NUCALA (mepolizumab), anti-IL5 monoclonal antibody

Minor improvement in the management of severe refractory eosinophilic asthma

Main points

- NUCALA has Marketing Authorisation as additional treatment, in severe refractory eosinophilic asthma.
- It must be prescribed by a physician experienced in the diagnosis and management of severe refractory eosinophilic asthma.
- It is reserved for adults with severe refractory eosinophilic asthma defined by a blood eosinophil level ≥ 300/µL in the last twelve months AND at least one of the 2 following criteria:
  - ≥ 2 episodes of asthmatic exacerbations having required treatment with oral corticosteroids (> 3 days each) in the last 12 months despite a basic treatment combining high-dose inhaled corticosteroids and a long-acting bronchodilator (LABA) (step 4/5 GINA);
  - a treatment with oral corticosteroid therapy for at least 6 months during the last 12 months.

Therapeutic use

- Severe asthma requires a basic treatment with a combination of moderate- or high-dose inhaled corticosteroids (ICS) and long-acting beta-2 agonist bronchodilator (LABA), possibly supplemented by other bronchodilator(s) or anti-inflammatory agent(s) (GINA classification treatment step 4);
- In case of severe asthma not controlled by the combination of ICS and LABA are added to the basic treatment: oral corticosteroids (OCS) or injectable corticosteroids, omalizumab in case of allergic asthma or mepolizumab in case of eosinophilic asthma.

Role of the medicinal product in the therapeutic strategy

NUCALA is an alternative in patients with severe refractory eosinophilic asthma. The Committee has defined the patients likely to benefit from mepolizumab (see “Main points”). Uncertainties remain about the definition of diagnostic criteria for eosinophilic asthma and the definition of criteria to identify the population of patients most likely to benefit from mepolizumab in clinical practice.

Clinical data

- The efficacy of mepolizumab was assessed versus placebo in the course of three randomised, double-blind clinical studies over a period ranging from 24 to 52 weeks:
  - One dose-finding study that included 616 patients with uncontrolled severe asthma showed a decrease in significant clinical exacerbations of asthma after 52 weeks in the mepolizumab groups compared to placebo: 2.40 exacerbations/year in the placebo group versus 1.15 to 1.46 in the mepolizumab groups, i.e. a reduction in the risk of exacerbations from 39% to 52% according to the dosages, corresponding to about one avoided exacerbation on average per year on mepolizumab compared to placebo. No dose-response relationship was observed.
  - One study that included 576 patients with uncontrolled severe eosinophilic asthma showed a decrease in clinical exacerbations of asthma after 32 weeks in the mepolizumab arms compared to placebo: 1.74 exacerbation/year in the placebo group versus 0.83 to 0.93 in the mepolizumab groups, i.e. a reduction in the risk of exacerbations from 47% to 53% according to the dosages, corresponding to about one avoided exacerbation on average per year per patient on mepolizumab compared to placebo.
A study evaluated the efficacy of mepolizumab on corticosteroid-sparing in 135 patients with uncontrolled severe eosinophilic asthma after 24 weeks. Mepolizumab was associated with a modest reduction in OCS doses: the OCS dose was reduced in 64% of patients in the mepolizumab group versus 44% in the placebo group and 54% of patients in the mepolizumab group achieved an OCS dose ≤ 5 mg/day versus 32% in the placebo group.

In the context of clinical studies, mepolizumab was not associated with an increased risk of infections, systemic reactions (allergic or not) and cancers. The incidence of anti-mepolizumab antibodies was 6% for mepolizumab 100 mg SC and 2% for all IV forms combined.

**Special prescribing conditions**

- Medicine requiring initial annual hospital prescription
- Initial prescription and renewal by respiratory medicine specialists only

**Benefit of the medicinal product**

- The actual benefit* of NUCALA is substantial only in additional treatment in severe refractory eosinophilic asthma in adults who meet the criteria defined below (see "Main points"): Patients whose asthma is not controlled due to unsuitable basic treatment, adherence problems, comorbidities or aggravating risk factors that fall outside of this scope. The actual benefit of NUCALA is insufficient in the other situations.
- Taking into account:
  - demonstration in both studies versus placebo of a significant and clinically relevant reduction in exacerbations of asthma in patients with severe asthma not controlled by a basic treatment combining high-dose inhaled corticosteroids in combination or oral corticosteroids; this effect was more marked when the blood level of eosinophils at enrolment was higher;
  - completion of a study on oral corticosteroid-sparing showing a modest decrease compared to placebo on the consumption of oral corticosteroids;
  - a clinically relevant effect on the quality of life evaluated using the Saint-Georges questionnaire in two studies;
  - the unmet treatment need in patients with uncontrolled severe asthma and the risks associated with exacerbations, their impact on quality of life and consumption of care they generate;
  - the lack of clear diagnostic criteria for eosinophilic asthma and the limitations associated with the determination of blood eosinophils;
  - uncertainties about the criteria to identify the population of patients most likely to benefit from mepolizumab in clinical practice;
  - the lack of clinically relevant effect on respiratory function evaluated by FEV1 and on control of asthma evaluated by the ACQ-5 questionnaire;
  - the absence of data concerning omalizumab failure.

NUCALA provides a minor improvement in actual clinical benefit** (IACB IV) in the management of severe refractory eosinophilic asthma.

- 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 Opinion of 22 June 2016 (CT-14895) and is available at [www.has-sante.fr](http://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. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The improvement of actual clinical benefit (IACB) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of IACB on a scale from I (major) to IV (minor). A level V IACB (equivalent of "no IACB") means "no clinical added value".

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