HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
16 SEPTEMBER 2020
The legally binding text is the original French opinion version

siltuximab
SYLVANT 100 and 400 mg powder for concentrate for solution for infusion

Reevaluation

Key points

Favourable opinion for reimbursement in the treatment of adult patients with multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpes virus-8 (HHV-8) negative.

What therapeutic improvement?

SYLVANT (siltuximab) provides a therapeutic improvement.

Role in the care pathway?

In the event of symptomatic and inflammatory disease, the first-line treatment is based on medicinal products targeting the IL6 / IL6 receptor axis. These treatments are suspensive only. Since siltuximab has a marketing authorisation (MA) in this indication, it is a first-line treatment (level-1 recommendation). The proprietary medicinal product ROACTEMRA (tocilizumab), another IL6 inhibitor, is also used, but does not have a MA in this indication in France. According to the guidelines, its use is recommended at the same stage in the care pathway as siltuximab with a lower level of evidence (category 2A or 2B depending on the guidelines) given the absence of comparative data.
An antibody targeting B lymphocytes, rituximab, may also be proposed off-label in non-severe forms with little inflammation or following the failure of IL6 inhibitors. Corticosteroids are also used in combination with immunotherapy to control the inflammatory syndrome.

Second-line therapy uses immunomodulating/immunosuppressant agents or chemotherapy.

Role of SYLVANT in the care pathway
Currently, SYLVANT (siltuximab) is the only biologic therapy with a marketing authorisation in France in the treatment of adult patients with MCD who are HIV negative and HHV-8 negative and therefore remains the biologic therapy of choice in this indication.
The role of SYLVANT (siltuximab) compared to tocilizumab used off-label cannot be defined in the absence of comparative data

Special recommendations

Due to the complexity of diagnosing idiopathic multicentric Castleman's disease (MCD), the Committee recommends that the decision to initiate SYLVANT (siltuximab) treatment be taken during a multidisciplinary review meeting at a Castleman's disease reference or expert centre.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Multicentric Castleman's disease (MCD) is a rare, heterogeneous lymphoproliferative syndrome that is difficult to diagnose and which, due to its complications, can be life-threatening for patients.
◗ This is a symptomatic treatment.
◗ The efficacy/adverse effects ratio remains moderate in view of the efficacy results currently available (from a phase II study and the ACCELERATE registry) and its safety profile.
◗ There are no alternatives with an MA in the indication concerned.
◗ SYLVANT (siltuximab) is a first-line treatment.

Public health impact

Considering:

- the seriousness of this disabling disease, which can lead to major complications that may be life-threatening to patients, and its rarity,
- the identified unmet medical need,
- the partial response to the medical need that siltuximab continues to provide,
- the demonstrated additional impact on morbidity and mortality in terms of durable tumour and symptomatic response,
- the absence of expected deterioration in the care and/or life pathway,

SYLVANT (siltuximab) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of SYLVANT (siltuximab) is substantial in the MA indication.

The Committee issues a favourable opinion for maintenance of inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and dosages.

Clinical Added Value

Considering:

- **the demonstrated superiority of siltuximab compared to placebo in terms of durable tumour and symptomatic response, with an improvement of + 34% (34% versus 0%, p = 0.0012),**
- **the absence of any demonstrated improvement to date in overall survival,**
- **the absence of any quality-of-life data with a demonstrative value,**
- **the safety profile marked, in particular, by secondary infections and important identified risks of hypertension and hyperlipidaemia,**
- **additional data with a descriptive value from the ACCELERATE registry,**

the Committee considers that SYLVANT (siltuximab) provides a minor clinical added value (CAV IV) in the treatment of adult patients with multicentric Castleman's disease (MCD) who are HIV negative and HHV-8 negative