HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
17 JANUARY 2022

The legally binding text is the original French opinion version

satralizumab
ENSPRYNG 120 mg solution for injection in pre-filled syringe

First assessment

Key points

Favourable opinion for reimbursement as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) only in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive, and who have a relapsing form of the disease not having responded to background immunosuppressive therapy (rituximab, azathioprine, mycophenolate mofetil).

Unfavourable opinion for reimbursement in the other clinical situations of the MA.

What therapeutic improvement?

- Therapeutic improvement in management of the disease in adults, in the same way as SOLIRIS (eculizumab),
- Therapeutic improvement in the treatment of the disease in adolescents aged 12 years and older.

Role in the care pathway?

According to the 2021 French national diagnostic and care protocol (PNDS) relative to NMOSD, the treatment of neuromyelitis optica (NMO) flare-ups is a therapeutic emergency, due to the risk of incapacitating sequelae, in addition to the functional threat and the potential threat to life. In parallel, long-term management (background treatment) is essential in order to reduce the risk of flare-ups, since repeated relapses can cause functional and serious sequelae.

Initial treatment in the event of flare-ups is based on intravenous corticosteroid therapy with high-dose methylprednisolone (1 g/d for adults and 30 mg/kg/day for children from 12 years of age) for 5 to 10 days, followed by long-term oral treatment (1 mg/kg/day) and plasma exchanges in serious flare-ups.

The background treatments used in practice (off-label) and recommended for the prevention of relapses are the following immunosuppressive therapies:

- Rituximab, an anti-CD20, administered IV every 6 months (beneficial effect on the prevention of relapses, significant reduction in annualised rate of relapses),
- Tocilizumab, an anti-IL6 used in NMOSD refractory to conventional immunosuppressive therapies,
- Azathioprine, in combination with an oral corticosteroid therapy for the first six months (reduction in the annualised rate of relapses in adults and children),
- mycophenolate mofetil in combination with an oral corticosteroid therapy for the first six months (reduction in the annualised rate of relapses in adults and children),
- mitoxantrone (reduction in the annualised rate of relapses).

Other medicinal products, such as methotrexate, cyclophosphamide, ciclosporin and tacrolimus, are also used to a more limited degree.

Treatments used in MS (interferons, glatiramer acetate, natalizumab or fingolimod) appear to be ineffective or detrimental.

SOLIRIS (eculizumab), an anti-C5 complement protein antibody, was granted an MA in NMOSD and was evaluated in September 2020 by the Transparency Committee, which restricted its reimbursement to the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody-positive with a relapsing form of the disease, and not responding to background immunosuppressive therapy (rituximab, azathioprine, mycophenolate mofetil).

However, no proprietary medicinal products have an MA in the treatment of NMOSD in adolescent patients. The treatment in adolescents is based on the same off-label immunosuppressive therapies as in adults.

Role of the medicinal product in the care pathway

Considering:

- the superiority of satralizumab as monotherapy and in combination with immunosuppressive therapy demonstrated in two double-blind, placebo-controlled studies, having included patients with a relapsing form of the disease, the majority of whom were anti-aquaporin-4 IgG seropositive and/or had received prior immunosuppressive therapy,
- the absence of direct comparative data versus the immunosuppressive therapies used in practice (off-label), in particular rituximab, or versus eculizumab in adult patients, with the latter having been developed concomitantly,

ENSPRYNG (satralizumab) as a monotherapy or in combination with immunosuppressive therapy is a background therapy for neuromyelitis optica spectrum disorders in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive, and who have a relapsing form of the disease not having responded to background immunosuppressive therapy (rituximab, azathioprine, mycophenolate mofetil).

It should be noted that in adults, this medicinal product is an additional treatment option, in the same way as SOLIRIS (eculizumab, with an MA in adults only), in the absence of direct comparative data versus the latter enabling them to be ranked in the therapeutic strategy. The choice between these treatments should be made on the basis of the clinical situation, the safety profile of the medicinal products, their methods of administration and patients' preferences.

ENSPRYNG (satralizumab) has no role in the other situations of the MA.

