

Clinical Policy: Antithrombin III (Thrombate III, Atryn)

Reference Number: CP.MP.179

Last Review Date: 10/19

[Coding Implications](#)

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Description

Medical necessity criteria for Antithrombin III (Thrombate III[®] and Atryn[®]).

Policy/Criteria

- I. It is the policy of health plans affiliated with Centene Corporation[®] that antithrombin III is **medically necessary** for the following indications:
 - A. Diagnosis of hereditary antithrombin deficiency and one of the following:
 1. Treatment or prevention of thromboembolism and human-derived antithrombin III (Thrombate III) is requested;
 2. Prevention of peri-operative and peri-partum thromboembolism and recombinant antithrombin III (Atryn) or Thrombate III is requested.
- II. It is the policy of health plans affiliated with Centene Corporation that Antithrombin III (Thrombate III or Atryn) is **not medically necessary** for all other indications, including but not limited to, disseminated intravascular coagulation (DIC) associated with sepsis or trauma.

Background

Deficiency of antithrombin III, also known as antithrombin, can be inherited or acquired, and is associated in some patients with a heightened risk of thromboembolism. Antithrombin can be replaced in patients who are deficient, but questions remain regarding the benefits, risks, and appropriate indications for use.

Thrombate

FDA-approved indications for Thrombate include the following:

Patients with hereditary antithrombin deficiency for:

- Treatment and prevention of thromboembolism
- Prevention of peri-operative and peri-partum thromboembolism

Atryn

FDA-approved indications for Atryn include prevention of peri-operative and peri-partum thromboembolic events in hereditary antithrombin deficient patients.

Antithrombin for disseminated intravascular coagulation (DIC)

In addition to the FDA-approved indications, antithrombin has been suggested for treatment of patients with DIC associated with trauma or sepsis. However, 2009 British guidelines for the diagnosis and management of DIC do not recommend antithrombin in patients with DIC without further prospective evidence in randomized controlled trials.³ More recent studies have not found clear benefit of antithrombin in treatment of DIC. A 2016 Cochrane review of antithrombin

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administration in critically ill patients concluded that there is insufficient evidence to support its use in any category of such patients, including those with sepsis and DIC.⁴

HCPCS Codes	Description
J7196	Injection, antithrombin recombinant, 50 IU
J7197	Antithrombin III (human), per IU

Reviews, Revisions, and Approvals	Date	Approval Date
Policy developed	10/19	10/19

References

1. Grifols Therapeutics LLC. Thrombate III prescribing information. Research Triangle Park, NC. January 2019.
2. GTC Biotherapeutics, Inc. ATryn prescribing information. Framingham Massachusetts. November 2010.
3. Levi M1, Toh CH, Thachil J, Watson HG. Guidelines for the diagnosis and management of disseminated intravascular coagulation. British Committee for Standards in Haematology. Br J Haematol. 2009 Apr;145(1):24-33.
4. Allingstrup M, Wetterslev J, Ravn FB, Møller AM, Afshari A. Antithrombin III for critically ill patients. Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD005370.
5. Warren BL, Eid A, Singer P, et al. Caring for the critically ill patient. High-dose antithrombin III in severe sepsis: a randomized controlled trial. JAMA 2001; 286:1869.
6. Leung L LK. Clinical features, diagnosis, and treatment of disseminated intravascular coagulation in adults. UpToDate. Mannuccio Mannucci P (Ed.) Waltham, MA. Accessed 10/11/14.
7. Schmidt GA, Clardy PF. Investigational and ineffective therapies for sepsis. UpToDate. Parsons PE, Sexton DJ (Eds.) Waltham, MA. Accessed 10/11/14.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage

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decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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.

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