Clinical Policy: Antithrombin III (ATryn, Thrombate III)

Reference Number: PA.CP.PHAR.564
Effective Date: 01/2022
Last Review Date: 01/2025

Description
The following are antithrombin products requiring prior authorization: antithrombin III, human (Thrombate III®) and antithrombin, recombinant (ATryn®).

FDA Approved Indication(s)
ATryn is indicated for the prevention of peri-operative and peri-partum thromboembolic events in hereditary antithrombin deficient patients.

Thrombate III is indicated in patients with hereditary antithrombin deficiency for:
- Treatment and prevention of thromboembolism
- Prevention of peri-operative and peri-partum thromboembolism

Limitation(s) of use: ATryn is not indicated for treatment of thromboembolic events in hereditary antithrombin deficient patients.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that ATryn and Thrombate III are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hereditary Antithrombin Deficiency (must meet all)**:**

1. Diagnosis of hereditary antithrombin deficiency;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Request is for Thrombate III for the treatment or prevention of thromboembolism;
   b. Request is for prevention of peri-operative or peri-partum thromboembolism.

Approval duration: 3 months (acute thrombosis or peri-operative/peri-partum prevention) or 6 months (prevention)

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Hereditary Antithrombin Deficiency (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
2. Member is responding positively to therapy.

Approval duration: 3 months (acute thrombosis or peri-operative/peri-partum prevention) or 6 months (prevention)

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy PA.CP.PMN.53 or evidence of coverage documents;

B. Disseminated intravascular coagulation (DIC).

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
DIC: disseminated intravascular coagulation
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to goat and goat milk proteins (*ATryn only*)
- Boxed warning(s): none reported

Appendix D: General Information

- 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. More recent studies have not found clear benefit of antithrombin in treatment of DIC. A 2016 Cochrane review of antithrombin 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. A 2022 statement from the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis (ISTH) on sepsis-induced coagulopathy in the management of sepsis concluded that although antithrombin is a candidate for anticoagulation, it has not proven to be effective with robust evidence, and future trials are warranted.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Antithrombin III [human] (Thrombate III)	Individualize dose to achieve antithrombin level of 80% to 120% of normal human plasma. Loading dose (IV infusion): 120% - baseline % x body weight (kg) / 1.4% Adjustment (as needed, IV infusion): Target % - trough % x body weight (kg) / 1.4% Maintenance: Loading dose x 0.6 IV every 24 hours as needed	Varies per baseline and target antithrombin levels
Antithrombin [recombinant] (ATryn)	Treatment goal is to restore and maintain functional antithrombin activity levels between 80% - 120% (0.8 - 1.2 IU/mL) of normal. For surgical patients: *Loading dose (IV infusion):* 100% - baseline % x body weight (kg) / 2.3% *Maintenance (IV infusion):* 100% - baseline % x body weight (kg) / 10.2% For pregnant women: *Loading dose (IV infusion):* 100% - baseline % x body weight (kg) / 1.3% *Maintenance (IV infusion):* 100% - baseline % x body weight (kg) / 5.4% Continue administration of ATryn until adequate follow-on anticoagulation has been established.	Varies per baseline and target antithrombin levels

VI. Product Availability

Drug Name	Availability
Antithrombin III [human] (Thrombate III)	Single-dose vial: approximately 500 units
Antithrombin [recombinant] (ATryn)	Single-dose vial: approximately 525 IU or 1,750 IU

VII. References

1. Thrombate III Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics LLC; October 2021. Available at: www.thrombate.com. Accessed November 1, 2024.
2. ATryn prescribing information. Framingham, MA: GTC Biotherapeutics, Inc; December 2013. Available at: www.ATryn.com. Accessed November 1, 2024.
3. Levi M, 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.
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. Iba T, Levi M, Thachil J, et al. Communication from the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis on sepsis-induced coagulopathy in the management of sepsis. J Thromb Haemost. 2023;21(1):145-153
7. Medical and Scientific Advisory Council (MASAC) of the National Bleeding Disorders (formerly National Hemophilia Foundation): Database of treatment guidelines. Available at: https://www.hemophilia.org/healthcare-professionals/guidelines-on-care/masac-documents. Accessed October 27, 2023.

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

Reviews, Revisions, and Approvals	Date
Policy created	01/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
1Q 2024 annual review: no significant changes; references reviewed and updated.	01/2024
1Q 2025 annual review: no significant changes; references reviewed and updated.	01/2025