HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

16 DECEMBER 2020

The legally binding text is the original French opinion version

catridecacog

NOVOTHIRTEEN 2,500 IU powder and solvent for solution for injection

First assessment

Key points

Favourable opinion for reimbursement in long-term prophylaxis of bleeding in patients with congenital Factor XIII A-subunit deficiency.

What therapeutic improvement?

No clinical added value compared to FIBROGAMMIN human plasma-derived factor XIII.

Role in the care pathway?

Therapeutic management is based on fresh frozen plasma and on FIBROGAMMIN human plasma-derived FXIII concentrate.

Bleeding episodes can be treated with factor XIII concentrate or, otherwise, with frozen fresh plasma.

Prophylactic replacement therapy with factor XIII concentrate is generally initiated in all diagnosed patients, often from the first inaugural bleeding episode, to prevent the most frequent and most serious bleeding, more particularly intracranial bleeding, which can occur spontaneously from childhood. In the absence of prophylaxis during pregnancy, the risk of spontaneous miscarriage is very high.

In practice, the use of fresh frozen plasma (FFP) is limited - and very rarely used prophylactically - as long-term treatment due to the long duration of the injections and the risk of volume overload and allergic reactions (large number of substances in addition to factor XIII). The advantages of FIBROGAMMIN compared to FFP are the FXIII concentration (62.5 IU/mL versus 1 IU/ml in FFP) making it possible to administer smaller volumes, the high degree of viral safety ensured by pasteurisation, and the good tolerance of the concentrate.

Role of the medicinal product in the care pathway

NOVOTHIRTEEN (catridecacog) is an alternative to the only FXIII concentrate currently available, FIBROGAMMIN, for the long-term prophylaxis of bleeding in patients with congenital Factor XIII A-subunit deficiency. Both are administered once monthly.

NOVOTHIRTEEN (catridecacog) is the first recombinant FXIII concentrate and therefore offers the advantage of a higher degree of safety compared to blood-derived products, such as FIBROGAMMIN, which expose patients to a potential risk of transmission of infectious diseases.

In addition, this recombinant FXIII is significantly more concentrated than the plasma-derived FXIII (FIBROGAMMIN) available (833 IU/ml versus 62.5 IU/ml after reconstitution), enabling the injection of a smaller volume and administration as a bolus injection. However, given this high concentration, for young children weighing less than 24 kg it is necessary to dilute the solution after reconstitution to allow the necessary dose to be taken, and consequently to use another volume calculation formula to be taken to that used in patients with a higher bodyweight.

It should be highlighted that NOVOTHIRTEEN (catridecacog) is only intended for the management of patients with FXIII A-subunit deficiency, unlike FIBROGAMMIN, which is also indicated in patients with B-subunit deficiency. Although A-subunit deficiency is largely more common (around 95% of cases), it is necessary to identify the type of subunit missing before using catridecacog to ensure that this concentrate is appropriate. This identification is currently not systematic across in all centres treating these patients.

The Committee recalls that, in accordance with the SPC, the data are very limited in pregnant women. Consequently, it considers that the use of NOVOTHIRTEEN (catridecacog) should only be considered if duly justified and following multidisciplinary discussion.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Factor XIII deficiency is a very rare congenital disease, characterised by bleeding episodes that likely to lead to a life-threatening prognosis.
◗ NOVOTHIRTEEN (catridecacog) is a preventive treatment for bleeding episodes.
◗ The efficacy/adverse effects ratio is high.
◗ There is a drug alternative for long-term prophylaxis: a human plasma-derived factor XIII (FIBROGAMMIN).
◗ This is a first-line treatment.

Public health impact:

Considering:
- the seriousness of the disease,
- its very low prevalence,
- the partially met medical need,
- the partial response to the identified need,
- the expected impact on the care and life pathway due to the method of production of this FXIII using a recombinant DNA technique, which presents the advantage of a better degree of viral safety and a reduction in injection volume and time needed compared to FIBROGAMMIN human plasma-derived FXIII,
- but in the absence of any demonstrated additional impact to date compared to FIBROGAMMIN in terms of morbidity and mortality and quality of life,

NOVOTHIRTEEN (catridecacog) is unlikely to have an additional impact on public health.

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

The Committee issues a favourable opinion for 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 demonstration of the efficacy of NOVOTHIRTEEN (catridecacog) on a clinically relevant endpoint (annualised rate of bleeding episodes requiring FXIII treatment) for prophylactic treatment in patients with congenital factor XIII A-subunit deficiency in two non-comparative phase 3 studies,**
- **its satisfactory safety profile, and**
- **its production process using a recombinant DNA technique, which provides a higher degree of safety for patients than the human plasma-derived FXIII concentrate currently available (FIBROGAMMIN),**

But taking into account:
- **the lack of comparative data versus FIBROGAMMIN,**
- **the absence of quality of life assessment for patients receiving this prophylactic treatment long term,**

the Committee considers that NOVOTHIRTEEN (catridecacog) provides no clinical added value (CAV V) compared to FIBROGAMMIN (human plasma-derived FXIII) in the prophylactic treatment of congenital factor XIII A-subunit deficiency.