HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
20 APRIL 2022

The legally binding text is the original French opinion version

mepolizumab
NUCALA 100 mg powder for solution for injection, solution for injection in pre-filled syringe and solution for injection in pre-filled pen

New indication

Key points

Favourable opinion for reimbursement as an add-on treatment for patients aged 6 years and older with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA).

What therapeutic improvement?

Therapeutic improvement in the management of relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA).

Role in the care pathway?

Eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss syndrome) is a rare disease belonging to the anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis group, affecting the small and medium-sized blood vessels.

In France, the therapeutic strategy to induce remission of EGPA in adults is based on the French national diagnostic and care protocol (PNDS) guidelines issued by the HAS, drawn up in 2019 under the aegis of the GFEV (French vasculitis study group) and the FAI²R (Rare auto-immune and auto-inflammatory diseases network). According to these guidelines, the main objectives of EGPA treatment are to:
- achieve remission and sometimes a cure;
- reduce the risk of relapses;
- limit and reduce the sequelae associated with the disease;
- limit adverse effects and complications related to the treatments used;
- improve the quality of life parameters affected by the disease;
- maintain socioprofessional and/or school integration and/or enable a rapid return to social and/or school and/or work activities.

According to the PNDS:
- the initial treatment of EGPA includes corticosteroid therapy initiated at a dose of 1 mg/kg/day of prednisone equivalent, capped at 60 mg per day, apart from in exceptional cases, potentially preceded by an intravenous (IV) bolus of methylprednisolone, depending on the severity and the patient's cardiovascular condition. After an initial 3-week treatment at a dose of 1 mg/kg/day of prednisone equivalent, corticosteroids should be tapered;
- the therapeutic strategy in EGPA is guided by the presence or absence of poor prognostic factors defined in the 1996 Five Factor Score (FFS), with systemic forms with an FFS = 0 warranting corticosteroids alone, and those with an FFS ≥ 1 requiring a combination of corticosteroids and immunosuppressants.

Forms without poor prognostic factors (FFS=0)
Immunosuppressive therapy is not warranted as first-line treatment in these forms. It is only prescribed to patients whose EGPA is not controlled by corticosteroids alone (non-achievement of remission or relapse of vasculitis), if it is necessary to obtain corticosteroid-sparing in the event of corticosteroid dependence on more than 7.5 to 10 mg/d of prednisone equivalent (in order to reduce the risk of adverse effects) or in the event of intolerance to corticosteroid therapy.

In situations where immunosuppressive therapy is indicated as second-line treatment:
- in the absence of signs of severity (FFS = 0), the choice of immunosuppressant should preferentially be oral azathioprine (at a dose of 2 to 3 mg/kg/day) or oral or subcutaneous methotrexate (at a dose of 0.3 mg/kg/week) for a duration of 12 to 18 months, by analogy with the treatment of ANCA-associated vasculitis;
- if signs of severity develop (FFS ≥ 1), the choice of immunosuppressant should preferentially be cyclophosphamide, according to the same treatment conditions as for forms with one or more poor prognostic factors on initial diagnosis, described below.

Forms with poor prognostic factors (FFS ≥ 1)
Immunosuppressive therapy, preferentially cyclophosphamide in IV bolus form, is warranted as first-line treatment in these forms, in combination with corticosteroid therapy.

In the event of disease refractory to conventional treatments, the use of plasma exchanges to control inflammatory flare-ups and/or other therapies should be discussed with a reference or expert centre.

Following induction therapy, it is essential to conduct a reassessment of the vasculitis, to investigate for signs of activity, in order to envisage switching to maintenance treatment only if the vasculitis is still active.

Children with EGPA should be managed in consultation with or directly within a paediatric "rare autoimmune diseases and systemic diseases" reference centre or expert centre, possibly with the involvement of an adult reference or specialist centre.

Role of the medicinal product in the care pathway

NUCALA (mepolizumab) is a first-line therapy as an add-on treatment for patients aged 6 years and older with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA).

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

- Eosinophilic granulomatosis with polyangiitis (EGPA) can have life-threatening complications.
- The proprietary medicinal product NUCALA (mepolizumab) is a symptomatic medicinal product.
- The efficacy/adverse effects ratio of NUCALA (mepolizumab) is high.
- There are no therapeutic alternatives.
- NUCALA (mepolizumab) is a first-line therapy as an add-on treatment for patients aged 6 years and older with relapsing-remitting or refractory EGPA.

Public health benefit

Considering:

- the seriousness of the disease;
- the low prevalence of EGPA;
- the unmet medical need in relapsing-remitting or refractory EGPA;
- the partial response to the identified need due to an additional impact on morbidity, despite the absence of a demonstrated impact on mortality and quality of life;
- the absence of demonstration of a potential impact on the organisation of care;

NUCALA (mepolizumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of NUCALA (mepolizumab) is substantial as an add-on treatment for patients aged 6 years and older with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA).

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use "as an add-on treatment for patients aged 6 years and older with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA)" and at the MA dosages.

- **Recommended reimbursement rate: 65%**

Clinical Added Value

Considering:

- demonstration of the superiority of NUCALA (mepolizumab) compared to placebo in a randomised, double-blind study, on the total accrued duration of remission (OR=5.91; CI95% [2.68; 13.03]; p < 0.001) and on the proportion of patients in remission at both 36 and 48 weeks (OR=16.74; CI95% [3.61; 77.56]; p < 0.001), clinically relevant co-primary endpoints, with a substantial effect size;
- demonstration of the superiority of mepolizumab compared to placebo on the ranked secondary endpoints (particularly the time to first confirmed relapse of EGPA and average daily oral corticosteroid dose during weeks 48 to 52);
- and its satisfactory safety profile;
- the unmet medical need in patients with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA);

but in view of:

- the lack of data on the evolution of organ involvement, in the absence of long-term data;
- the absence of robust data on quality of life,

the Transparency Committee considers that NUCALA (mepolizumab) provides a minor clinical added value (CAV IV) in the care pathway for relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA).