Drug Coverage Policy

Effective Date.....3/15/2025
Coverage Policy Number.....IP0342
Policy Title.....Hematology - Ceprotin

Hematology – Ceprotin

- Ceprotin® (protein C concentrate [human] intravenous infusion – Baxalta/Shire)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Medical Necessity Criteria

Ceprotin is considered medically necessary when the following criteria are met:

1. **Protein C Deficiency, Severe.** Individual meets **ALL** of the following criteria:
   A. Documented diagnosis of protein C deficiency is confirmed by documentation of **ONE** of the following:
      i. Plasma protein C activity below the lower limit of normal based on age-specific reference range for the reporting laboratory
      ii. Plasma protein C antigen below the lower limit of normal based on age-specific reference range for the reporting laboratory
      iii. Genetic testing demonstrating biallelic pathogenic variants in the PROC gene

B. Acquired causes of protein C deficiency have been excluded (for example, recent use of vitamin K antagonists within 30 days, vitamin K deficiency, chronic liver disease, recent thrombosis, recent surgery or disseminated intravascular coagulation)
C. Current or prior history of symptoms associated with severe protein C deficiency (for example, purpura fulminans, thromboembolism)
D. Medication is prescribed by or in consultation with a hematologist

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

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Continuation of Ceprotin is considered medically necessary for Protein C Deficiency, Severe when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J2724	Injection, protein C concentrate, intravenous, human, 10 IU

Background

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 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 to 120 IU/kg by intravenous infusion. The subsequent three doses should be 60 to 80 IU/kg once every 6 hours by intravenous infusion. The maintenance dose is 45 to 60 IU/kg once every 6 to 12 hours.[1]

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.
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 November 27, 2024.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	• No criteria change • Updated coverage policy title	5/1/2024

	• Added dosing information	
Selected Revision	No criteria changes	3/15/2025

The policy effective date is in force until updated or retired.