

Clinical Policy: Antithrombin III (ATryn, Thrombate III)

Reference Number: LA.PHAR.564

Effective Date:

Last Review Date: 05.01.23
Line of Business: Medicaid

Coding Implications
Revision Log

See <u>Important Reminder</u> 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 \geq 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 (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.

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)

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



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

Dosage and Administration						
Drug Name	Dosing Regimen	Maximum Dose				
Antithrombin III	Individualize dose to achieve antithrombin	Varies per baseline				
[human]	level of 80% to 120% of normal human	and target				
(Thrombate III)	plasma.	antithrombin levels				
	<u>Loading dose (IV infusion):</u> 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					
Antithrombin	Treatment goal is to restore and maintain	Varies per baseline				
[recombinant]	functional antithrombin activity levels	and target				
(ATryn)	between 80% - 120% (0.8 - 1.2 IU/mL) of	antithrombin levels				
	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.					

VI. Product Availability



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

VII. References

- 1. Thrombate III Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics LLC; October 2021. Available at: www.thrombate.com. Accessed November 8, 2022.
- 2. ATryn prescribing information. Framingham, MA: GTC Biotherapeutics, Inc; December 2013. Available at: www.ATryn.com. Accessed November 8, 2022.
- 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.

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	Description
Codes	
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	

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. 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.

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 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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

©2023 Louisiana Healthcare Connections. All rights reserved. All materials are exclusively owned by Louisiana Healthcare Connections and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Louisiana Healthcare Connections. You may not alter or remove any trademark, copyright or other notice contained



herein. Louisiana Healthcare Connections is a registered trademark exclusively owned by Louisiana Healthcare Connections.