PRIOR AUTHORIZATION POLICY

POLICY: Hematology – Ceprotin Prior Authorization Policy
- Ceprotin® (protein C concentrate [human] intravenous infusion – Takeda)

REVIEW DATE: 12/04/2024

OVERVIEW

Ceprotin is indicated for **severe congenital protein C deficiency** for the prevention and treatment of venous thrombosis and purpura fulminans in neonates, pediatric and adult patients.[1]

Disease Overview

Severe congenital protein C deficiency is an autosomal recessive disorder associated with biallelic loss-of-function variants in the protein C (*PROC*) gene which result in a deficiency of protein C, a natural anticoagulant.[2-4] The predicted incidence is 1 per 4 million births.[2] The prevalence is likely lower due to early fetal death or undiagnosed neonatal deaths. The condition typically presents with purpura fulminans and disseminated intravascular coagulation within 72 hours of birth, but may occur in later infancy. Many infants experience retinal and cerebral vessel thrombosis. The normal adult range for plasma protein C levels is 0.65 to 1.35 IU/mL. In severe congenital protein deficiency, protein C levels by definition are < 0.01 IU/mL and are often undetectable. In some cases, biallelic *PROC* variants results in moderate reduction of protein C levels (0.01 to 0.2 IU/mL) and may present in infancy with purpura fulminans or in adolescence or adults with recurrent various thromboembolic disease. Diagnosis is based on characteristic symptoms and detailed family history, in addition to measurement of protein C activity or antigen levels.[3] It is critical to exclude any acquired reason for protein C deficiency, which is more common than congenital protein C deficiency.[2,3] Potential causes of acquired deficiency include vitamin K antagonists (e.g., warfarin), vitamin K deficiency, chronic liver disease, severe infection, or disseminated intravascular coagulopathy.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Ceprotin. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Ceprotin as well as the monitoring required for adverse events and long-term efficacy, approval requires Ceprotin to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ceprotin is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Protein C Deficiency, Severe.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D)
   A) The diagnosis of protein C deficiency is confirmed by at least ONE of the following (i, ii, or iii):

i. Plasma protein C activity below the lower limit of normal based on the age-specific reference range for the reporting laboratory; OR
ii. Plasma protein C antigen below the lower limit of normal based on the age-specific reference range for the reporting laboratory; OR
iii. Genetic testing demonstrating biallelic pathogenic variants in the *PROC* gene; AND

B) Acquired causes of protein C deficiency have been excluded; AND
Note: Examples of acquired causes of protein C deficiency include recent use of vitamin K antagonists (e.g., warfarin) within 30 days, vitamin K deficiency, chronic liver disease, recent thrombosis, recent surgery, or disseminated intravascular coagulation.

C) According to the prescriber, patient has a current or prior of symptoms associated with severe protein C deficiency (e.g., purpura fulminans, thromboembolism); AND

D) Ceprotin is being prescribed by or in consultation with a hematologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Ceprotin is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Ceprotin® intravenous infusion [prescribing information]. Lexington, MA: Takeda; March 2023.
2. Minford A, Brandao LR, Othman M, et al. Diagnosis and management of severe congenital protein C deficiency (SCPCD): communication from the SCC of the ISTH. *J Thromb Haemost*. 2022;20:1735-1743.
3. Cooper PC, Pavlova A, Moore GW, et al. Recommendations for clinical laboratory testing for protein C deficiency, for the subcommittee on plasma coagulation inhibitors of the ISTH. *J Thromb Haemost*. 2020;18(2):271-277.
4. Siffel C, Wadhwa A, Tongbram V, et al. Comprehensive literature review of protein C concentrate use in patients with severe congenital protein C deficiency. *Res Pract Thromb Haemost*. 2024;8:e102542.