

## Clinical Policy: Antithrombin III (ATryn, Thrombate III)

Reference Number: LA.PHAR.564

Effective Date: 09.29.23

Last Review Date: 03.25.24 ~~05.01.23~~

Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**\*\*Please note:** This policy is for medical benefit\*\*

### 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 Louisiana Healthcare Connections® 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)**

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

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1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

## II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections benefit 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)**

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

## 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 policies – LA.PMN.53 for Medicaid, 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

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#### 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. <u>Loading dose (IV infusion):</u> 120% - baseline % x body weight (kg) / 1.4% <u>Adjustment (as needed, IV infusion):</u> Target % - trough % x body weight (kg) / 1.4% <u>Maintenance:</u> 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. <u>For surgical patients:</u> <u>Loading dose (IV infusion):</u> 100% - baseline % x body weight (kg) / 2.3% <u>Maintenance (IV infusion):</u> 100% - baseline % x body weight (kg) / 10.2% <u>For pregnant women:</u> <u>Loading dose (IV infusion):</u> 100% - baseline % x body weight (kg) / 1.3% <u>Maintenance (IV infusion):</u> 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

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#### VI. Product Availability

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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](http://www.thrombate.com). Accessed ~~November 8, 2022~~October 11, 2023.
2. ATryn prescribing information. Framingham, MA: GTC Biotherapeutics, Inc; December 2013. Available at: <https://www.ATryn.com-fda.gov/media/75529/download?attachment..> Accessed ~~November 8, 2022~~October 30, 2023.
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. 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	LDH Approval Date
Policy created	05.01.23	<u>08.28.23</u>
<u>Annual review: no significant changes; references reviewed and updated.</u>	<u>03.25.24</u>	

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#### **Important Reminder**

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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. LHCC 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.

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