CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hematology – Ceprotin Utilization Management Medical Policy
- Ceprotin® (protein C concentrate [human] intravenous infusion – Takeda/Baxalta)

REVIEW DATE: 12/10/2025

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.

Dosing Information

Dosing is highly individualized. The National Hemophilia Foundation Medical and Scientific Advisory Council (MASAC) provides recommendations regarding doses of clotting factor concentrate in the home (2016).[5] The number of required doses varies greatly and is dependent on the severity of the disorder and the prescribed regimen. Per MASAC guidance, patients on prophylaxis should also have a minimum of one major dose and two minor doses on hand for breakthrough episodes in addition to the prophylactic doses used monthly. The guidance also notes that an adequate supply of clotting factor concentrate is needed to accommodate weekends and holidays. Therefore, maximum doses in this policy allow for prophylactic dosing plus three days of acute episodes or perioperative management per 28 days. Doses exceeding this quantity will be reviewed on a case-by-case basis by a clinician.

Dosing considerations for individual indications are as follows:

- **Protein C Deficiency, Severe:** For long-term prophylaxis, the maintenance dose is 45 IU/kg to 60 IU/kg once every 12 hours by intravenous infusion.[1] For acute episodes or short-term prophylaxis, the prescribing information recommends an initial dose of 100 IU/kg to 120 IU/kg by intravenous infusion. The subsequent three doses should be 60 IU/kg to 80 IU/kg once every 6 hours by intravenous infusion. The maintenance dose is 45 IU/kg to 60 IU/kg once every 6 to 12 hours.[1]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Ceprotin. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). 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

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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 history 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.

   Dosing. Approve up to 4,440 IU/kg intravenously per 28 days.

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]. Cambridge, MA: Takeda/Baxalta; September 2024.
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.
5. MASAC (Medical and Scientific Advisory Council) recommendations regarding doses of clotting factor concentrate used in the home. MASAC Document #242. Adopted on June 7, 2016. Available at: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendations-Regarding-Doses-of-Clotting-Factor-Concentrate-in-the-Home. Accessed on December 7, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/08/2023
Annual Revision	**Protein C Deficiency, Severe:** The word "mutations" was changed to "pathogenic variants".	12/04/2024
Annual Revision	No criteria changes.	12/10/2025