SUMMARY

emicizumab

HEMLIBRA 30 and 150 mg/ml

solution for injection

Indication extension

Original French opinion adopted by the Transparency Committee on 10 May 2023

The legally binding text is the original French opinion version

Transparency Committee's conclusions

Clinical Benefit

- Haemophilia A is an X-linked, recessive, constitutional, genetic bleeding disorder resulting from a coagulation factor VIII deficiency. It is mainly characterised by spontaneous joint bleeding (haemarthrosis) and muscle bleeding (haematoma) or extensive bleeding after an injury. Irrespective of the severity of the haemophilia, the condition can be life-threatening in the event of internal bleeding, following injury or surgery.
- This is a preventive medicinal product.
- The efficacy/adverse effects ratio is high.
- In patients with moderate congenital haemophilia A with severe bleeding phenotype without factor VIII inhibitors, in whom long-term prophylaxis of bleeding episodes is indicated, HEMLIBRA (emicizumab) is a first-line treatment, in the same way as FVIII concentrates (see 5.1).

- **Public health benefit**

Considering:

- the seriousness of the disease and its low prevalence (orphan disease);
- the identified medical need partially met by FVIII concentrates;
- the partial response to the identified need given the expected additional impact on quality of life compared to FVIII concentrates and the potential impact on the organisation of care given the simplification of treatment (subcutaneous injections weekly, or every 2 or

4 weeks, versus intravenous infusions several times per week), not demonstrated at this stage by the data presented;
- but in the absence of a demonstrated additional impact on morbidity and mortality;

HEMLIBRA (emicizumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of HEMLIBRA 30 mg/ml and 150 mg/ml (emicizumab) solution for injection is substantial in the MA indication "prophylaxis of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency), without factor VIII inhibitors who have moderate disease (FVIII ≥ 1% and ≤ 5%) with severe bleeding phenotype".

The Committee issues a favourable opinion for inclusion of HEMLIBRA 30 mg/ml and 150 mg/ml (emicizumab) solution for injection in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and at the MA dosages.

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

Clinical Added Value

Considering:

- the efficacy of HEMLIBRA (emicizumab) observed in long-term prophylaxis in patients with moderate haemophilia A in the HAVEN 6 clinical study, in which the primary endpoint was assessment of safety, with an annualised bleeding rate (primary efficacy endpoint) estimated at 0.9 (CI95%, 0.50-1.78) with 68.6% of patients having had no treated bleeds,
- the low quality of this evidence given the study's major methodological limitations, in particular its open-label nature, with no control of sources of bias for estimation of the treated bleed rate, the purely descriptive nature of the results in the absence of any hypothesis with respect to the expected effect of emicizumab, and the small patient sample on which the assessment was based (data from a subgroup of 51 patients),
- uncertainties with respect to the representativity of the population included compared to that validated by the MA "patients with haemophilia A without factor VIII inhibitors, who have moderate disease with severe bleeding phenotype", given the high level of heterogeneity of the patients included, particularly in terms of bleeding profile, and the fact that the endogenous FVIII levels at the time of inclusion were not known for all these patients, which may have led to underestimation of the number of patients included with mild haemophilia,
- the absence of robust data enabling assessment of the benefit of prophylaxis with emicizumab in comparison with conventional factor VIII prophylaxis,

and despite:

- the expected benefit on quality of life due to the reduced burden of prophylactic treatment compared to FVIII,

The Committee deems that HEMLIBRA 30 mg/ml and 150 mg/ml (emicizumab) solution for injection provides no clinical added value (CAV V) in the current care pathway.