SUMMARY

human protein C

CEPROTIN 500 IU/5 mL and 1,000 IU/10 mL,

powder and solvent for solution for injection

Indication extension

Original French opinion adopted by the Transparency Committee on 19 July 2023

The legally binding text is the original French opinion version

Transparency Committee's conclusions

Clinical Benefit

- This is a preventive medicinal product.
- The efficacy/adverse effects ratio is high given the available study results in favour of the efficacy of human protein C in the long-term prophylaxis of thrombotic events in patients with severe congenital protein C deficiency, despite the absence of robust and demonstrative data (exploratory endpoint in the pivotal study and observational studies).
- The product is a first-line treatment in view of the therapies available for the long-term prophylaxis of thrombotic events in patients with severe congenital protein C deficiency (see 5.1).

Public health benefit

Considering:

- the seriousness of the disease and its very low prevalence;
- the medical need partially met by protein C concentrates used off-label;
- the partial response to the identified need:
  - with an additional impact of CEPROTIN (human protein C) on morbidity and mortality and on quality of life that has not been demonstrated to date, but for which the Committee highlights the development efforts in a very rare disease, which provide a framework for the off-label use cited in the recommendations;

- the lack of evidence of an additional impact on the organisation of care and the patient's life pathway;

CEPROTIN (human protein C) 500 IU/5 mL and 1,000 IU/10 mL powder and solvent for solution for injection is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of CEPROTIN (human protein C) 500 IU/5 mL and 1,000 IU/10 mL powder and solvent for solution for injection is substantial in the long-term prophylaxis of *purpura fulminans,* coumarin-induced skin necrosis and venous thrombotic events in patients with severe congenital protein C deficiency.

The Committee issues a favourable opinion for inclusion of CEPROTIN (human protein C) 500 IU/5 mL and 1,000 IU/10 mL powder and solvent for solution for injection in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the long-term prophylaxis of *purpura fulminans,* coumarin-induced skin necrosis and venous thrombotic events in patients with severe congenital protein C deficiency, 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:

- data suggesting the efficacy of CEPROTIN (human protein C) in the long-term prophylaxis of acute thrombotic episodes in patients with severe congenital protein C deficiency, given the absence of episodes of purpura fulminans and thrombotic episodes observed in the study over the prophylaxis period with an average duration of 7 months (exploratory endpoint of the phase II/III study - 400101 - part 3),
- the safety profile, which is already known and deemed to be acceptable,
- the medical need partially met by the available protein C concentrates used off-label in this indication,

but given:

- the low level of evidence of the available efficacy and quality of life data (descriptive, open-label, non-randomised study of short duration),
- uncertainties with respect to safety in view of the limited long-term data in the studies supplied, in a context in which this treatment can be used for life,

the Transparency Committee deems that CEPROTIN (human protein C) 500 IU/5 mL and 1,000 IU/10 mL powder and solvent for solution for injection provides a minor clinical added value (CAV IV) in the care pathway for the long-term prophylaxis of *purpura fulminans,* coumarin-induced skin necrosis and venous thrombotic events in patients with severe congenital protein C deficiency.