PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 11/02/2022

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

Disease Overview
Mutations in the *PROC* gene lead to deficiency of protein C, which is a natural anticoagulant.[2] Individuals with heterozygous *PROC* mutation present with milder disease but are at risk for development of venous thromboembolism. Those who have mutations in both *PROC* genes develop severe symptoms within a few hours to days after birth. In severe protein C deficiency, a complication called purpura fulminans may arise in which blood clots form throughout the body. Blood clots affect the extremities most often but can become widespread (disseminated intravascular coagulation), leading to tissue necrosis.

Diagnosis is based on characteristic symptoms and detailed family history, in addition to measurement of protein C activity or antigen levels.[3,4] It is critical to exclude any acquired reason for protein C deficiency, which is more common than congenital protein C deficiency.[3] Potential causes of acquired deficiency include vitamin K antagonists (e.g., warfarin), vitamin K deficiency, chronic liver disease, recent thrombosis, recent surgery, or disseminated intravascular coagulation. Diagnostic recommendations from the International Society of Thrombosis and Hemostasis recommend waiting until 30 days after vitamin K antagonist treatment ends to perform protein C assay testing.[4] Molecular genetic testing is only available in a few research laboratories and is not routinely used in clinical diagnosis.[3]

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 the following criteria (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 mutations 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: Baxalta/Shire; August 2021.
2. Protein C Deficiency. National Organization of Rare Disorders. Updated 2016. Available at: https://rarediseases.org/rare-diseases/protein-c-deficiency/. Accessed on October 28, 2022.
3. Dinarvand P, Moser KA. Protein C deficiency. *Arch Pathol Lab Med*. 2019 Oct;143(10):1281-1285.
4. 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 Feb;18(2):271-277.