HAUTE AUTORITÉ DE SANTÉ

**DERMATOLOGY**
**New indication**
**April 2015**

**BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION**

# **XOLAIR** (omalizumab), anti-IgE

**Minor improvement in the treatment of spontaneous chronic urticaria unresponsive to anti-H1 antihistamines**

## Main points

- XOLAIR now has Marketing Authorisation, as an additional treatment, in the treatment of spontaneous chronic urticaria (SCU) in patients from the age of 12 years with an inadequate response to anti-H1 antihistamine treatments.
- Its efficacy has been demonstrated versus placebo as an additional treatment, particularly in terms of the percentage of patients with good control of the disease. The effects observed are purely transient and resolve as soon as treatment is stopped, in the 6$^{th}$ month.
- Omalizumab was well tolerated in the studies, however cardiovascular risks and those related to the immunosuppressive effect (particularly carcinogenic) have not been evaluated in the long term.

## Pre-existing indication

Severe persistent allergic asthma.
This summary does not cover this indication.

## Therapeutic use

As a first step, the factors aggravating the SCU should be eliminated.
In first-line treatment, the medication management comprises anti-H1 antihistamines, preferably non-sedating second-generation ones, taken daily for prevention (even in the absence of symptoms) at a dose of 1 tablet/day.
If symptoms persist after 2 weeks of treatment, the anti-H1 dosage may be increased up to 4 times the recommended dose (off-label dosage).
If symptoms persist 1 to 4 weeks after this therapeutic modification, omalizumab or other off-label treatments (cyclosporin or montelukast) can be added to the anti-H1 taken up to 4 times the dose recommended by the Marketing Authorisation.

### Role of the medicinal product in the therapeutic strategy

XOLAIR is a second-line treatment in SCU, in adults and adolescents from the age of 12 years, as an additional treatment to anti-H1 antihistamines, in the event of inadequate response to the latter, despite optimised treatment.

## Clinical data

- The evaluation of the efficacy and safety of omalizumab as an additional treatment for SCU unresponsive to anti-HI antihistamine is based on three randomised, double-blind, placebo-controlled studies, two of which are efficacy studies, ASTERIA I (24 weeks) and ASTERIA II (12 weeks), and one a safety study, GLACIAL (24 weeks). In the safety study, patients were exposed to an anti-H1 antihistamine dose up to 4 times the dose recommended by the Marketing Authorisation and efficacy was a secondary endpoint.

- Omalizumab was superior to placebo in terms of the variation in the weekly ISS pruritus score (score evaluating the severity of the pruritus by the patient, ranging from 0 to 21) at 12 weeks compared with inclusion (primary endpoint). However, the difference observed between the groups only reached the threshold for clinical relevance (difference ≥ 5 points) in the ASTERIA I study.

The effect of omalizumab in terms of the percentage of patients with good control of the disease (UAS7 score ≤ 6; composite score based on the self-assessment by the patient, the intensity of the pruritis and the number of papules, it ranges from 0 to 42) compared with placebo, the most relevant criterion in severe cases, may be considered as substantial: 52% versus 11% in ASTERIA I and 66% versus 19% in ASTERIA II. However, this assessment should be tempered by the fact that the effect of omalizumab is purely transient; the ISS and UAS7 scores gradually reach the values observed with placebo after stopping treatment at W40. Furthermore, the data are time-limited (6 months maximum).

The percentage of complete remissions (UAS7 = 0) was from 34 to 44% in the omalizumab 300 mg group versus 5 to 9% in the placebo group.

- In all studies, the main adverse effects reported following use of omalizumab 300 mg included: reactions at the injection site, headaches, arthralgia and myalgia. However, there is no long-term safety data evaluating the cardiovascular risks and the risks related to the immunosuppressive effect of omalizumab, in particular the carcinogenic effect.

## Special prescribing conditions

- Exception drug status

## Benefit of the medicinal product

- The actual benefit* of XOLAIR is moderate
- XOLAIR provides clinical added value (IAB IV, minor) in the treatment of spontaneous chronic urticaria, as an additional treatment, in adults and adolescents (from the age of 12 years) with an inadequate response to anti-H1 antihistamine treatments.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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[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".