Special recommendations

The Committee recommends that treatment with ENSPRYNG (satralizumab) be administered in a multiple sclerosis resource and expertise centre or in a centre specialising in rare inflammatory brain and spinal cord diseases, with prescription restricted to neurologists in the context of a multidisciplinary team meeting justified in view of the risk of using ENSPRYNG (satralizumab) outside the reimbursement scope defined by the Committee on the basis of available efficacy and safety data, particularly first-line use or use in patients who do not have anti-AQP4 antibodies (off-label).

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Neuromyelitis optica spectrum disorder (NMOSD) is a serious, disabling disease that can be life-threatening in some cases.

◗ The proprietary medicinal product ENSPRYNG (satralizumab) as a monotherapy or in combination with immunosuppressive therapy is a symptomatic background therapy.

◗ The efficacy/adverse effects ratio of ENSPRYNG (satralizumab) is:

- substantial as a monotherapy or in combination with immunosuppressive therapy in the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive, and who have a relapsing form of the disease not having responded to background immunosuppressive therapy (rituximab, azathioprine, mycophenolate mofetil) in view of the available data,
- not established in the other situations due to a lack of data.

◗ There are therapeutic alternatives (see chapter 05 "Clinically relevant comparators").

◗ ENSPRYNG (satralizumab) as a monotherapy or in combination with immunosuppressive therapy is a background therapy for neuromyelitis optica spectrum disorders in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive, and who have a relapsing form of the disease not having responded to background immunosuppressive therapy (rituximab, azathioprine, mycophenolate mofetil). It should be noted that in adults, this medicinal product is an additional treatment option, in the same way as SOLIRIS (eculizumab, with an MA in adults only), in the absence of direct comparative data versus the latter enabling them to be ranked in the therapeutic strategy.
ENSPRYNG (satralizumab) has no role in the other situations of the MA.

Public health impact

Considering:

- the seriousness of the disease and its low prevalence,
- the partially met medical need,
- the partial response to the identified need, due to:
  - the additional demonstrated impact on morbidity in terms of time to first relapse, with no demonstrated impact on mortality,
  - the lack of demonstrated impact on quality of life in the absence of robust data,
- the absence of any demonstrated impact on the organisation of care,

ENSPRYNG (satralizumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of ENSPRYNG (satralizumab) is:

- **Substantial as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) only in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive, and who have a relapsing form of the disease not having responded to background immunosuppressive therapy (rituximab, azathioprine, mycophenolate mofetil).**
- **Insufficient in the other clinical situations of the MA.**

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 a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive, and who have a relapsing form of the disease not having responded to background immunosuppressive therapy (rituximab, azathioprine, mycophenolate mofetil), and at the MA dosages.

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the other clinical situations of the MA.

- **Recommended reimbursement rate: 65%**

Clinical Added Value

In patients with NMOSD who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive and who have a relapsing form of the disease not having responded to background immunosuppressive therapy (rituximab, azathioprine, mycophenolate mofetil), considering:

- demonstration of the superiority of satralizumab as monotherapy or in combination with immunosuppressive therapy versus placebo in the treatment of NMOSD in patients who have a relapsing form of the disease, in terms of time to relapse, a clinically relevant primary endpoint,
- the need to have access to authorised medicinal products with demonstrated efficacy in view of the current strategy based on immunosuppressive therapies prescribed off-label as first-line treatment in adults and adolescents, and on eculizumab, authorised in adults but reserved for relapsing forms not having responded to immunosuppressive therapies,

and despite:

- the absence of robust data on the annualised relapse rate, this having been assessed as an exploratory endpoint,
- the absence of a demonstrated benefit on disability and patients' quality of life,
- remaining uncertainties concerning the efficacy and long-term safety, as well as the optimal treatment duration and use strategy in the absence of comparison with the background therapies used in clinical practice, in particular rituximab,

the Transparency Committee considers that **ENSPRYNG (satralizumab) provides a moderate clinical added value (CAV III):**

- **in the care pathway in adolescents aged 12 years and older,**
- **in the care pathway, in the same way as SOLIRIS (eculizumab), in adults, for whom this medicinal product is authorised.**