Clinical Policy: Antithrombin III (ATryn, Thrombate III)

Reference Number: ERX.SPA.461
Effective Date: 03.01.22
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

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

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 per-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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Hereditary Antithrombin Deficiency (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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.

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%	Varies per baseline and target antithrombin levels

Drug Name	Dosing Regimen	Maximum Dose
	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.	

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; January 2019. Available at: www.thrombate.com. Accessed October 29, 2021.
2. ATryn prescribing information. Framingham, MA: GTC Biotherapeutics, Inc; December 2013. Available at: www.ATryn.com. Accessed October 29, 2021.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.29.21	02.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.