HAUTE AUTORITÉ DE SANTÉ

ASSESSING HEALTH TECHNOLOGIES

OPINION ON MEDICINAL PRODUCTS

(eptacog beta - FVIIa)

CEVENFACTA 1 mg, 2 mg and 5 mg,

powder and solvent for solution for injection

First assessment

Adopted by the Transparency Committee on 18 January 2023

SUMMARY

The legally binding text is the original French opinion version

Key points

Disapproval of reimbursement for the marketing authorisation indication:

"CEVENFACTA is indicated for adult and adolescent patients (aged 12 years and over) for the treatment of bleeding episodes and for the prevention of bleeds occurring during surgery or invasive procedures in the following patient cohorts:

- High-responder patients with congenital haemophilia with high-titre clotting factor VIII or IX inhibitors (i.e. titre ≥5 Bethesda units (BU));
- Patients with congenital haemophilia with low-titre inhibitors (BU <5), but for whom a strong response to the administration of factor VIII or factor IX is expected, or who may be refractory to increasing the FVIII or FIX dose"

Role in therapeutic strategy?

Timely control of spontaneous or trauma-induced bleeding events is key in delaying and/or preventing irreversible tissue and joint damage.

For haemophilia patients with inhibitors, the therapeutic options available to treat bleeds or prevent them from occurring during surgery are limited. They essentially consist of “bypass” agents:

- rFVIIa (NOVOSEVEN) and CCPa (FEIBA). The rFVIIa available, NOVOSEVEN, can be used as a first-line treatment in these contexts.
- the use of CCPa (FEIBA) is limited, in accordance with its marketing authorisation, to haemophilia A and B patients exhibiting high-responder inhibitors, as a first-line treatment for haemophilia A, and only in the event of failure to respond to rFVIIa for haemophilia B patients (risk of anamnestic boost of inhibitors).

Note that the availability in 2019 of emicizumab (HEMLIBRA), a medicinal product indicated for the long-term prophylaxis of haemophilia A patients in the presence of anti-FVIII inhibitors, has required adaptation of the care regimen for bleeds, suspected bleeds, and for emergency or scheduled invasive procedures. This has led to the drafting of proposals, by various learned societies in consultation, in respect of the care of haemophilia A patients with inhibitors. For haemorrhagic accident treatment, tranexamic acid is proposed as a first-line treatment alone for isolated mucosal bleeding and rFVIIa for major bleeding as defined by ISTH criteria. For surgical procedures for which the bleeding risk is deemed to be minor and in the absence of any added bleeding risk, it is proposed to envisage prescribing an additional haemostatic medicinal product such as rFVIIa (NOVOSEVEN). rFVIIa is a first-line treatment for major surgical procedures and in the event of postoperative bleeding that is deemed to be abnormal in the context of minor surgery. The role of CCPa is restricted to cases of inefficacy of rFVIIa or human FVIII or where FVIII cannot be used, under strict clinical and biological medical monitoring, on account of the synergistic action and risk of thrombotic microangiopathy when CCPa and emicizumab are used concomitantly

Role of the medicinal product

Considering:

- The insufficient clinical efficacy data available to establish its efficacy in the treatment of major bleeding and in the prevention of bleeding during major surgical procedures; moreover, there are weaknesses in the evidence of its efficacy in the treatment of minor to moderate episodes,
- The need partially met by the alternatives available, in particular the rFVIIa NOVOSEVEN for which significant follow-up of use is available (used in France since 1996), and which offers the advantage of being suitable for use in children under 12 years, unlike CEVENFACTA (eptacog beta - rFVIIa) for which marketing authorisation was denied due to lack of evidence of efficacy in the PERSEPT-2 study,
- The inability, due to a lack of comparative data, to rule out a loss of chance for patients with CEVENFACTA (eptacog beta - rFVIIa) compared to the use of the rFVIIa already available (NOVOSEVEN),
- And despite an acceptable safety profile,

the Committee deems that CEVENFACTA (eptacog beta - rFVIIa) has no role in the current therapeutic strategy.

Committee's conclusions

Clinical Benefit

- Haemophilia is a disease associated with potentially major bleeds, which can cause incapacitating clinical manifestations. The onset of an inhibitor can give rise to more frequent hospitalisation and accelerated osteoarticular damage resulting in impaired quality of life and an increased therapeutic burden.
- The proprietary medicinal product CEVENFACTA (eptacog beta - rFVIIa) is a curative and preventive medicinal product.
- The efficacy/adverse effect ratio is considered to be poorly defined on account of:
  - Insufficient clinical data to establish its efficacy in the treatment of major bleeds (only 3 of the 468 bleeds treated, analysed descriptively) and in the context of major surgery (only 5 major surgical procedures assessed, including 2 failures to respond to treatment); moreover, there are weaknesses in the evidence of its efficacy in the treatment of minor to moderate episodes (non-conservative primary analysis, partially subjective nature of the primary outcome measure in an open-label study context essentially relating to non-major bleeds, etc.),
  - And despite an acceptable safety profile.
- Therapeutic alternatives are available (NOVOSEVEN recombinant activated FVII and FEIBA activated CCP).
- CEVENFACTA (eptacog beta - rFVIIa) has no role in the therapeutic strategy (see Section 8).

Public health benefit

Considering:

- the severity of the disease and its low prevalence,
- the identified partially met medical need,
- the lack of response to the identified need considering the lack of the evidence of an additional impact on morbidity-mortality or on quality of life,
- the lack of expected additional impact on the care and/or life pathway, or on delivery of care,

CEVENFACTA (eptacog beta - rFVIIa) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the actual clinical benefit of CEVENFACTA (eptacog beta - FVIIa) is insufficient in the marketing authorisation indication to justify public funding in view of the alternatives available.

The Committee disapproves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for the indications and at the dosages of the marketing authorisation.