OPINION ON MEDICINAL PRODUCTS

mepolizumab

NUCALA 40 and 100 mg, Injectable solution - 5 October 2022

Injectable solution

Reassessment and availability of new dosage form(s)

Adopted by the Transparency Committee on 5 October 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Positive opinion on the reimbursement of NUCALA (mepolizumab) as an additional treatment for severe refractory eosinophilic asthma in children aged six years and over and in adolescents meeting the following criteria

- **a blood eosinophil level ≥ 150/µL within the last 12 months**;

AND

- at least two asthma exacerbation episodes requiring oral corticosteroid treatment (≥ 3 days each) in the last 12 months despite basic treatment with a combination of high-dose inhaled corticosteroids and a long-acting bronchodilator (LABA);
- OR treatment with oral corticosteroids for at least 6 months in the last 12 months.

Not recommended for reimbursement in other clinical situations for the additional treatment of severe refractory eosinophilic asthma in children aged 6 years and over and adolescents.

Therapeutic improvement?

A therapeutic advance in the management of severe refractory eosinophilic asthma in children aged six years and older and adolescents.

Role in therapeutic strategy?

As in adults, the aim of the pharmacological management of asthma in children aged six years and older and in adolescents is to maintain sustained control of the disease, including: reduction of symptoms, prevention of exacerbations, reduction of limitations in daily life, and limitation of adverse effects due to pharmacological treatments.

Treatment is adapted to the severity of the disease. International consensus has identified five levels of severity with escalation of therapy in case of non-control or partial control of asthma. Severe asthma corresponds to levels 4 and 5:

- tier 4 – asthma requiring basic treatment with a combination of medium-dose ICS and LABA (preferred basic treatment);
- tier 5 – tier 4 asthma requiring basic treatment with a combination of high-dose ICS and LABA, with the addition of biologic treatment if necessary, depending on the asthma phenotype.

Escalation of therapy for severe asthma in children over six years of age and adolescents involves oral corticosteroids and biotherapies as a last resort. However, in paediatrics, oral corticosteroids can only be occasionally used as a short course of treatment due to the risk of adverse effects. Among the biotherapies, omalizumab (XOLAIR) for severe allergic asthma, mepolizumab (NUCALA) for severe refractory eosinophilic asthma and dupilumab (DUPIXENT) for severe asthma associated with type-2 inflammation are currently approved for use in children aged six and over in France.

Role of the medicinal product:

According to the recommendations of the *European Respiratory Society/American Thoracic Society (*ERS/ATS) and the *European Academy of Allergy and Clinical Immunology (*EAACI), the eosinophil count should be ≥ 150/µL for the initiation of NUCALA (mepolizumab) therapy. This level should be ≥ 150/µL or ≥ 300/µL for the initiation of NUCALA (mepolizumab) therapy according to the GINA.

The Committee defines children aged six years and over and adolescents who may benefit from NUCALA (mepolizumab) in the following manner:

- patients with a blood eosinophil level ≥ 150/µL in the last 12 months;

AND

- patients with at least two asthma exacerbation episodes requiring oral corticosteroid treatment (≥ 3 days each) in the last 12 months despite basic treatment with a combination of high-dose inhaled corticosteroids and a long-acting bronchodilator (LABA);
- OR patients treated with oral corticosteroids for at least six of the last 12 months.

Children aged 6 years and older and adolescents whose asthma is not controlled due to inadequate basic treatment, compliance problems, comorbidities or unmanaged aggravating risk factors, are not included.

Due to the lack of a direct comparison between NUCALA (mepolizumab) and the biotherapies (DUPIXENT [dupilumab] and XOLAIR [omalizumab]), the role of NUCALA (mepolizumab) among the other available biotherapies for severe asthma still needs to be clarified.

Committee's conclusions

Clinical Benefit

- Uncontrolled severe asthma has a major impact on quality of life and is associated with a risk of severe, life-threatening exacerbations.
- NUCALA (mepolizumab) is used as a basic treatment for symptoms in children aged six years and older and in adolescents with severe refractory eosinophilic asthma.
- The efficacy/adverse effect ratio of NUCALA (mepolizumab) is substantial.
- Therapeutic alternatives (other biotherapies) are available.
- NUCALA (mepolizumab) is an additional treatment option for severe refractory eosinophilic asthma limited to certain children from 6 years of age, and adolescents.
- **Public health benefit**

Considering:

- the severity of severe asthma,
- its prevalence,
- the partially met medical need in children and adolescents with severe uncontrolled asthma;
- the partial response to the identified need, given:
  - the expected additional impact on morbidity but with no evidence of impact on mortality and quality of life;
  - the lack of evidence of an additional impact on delivery of care;

NUCALA (mepolizumab) is not likely to have an additional impact on public health.

Taking into account all these elements, the Committee deems that the actual clinical benefit of NUCALA (mepolizumab) is substantial only as additional treatment in severe refractory eosinophilic asthma for children aged 6 years of age and older and in adolescents meeting the following criteria

- **a blood eosinophil level ≥ 150/µL within the last 12 months;**

AND

- **at least two asthma exacerbation episodes requiring oral corticosteroid treatment (≥ 3 days each) in the last 12 months despite basic treatment with a combination of high-dose inhaled corticosteroids and a long-acting bronchodilator (LABA);**
- **OR treatment with oral corticosteroids for at least 6 months in the last 12 months.**

Children aged 6 years and older and adolescents whose asthma is not controlled due to inadequate basic treatment, compliance problems, comorbidities or unmanaged aggravating risk factors, are not included.

In other clinical situations, the actual clinical benefit of NUCALA (mepolizumab) is insufficient to justify public funding.

The Committee approves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary medicinal products approved for community use for the marketing authorisation indication for children aged 6 years and over and adolescents meeting the aforementioned criteria, for whom the actual clinical benefit is substantial.

The Committee disapproves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary medicinal products approved for community use in the other clinical situations for children aged 6 years and over and for adolescents.

Recommended reimbursement rate: 65%

Clinical Added Value

Considering:

- the evidence of superiority of NUCALA (mepolizumab) over placebo in a randomised, double-blind study, for children aged 6-17 years, concerning the annualised rate of severe asthma exacerbations at 52 weeks, a clinically relevant outcome measure with a modest effect size (rate ratio = 0.73; 95% CI [0.56; 0.96], p=0.027);
- its acceptable safety profile;
- the partially met medical need for children aged 6 years and over with severe uncontrolled asthma, despite optimised treatment;

but in the light of:

- the health, social and environmental conditions (overweight, stress, inadequate medical follow-up, pollution) of the children included in the MUPPITS-2 study, which may limit the extrapolation of the results to the French population;
- the lack of available long-term data (52-week study) on the evolution of asthma in children treated with mepolizumab;
- the lack of robust quality-of-life data;

the Transparency Committee deems that NUCALA (mepolizumab) provides minor clinical added value (CAV IV) in the management of severe refractory eosinophilic asthma for children aged 6 years and older and in adolescents.