SUMMARY

sutimlimab

ENJAYMO 50 mg/ml,

solution for infusion

Initial inclusion

Original French opinion adopted by the Transparency Committee on 30 August 2023

The legally binding text is the original French opinion version

Transparency Committee's conclusions

Clinical Benefit

- CAD is a rare form of chronic autoimmune haemolytic anaemia in which the clinical signs (cold-induced acrocyanosis and/or haemolytic anaemia) can impair quality of life but are rarely life-threatening. The long-term prognosis is most often favourable but may depend on the type and progression of the underlying lymphoid blood disorder in forms resulting from a duly characterised lymphoid blood disorder, as well as on the severity and frequency of haemolysis flare-ups.
- This is a symptomatic medicinal product.
- The efficacy/adverse effects ratio is:
  - high in the MA indication only in patients with Hb levels ≤ 10 g/dl,
  - not established in other clinical situations of the MA, i.e. in patients with Hb levels > 10 g/dl, in the absence of clinical data in this population.
- The product is a treatment option in the MA indication only in patients with Hb levels ≤ 10 g/dl. In the absence of data, ENJAYMO (sutimlimab) has no role in the care pathway for patients with Hb levels > 10 g/dl.

Public health benefit

Considering:

- the severity of the disease, which may impair quality of life but is rarely life-threatening and for which the long-term prognosis is most often favourable;
- the low prevalence of the disease;
- the medical need partially met by the available alternatives used off-label;
- the partial response to the identified need, due to:

- a demonstrated additional impact versus placebo on morbidity in terms of increase in Hb levels and reduction of symptoms of fatigue, but without a demonstrated impact on the need for transfusions or vasomotor disorders of the extremities despite these being some of the dominant symptoms,
- the lack of evidence to support an improvement in the care or life pathway. It should be noted that since this is a chronic treatment, use of sutimlimab could prove to be restrictive in the long term, given that the dosing regimen is an IV infusion over 1 to 2 hours every 2 weeks (with the need for patient monitoring during the hour following the infusion), which must be administered by a healthcare professional and in a hospital setting for the first 3 months.

ENJAYMO (sutimlimab) is unlikely to have an additional impact on public health.

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

- **substantial in the indication "treatment of haemolytic anaemia in adult patients with cold agglutinin disease (CAD) only in patients with Hb levels ≤ 10 g/dl",**
- **insufficient to justify public funding cover in the other clinical situations of the MA indication (patients with Hb levels > 10 g/dl).**

The Committee issues a favourable opinion for inclusion of ENJAYMO (sutimlimab) in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication "treatment of haemolytic anaemia in adult patients with cold agglutinin disease (CAD) only in patients with Hb levels ≤ 10 g/dl" 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 other clinical situations of the MA indication (patients with Hb levels > 10 g/dl).

➔ **Recommended reimbursement rate for inclusion in the retail list of reimbursed proprietary medicinal products approved for use: 65%**

Clinical Added Value

In adult patients with Hb levels ≤ 10 g/dl

Considering:

- demonstration - after 26 weeks of treatment in the phase 3 CADENZA study - of the superiority of sutimlimab compared to placebo, in patients with symptomatic haemolytic anaemia (haemoglobin ≤ 10 g/dl) without a recent history of transfusion, in terms of the percentage of responder patients (primary outcome measure defined by an increase of 1.5 g/dl of Hb, without transfusion and without a prohibited therapy), of an increase in hemoglobin levels and improvement of fatigue (FACIT-Fatigue score);
- the results of the open-label, non-comparative study (CARDINAL) conducted in patients with a recent history of transfusion (median of 2 in the past 12 months), which also suggest an improvement in hemoglobin levels under sutimlimab;
- the medical need partially met by the available alternatives, all used off-label;

but also taking into account:

- the non-comparative nature of the CARDINAL study, which included more severe patients (patients with a recent history of transfusions) than those included in the CADENZA study and hence more representative of the population likely to fall under this treatment in routine practice;
- the absence of direct or indirect comparison versus the maintenance therapies currently used in practice and recommended in the French national diagnostic and care protocol (PNDS), particularly rituximab as monotherapy or in combination, making it impossible to position the role of this treatment in the current care pathway;
- the absence of robust evidence of a reduced need for transfusions thanks to sutimlimab in patients with a history of transfusion;
- uncertainties regarding the effect size of sutimlimab, particularly due to the low numbers of patients enrolled in the studies, the short duration of the studies in a context where CAD is a chronic disease with a seasonal course, with predominantly wintertime flare-ups, and the proportion of patients having received an unauthorised therapy (including iron and erythropoietin - EPO) having potentially contributed to the efficacy observed (higher proportion in the sutimlimab group than in the placebo group in the CADENZA study);
- demonstration of an improvement in symptoms only in terms of fatigue versus placebo, without any demonstration for the other symptoms that can be associated with anaemia (in particular shortness of breath and palpitations);
- the absence of an expected benefit, in view of the mechanism of action of sutimlimab, on vasomotor signs affecting the extremities – among the dominant symptoms in CAD that can be very disabling for patients;

the Committee deems that ENJAYMO (sutimlimab) provides no clinical added value (CAV V) in the care pathway for the treatment of hemolytic anemia in adult patients with cold agglutinin disease (CAD) only in patients with Hb levels ≤ 10 g/dl.

Other situations of the MA indication (adult patients with Hb levels > 10 g/dl)

Not applicable.