGY
New medicinal product
June 2017

**BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION**

# **OLUMIANT** (baricitinib), anti-JAK 1 and 2

**No clinical benefit demonstrated in the treatment of rheumatoid polyarthritis after failure of one or more disease-modifying treatments**

## Main points

- OLUMIANT has marketing authorisation in the treatment of rheumatoid polyarthritis (RP) 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 biotherapy) or beyond (failure of multiple conventional disease-modifying and/or biological treatments).
- Its superiority has been demonstrated in combination with MTX compared with adalimumab in combination with MTX in second-line (MTX failure). OLUMIANT has not been compared to available third-line alternatives (in particular tocilizumab, abatacept, rituximab).
- There are concerns in terms of long-term safety, in particular in relation to risks of infection and cardiovascular and carcinogenic risks.

## Therapeutic strategy

- Treatment of PR 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 methotrexate. 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 proprietary medicinal product in the therapeutic strategy**
  Considering, on one hand, the concerns in terms of safety (especially long-term) related to this new mechanism of action and, on the other hand, the more significant decline in biotherapies in terms of efficacy and safety, the Committee recommends that OLUMIANT be used preferably in third-line (namely, after failure of a biotherapy) or beyond. Preference must be given to the combination of MTX and monotherapy should be reserved for situations of intolerance to MTX or when continued treatment with MTX is inappropriate.

## Clinical data

- In one study, conducted in patients who failed MTX, the superiority (planned in the non-inferiority study protocol) of oral baricitinib 4 mg compared with adalimumab 40 mg in SC injection every 2 weeks both in combination with MTX was demonstrated in terms of ACR 20 response. The proportion of responders was 69.6% with baricitinib+MTX, 61.2% with adalimumab+MTX and 40.2% with placebo+MTX, i.e. an absolute difference for baricitinib-placebo of 29.4% [23.5; 35.4] and baricitinib-adalimumab of 8.5 [1.6; 15.3], $p \leq 0.001$ (per-protocol analysis). The superiority of baricitinib 4 mg/day compared with placebo on the radiographic score was also demonstrated. The data at 52 weeks are in favour of a maintained effect of the treatment.
- In a second study conducted in patients who failed conventional disease-modifying treatments (csDMARD), the superiority of baricitinib at dosages of 4 mg and 2 mg/day in combination with a csDMARD compared with placebo+csDMARD was evidenced in terms of ACR 20 response at 12 weeks. The proportion of ACR 20 responders was 61.7% with baricitinib 4 mg/day and 65.9% with baricitinib 2 mg/day compared with 39.5% with placebo, $p \leq 0.001$ (modified intention-to-treat analysis).
- In a third study conducted in patients who failed biological disease-modifying treatments (bDMARD), the superiority of baricitinib at dosages of 4 and 2 mg/day in combination with a csDMARD compared with

placebo+csDMARD was demonstrated in terms of the proportion of patients who obtained an ACR 20 response at 12 weeks: 55.4% with baricitinib 4 mg/day and 48.9% with baricitinib 2 mg/day compared with 27.3% with placebo, p ≤ 0.001 (modified intention-to-treat analysis).

- A fourth study with a 52-week duration was conducted outside of the marketing authorisation indication field, namely as first-line (DMARD-naïve patients), but made it possible to validate the use of baricitinib in monotherapy. In this study, the non-inferiority and the superiority of baricitinib 4 mg/day compared with methotrexate in monotherapy was demonstrated in the ACR 20 response at week 24. However, the efficacy of the monotherapy in terms of slowing radiographic progression (ranked secondary endpoint) was not demonstrated.
- There are concerns about the safety of baricitinib, especially long-term, in particular in relation to the potential carcinogenic and cardiovascular risks related to hyperlipidaemia.

## Special prescribing conditions

- Medicinal product for initial annual hospital prescription
- Initial prescription and renewal by rheumatology specialists only

## Benefit of the medicinal product

- The actual clinical benefit* of OLUMIANT is substantial.
- OLUMIANT does not provide any clinical added value** (CAV V) in the management of moderate to severe active rheumatoid polyarthritis in adults 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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* 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. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement of the medicinal product 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 (equivalent to “no CAV”) means “no clinical added value”.