Clinical Policy: Protein C Concentrate, Human (Ceprotin)

Reference Number: CP.PHAR.330
Effective Date: 03/17
Last Review Date: 03/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of these criteria is to ensure that patients follow selection elements established by Centene® clinical policy for Protein C concentrate, human (Ceprotin®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Ceprotin is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Congenital Protein C Deficiency (must meet all):

1. Prescribed by or in consultation a hematologist or physician with expertise in inherited thrombophilias*;
2. Diagnosis of severe congenital protein C deficiency and one of the following (a or b):
   a. Prescribed for use in an acute setting**;
   b. Lab result confirming low protein C activity (due to low protein C levels or function or both).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 – Global Biopharm Policy.

II. Continued Approval

A. Congenital Protein C Deficiency (must meet all):

1. Previously received this medication via Centene benefit or member has previously met all initial approval criteria;
2. Documentation supports a positive response to therapy;
3. If not previously determined, lab result confirms low protein C activity (due to low protein C levels or function or both)

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

**Common causes of inherited thrombophilias include Factor V Leiden, prothrombin gene mutation, and deficiencies in protein S, protein C, and antithrombin.*

***Treatment should not be delayed by testing requirements in the acute setting nor should testing be performed in the presence of acute thrombosis or initial anticoagulation therapy (at least three months) as these factors will influence the results.*

Background

Description/Mechanism of Action:

Ceprotin (Protein C Concentrate [Human]) is manufactured from human plasma purified by a combination of filtration and chromatographic procedures, including a column of immobilized mouse monoclonal antibodies on gel beads.

Protein C is the precursor of a vitamin K-dependent anticoagulant glycoprotein (serine protease) that is synthesized in the liver. It is converted by the thrombin/thrombomodulin-complex on the endothelial cell surface to activated Protein C (APC). APC is a serine protease with potent anticoagulant effects, especially in the presence of its cofactor protein S. APC exerts its effect by the inactivation of the activated forms of factors V and VIII, which leads to a decrease in thrombin formation. APC has also been shown to have profibrinolytic effects.

The Protein C pathway provides a natural mechanism for control of the coagulation system and prevention of excessive procoagulant responses to activating stimuli. A complete absence of protein C is not compatible with life. A severe deficiency of this anticoagulant protein causes a defect in the control mechanism and leads to unchecked coagulation activation, resulting in thrombin generation and intravascular clot formation with thrombosis.

Formulations:

Ceprotin (Protein C concentrate [human]) is a lyophilized powder* for IV injection available in the following nominal product strengths:

- 500 IU** per vial
- 1000 IU** per vial

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**For reconstitution with Sterile Water for Injection to a concentration of 100 IU/mL of Ceprotin.*
***One international unit (IU) of protein C corresponds to the amidolytically measured activity of protein C in 1 mL of normal plasma.*

FDA Approved Indications:

Ceprotin is a Protein C concentrate (human)/intravenous formulation indicated for:

- Pediatric and adult patients with severe congenital Protein C deficiency for the prevention and treatment of venous thrombosis and purpura fulminans.

Appendices

Appendix A: Abbreviation Key

APC: activated Protein C

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-

date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.183.Excellus Other Specialty Pharmacy. Added that prescriber with expertise in inherited thrombophilias may treat in addition to hematologist. Added a pathway to approval for presumptive diagnosis in acute setting. Extended approval criteria to 6 months for initial treatment.	02/17	03/17

References

1. Ceprotin prescribing information. Westlake Village, CA: Baxalta US, Inc.; September 2015. Available at http://www.shirecontent.com/PI/PDFs/CEPROTINPATIENT_USA_ENG.pdf. Accessed February 27, 2017.
2. Bauer KA. Screening for inherited thrombophilia in asymptomatic individuals. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.UpToDate.com. Accessed February 27, 2017.
3. Bauer KA. Protein C deficiency. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.UpToDate.com. Accessed February 27, 2017.
4. Stevens SM, Woller SC, Bauer KA, et al. Guidance for the evaluation and treatment of hereditary and acquired thrombophilia. J Thromb Thrombolysis. January 2016; 41(1): 154-164.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.