Original French opinion adopted by the Transparency Committee.

The legally binding text is the original French opinion version.

SUMMARY

concizumab

ALHEMO 15 mg/1.5 ml, 60 mg/1.5 ml, 150 mg/1.5 ml, 300 mg/3.0 ml,

Solution for injection in pre-filled pen

Inclusion on list

Adopted by the Transparency Committee on 2 September 2025

Summary of opinion

Favourable opinion for reimbursement only in prophylaxis for the prevention of bleeding episodes in patients with haemophilia B (congenital factor IX deficiency) with FIX inhibitors and aged 12 years and over.

Unfavourable opinion for reimbursement in the other situations covered by the MA indication.

Transparency Committee's conclusions

Clinical Benefit

Haemophilia A with inhibitor

- In patients with haemophilia A or B, the condition can be life-threatening in the event of bleeding, following injury or surgery. The occurrence of an inhibitor remains the most serious complication feared to date. It is manifested by an inadequate clinical response. The clinical impact depends on the inhibitor titre and its anamnestic response. This complication has a major impact in terms of vital and functional prognosis and quality of life, particularly for high-responder patients.
- This is a preventive medicinal product.
- The efficacy/adverse effects ratio of ALHEMO (concizumab) is inadequately established compared to the alternatives available for prophylaxis (emicizumab and bypass agents), which means that a loss of opportunity for the patient cannot be ruled out, either in terms of efficacy or safety, due notably to:
  - the absence of robust comparative data relative to these alternatives, particularly the conventional treatment HEMLIBRA (emicizumab), whose efficacy has been demonstrated more robustly in clinical trials and is now well established in clinical practice;

- uncertainties regarding the safety profile of concizumab, especially with regard to thrombo-embolic risk.

➔ In patients over 12 years of age with haemophilia A (congenital factor VIII deficiency) who have developed FVIII inhibitors, ALHEMO (concizumab) has no role in the therapeutic strategy in view of the available therapies.

➔ Public health benefit

Considering:

- the seriousness of the condition and its prevalence;
- the partially met medical need;
- the lack of response to the identified need, given:
  - the lack of evidence of an additional impact on morbidity and mortality and on quality of life;
  - the lack of evidence of an impact on the organisation of care, and the care and/or life pathway for patients or their families;

ALHEMO (concizumab) is unlikely to have an additional impact on public health.

Haemophilia B with inhibitor

➔ In patients with haemophilia A or B, the condition may be life-threatening in the event of bleeding, following injury or surgery. The occurrence of an inhibitor remains the most serious complication feared to date. It is manifested by an inadequate clinical response. The clinical impact depends on the inhibitor titre and its anamnestic response. This complication has a major impact in terms of vital and functional prognosis and quality of life, particularly for high-responder patients. The occurrence of an inhibitor in haemophilia B patients is frequently associated with an allergic or anaphylactic reaction and may be complicated by the onset of a nephrotic syndrome when immune tolerance is induced.

➔ This is a preventive medicinal product.

➔ The efficacy/adverse effects ratio is high.

➔ In patients over 12 years of age with haemophilia B (congenital factor IX deficiency) who have developed FIX inhibitors, ALHEMO (concizumab) is a first-line treatment in view of the available therapies.

➔ Public health benefits

Considering:

- the seriousness of the condition and its prevalence;
- the partially met medical need;
- the lack of response to the identified need, given:
  - the lack of evidence of an additional impact on morbidity and mortality and on quality of life;
  - the lack of evidence of an impact on the organisation of care, and the care and/or life pathway for patients or their families;

ALHEMO (concizumab) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of ALHEMO (concizumab), solution for injection in pre-filled pen, is:

- **substantial in prophylaxis for the prevention of bleeding episodes in patients suffering from haemophilia B (congenital factor IX deficiency) with FIX inhibitors and aged 12 and over. The Committee has made the maintenance of the substantial clinical benefit conditional on its reassessment within a maximum period of three years, based on the final results of the EXPLORER 7 study assessing the longer-term efficacy and safety of ALHEMO (end of study planned for February 2027), the data from the PUT-RD (Therapeutic Use Protocol-Data Collection) and any new data available.**
- **insufficient to justify public funding in view of the available alternatives in the other situations covered by the MA for prophylaxis to prevent bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors and aged 12 or over.**

The Committee issues the following opinion:

- **favourable for inclusion of ALHEMO (concizumab), solution for injection in pre-filled pen, in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use only within the scope retained and at the MA dosages.**
- **unfavourable for inclusion of ALHEMO (concizumab), solution for injection in pre-filled pen in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the other situations covered by the MA indication.**

➔ **Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%**

Clinical Added Value

Considering:

- the evidence of the superiority of prophylaxis with concizumab alone versus no prophylaxis (on-demand treatment with bypassing agents) in reducing the number of bleeding episodes in 52 randomised adult and adolescent patients aged 12 years and over with haemophilia A or B with inhibitors;
- the sub-optimal quality of this demonstration, raising uncertainties about the observed benefit, which may be overestimated;
- the lack of robust comparative data relative to prophylaxis using bypass agents;
- uncertainties regarding the safety profile of concizumab, especially with regard to thromboembolic risk;
- the absence of long-term data;

The Committee considers that ALHEMO (concizumab), solution for injection in pre-filled pen, provides no clinical added value (CAV V) in the current care pathway for prophylaxis for the prevention of bleeding episodes in patients with haemophilia B (congenital factor IX deficiency) with FIX inhibitors and aged 12 years or more, which includes the relevant comparators (NOVOSEVEN (rFVIIa) and FEIBA (CCPa)).