OPINION ON MEDICINAL PRODUCTS

avacopan
TAVNEOS 10 mg,

capsule

First assessment

Adopted by the Transparency Committee on 21 September 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement of TAVNEOS (avacopan) in the treatment of adult patients with severe and active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA), in combination with rituximab or cyclophosphamide.

Therapeutic progress?

A therapeutic advance in the management of adult patients with severe and active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MP).

Role in therapeutic strategy?

The goals of ANCA vasculitis management are to induce remission and prevent relapse, while limiting treatment-related adverse events and disease sequelae.

In France, the therapeutic strategy for inducing remission in severe and active GPA and PAM is based on the French recommendations of the French Vasculitis Study Group (GFEV) (2013), the EULAR European recommendations (2016), and the HAS national diagnosis and care protocol (PNDS 2019). Management is multidisciplinary and coordinated by a hospital doctor in conjunction with a reference centre for rare autoimmune and systemic diseases or a centre of expertise.

The treatment of severe forms of GPA and PAM combines corticosteroids with long-term immunosuppressive agents for more than 18 months. An initial induction therapy phase of approximately 3 to 6 months aims to attain remission of the disease.

In the induction therapy for remission of systemic GPA and PAM, rituximab can be prescribed as a first-line treatment along with cyclophosphamide. The choice of treatment is left to the clinician's discretion when patients are managed for a first episode of the disease. The decision takes into account the patient's history, pre-existing morbidity factors, the disease to be treated and the patient's opinion. Rituximab should be prescribed preferentially for women of childbearing age, particularly those over 30 years of age. These immunosuppressive treatments are given in combination with a high initial dose of corticosteroids. After an initial three-week course of treatment at a dose of 1 mg/kg/day of prednisone equivalent, the aim is to reduce and then discontinue corticosteroids on a tapering schedule, while maintaining remission. The total duration of corticosteroid therapy varies from six months (North American protocols) to 18-24 months (European protocols). In France, it is usually 6 to 12 months according to a tapering schedule in which the main benchmarks are approximately 20 mg/day at 3 months, 10 mg/day at 6 months and 5 mg/day at one year of prednisone equivalent.

Current induction therapy achieves remission in more than 80% of GPA and PAM cases. After remission has been achieved, relapses, which occur in more than half of GPA patients and in about 30% of PAM patients at 5 years, warrant maintenance therapy (with rituximab as the conventional treatment) in order to consolidate remission and limit the risk of relapse.

Role of the medicinal product

TAVNEOS (avacopan), the first selective human complement receptor 5a (C5aR1) antagonist, is a new first-line treatment option in combination with rituximab or cyclophosphamide for the treatment of adult patients with severe and active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA).

TAVNEOS (avacopan) is particularly indicated for adult patients with severe and active GPA or PAM who are at risk of decompensation from high-dose corticisteroids, or who are identified as being at high risk of developing complications from high-dose corticosteroids.

However, the Committee notes that TAVNEOS (avacopan) has no role for patients with GPA or PMA who are intubated/ventilated due to severe intra-alveolar haemorrhage and/or severe renal impairment (estimated glomerular filtration rate < 15 ml/min), as these patients were not evaluated in the phase III ADVOCATE study.

Special recommendations

➔ Other requests

The Committee regrets the lack of data on the use of TAVNEOS (avacopan) in the paediatric population in which the partial cortisone sparing provided by avacopan may be of interest.

Furthermore, the Committee hopes that clinical studies on this treatment can soon be put in place in the paediatric population.

Committee's conclusions

Clinical Benefit

- ANCA vasculitides such as granulomatosis with polyangiitis and microscopic polyangiitis can be life threatening and cause permanent organ damage.
- The proprietary medicinal product TAVNEOS (avacopan) is a curative medicinal product.
- The efficacy/adverse effect ratio of TAVNEOS (avacopan) is substantial.
- The conventional alternatives currently available are corticosteroids combined with immunosuppressive agents or immunomodulators.

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Public health benefit

Considering:

- the severity of granulomatosis with polyangiitis and microscopic polyangiitis;
- the low prevalence of these diseases;
- the partially covered medical need;
- the partial response to the identified need with a demonstrated additional impact on morbidity despite the lack of demonstrated impact on mortality and quality of life;

TAVNEOS (avacopan) is not likely to have a public health benefit.

Considering all of these elements, the Committee deems that the actual clinical benefit of TAVNEOS (avacopan) is substantial in the marketing authorisation indication.

The Committee approves the inclusion of TAVNEOS (avacopan) 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 and dosages.

Proposed reimbursement rate: 65%

Clinical Added Value

Considering:

- the evidence of non-inferiority of avacopan in relation to prednisone in tapering dosage on the proportion of patients in complete remission at 26 weeks (72.3% *versus* 70.1%,respectively ; 95% CI [-6.0; 12.8]; p<0.0001);
- the evidence of superiority of avacopan over prednisone in tapering dosage on the proportion of patients with maintenance of remission at 52 weeks (65.7% *versus* 54.9%, respectively; 95% CI [2.6; 22.3]; p = 0.0066);
- the lesser use (mean total cumulative dose of corticosteroids approximately 2.7 times higher in the control group) and lower corticosteroid toxicity in the avacopan group compared to the prednisone group;
- the acceptable safety profile of avacopan;

but in the light of:

- results which demonstrate that avacopan treatment has enabled a clear reduction in corticosteroid use without giving rise to complete cortisone sparing;
- the lack of long-term data to enable an assessment of the long-term benefit and safety of avacopan (study duration: 52 weeks);

the Committee deems that TAVNEOS (avacopan), in combination with rituximab or cyclophosphamide, provides minor clinical added value (CAV IV) in the management of adult patients with severe and active polyangiitis granulomatosis (GPA) or microscopic polyangiitis (MP).