HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY
7 JULY 2021

The legally binding text is the original French opinion version

human coagulation factor X
COAGADEX 250 IU and 500 IU powder and solvent for solution for injection

First assessment

Key points

Favourable opinion for reimbursement in the treatment and prophylaxis of bleeding episodes and for perioperative management in patients with hereditary factor X deficiency.

What therapeutic improvement?

Therapeutic improvement in the management of the condition.

Role in the care pathway?

The management of patients with hereditary factor X deficiency is determined by the severity of the disease and the associated bleeding risk. Therapies used to treat or prevent bleeding include non-specific medications (antifibrinolytics for mucous membrane bleeding, hormonal treatments to control menorrhagia) and factor X replacement therapy.

On-demand treatment for bleeding is sometimes sufficient, when bleeding is rare and non-severe, but variable-term prophylaxis may be indicated, for example in patients having presented a life-threatening haemorrhage, those presenting spontaneous bleeding such as haemarthrosis, women whose menstrual periods cannot be or are not controlled by other treatments (hormones, antifibrinolytics), or in pregnant women having presented obstetric complications associated with their deficiency.

Where it is necessary, factor X replacement therapy is therefore based on the administration of human prothrombin complex concentrate (PCC) or frozen fresh plasma (FFP), for which the MA in hereditary coagulation factor deficiency is limited to situations in which the specific coagulation factor is not available. These treatment options contain other coagulation factors in addition to the deficient FX and do not contain a precise factor X concentration. PCCs are more specifically associated with a potential risk of thrombosis, particularly in the event of repeated administration, and FFPs with a risk of fluid overload and hypersensitivity.

There are no French guidelines for the management of hereditary FX deficiencies. The international guidelines, in particular, those of the World Federation of Haemophilia, recommend the administration of specific coagulation factor concentrates where these are available and, in their absence, human prothrombin complex concentrate or frozen fresh plasma.

Role of the medicinal product in the care pathway

COAGADEX (human coagulation factor X), the only purified factor X concentrate to have a MA, is the first-line treatment for hereditary factor X deficiencies requiring replacement therapy.

Unlike PCC and FFP - the treatment options currently used in the absence of a purified specific factor - COAGADEX (human coagulation factor X) corrects only the factor X deficiency and therefore avoids the unnecessary administration of other coagulation factors. In addition, COAGADEX (human coagulation factor X) presents the advantage of having a precise formulation (100 IU/ml of factor X after reconstitution) and a low injection volume, which also reduces injection times.

The patients who could derive the greatest benefit from this treatment are those exposed to repeated administration of factor X, in whom the administration of PCC could lead to an increased thrombotic risk due to accumulation of other factors with a long half-life (mainly prothrombin, which has a half-life twice as long as that of factor X). The fact that caregivers and patients are less concerned about the thrombotic risk and the shorter injection times could also facilitate the initiation of prophylaxis when this is deemed necessary.

It is regrettable that there is no clinical data concerning use during pregnancy, a situation in which the administration of COAGADEX (human FX) should not therefore be considered unless absolutely necessary, in accordance with the SPC. In fact, in pregnant women with severe factor X deficiency for whom prophylaxis may be justified due to the risk of obstetric complications and given the fact that pregnancy is by its very nature a prothrombotic condition, it would be more convenient to implement treatment with a purified factor X than with a mixture of factors.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Hereditary coagulation factor X deficiency is a rare disease, characterised by bleeding episodes that can be life-threatening.

◗ The proprietary medicinal product COAGADEX (human coagulation factor X) is a preventive or curative replacement therapy.

◗ The efficacy/adverse effects ratio is high.

◗ COAGADEX (human coagulation factor X) is the only purified factor X concentrate with a MA in France. The available therapeutic alternatives (PCC and FFP) do not enable specific administration of factor X and their use is reserved for situations in which no specific coagulation factor concentrate is available.

◗ It is a first-line treatment for hereditary factor X deficiencies requiring replacement therapy.

Public health impact

Considering:

- the seriousness of the disease and its very low prevalence,
- the unmet medical need to have access to purified factor X concentrates,
- the response provided to the identified need with:
    - an expected impact on morbidity and quality of life, particularly for patients requiring long-term prophylaxis, related to potential improvements in care conditions thanks to exclusive administration of factor X, at a precise dosage, and with reduced injection volumes and times compared to the treatments currently used (PCC and FFP, which involve the administration of other unnecessary and potentially thrombogenic coagulation factors, particularly in the event of repeated administrations, and do not enable precise titration of factor X). It should be noted that this impact is not currently demonstrated.
    - an expected impact on the patient's care pathway related to the characteristics of this purified and precisely titrated factor, which may facilitate compliance with treatment and the initiation of prophylaxis when this is deemed necessary,

COAGADEX (human FX) is likely to have an impact on public health.

Given all these elements, the Committee deems that the clinical benefit of COAGADEX (human FX) 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 "treatment and prophylaxis of bleeding episodes and for perioperative management in patients with hereditary factor X deficiency" and at the MA dosages.

Clinical Added Value

Considering:
- The unmet need to have access to highly purified specific coagulation factors, the reference replacement therapies recommended in hereditary coagulation factor deficiencies,
- Available clinical data demonstrating the efficacy of COAGADEX (human coagulation factor X) to prevent and treat bleeding,
- The satisfactory safety profile although the data is limited, in particular the absence of thrombotic events and anti-FX inhibitors during clinical studies,
- The expected impact on morbidity and patients' quality of life, particularly in long-term prophylaxis, related to the potential improvement in care conditions thanks to exclusive administration of factor X, at a precise dosage, and with reduced injection volumes and times compared to the treatments currently available (PCC and FFP, which involve the administration of other unnecessary and potentially thrombogenic coagulation factors, particularly in the event of repeated administrations, and do not enable precise titration of factor X),

The Committee considers that COAGADEX (human coagulation factor X) provides a moderate clinical added value (CAV III) in the care pathway for the treatment and prophylaxis of bleeding episodes and for perioperative management in patients with hereditary factor X deficiency.