**LETTER OF MEDICAL NECESSITY FOR**

**INHERITED THORACIC AORTIC ANEURYSMS AND DISSECTIONS (TAAD) GENETIC TESTING**

Date: Date of Service/claim

To: Utilization Review Department

Insurance Company Name, Address, City, State

Re: Patient Name, DOB, ID #

ICD-10 Codes:

The ICD-10 codes listed below are commonly received by Ambry from ordering providers for the testing described in this letter. Ambry provides this information as a customer service but makes no recommendations regarding the use of any diagnosis codes. As a reminder, it is the ordering provider’s responsibility to always determine, for the specific date of service, the appropriate diagnostic codes based on the patient’s signs and symptoms.

Code Description

I71.2 THORACIC AORTIC ANEURYSM, WITHOUT RUPTURE

M35.9 SYSTEMIC INVOLVEMENT OF CONNECTIVE TISSUE, UNSPECIFIED

I77.810 THORACIC AORTIC ECTASIA

I71.01 DISSECTION OF THORACIC AORTA

I70.0 ATHEROSCLEROSIS OF AORTA

Z80.3 FAMILY HISTORY OF MALIGNANT NEOPLASM OF BREAST

Z82.49 FAMILY HISTORY OF ISCHEMIC HEART DISEASE AND OTHER DISEASES OF THE CIRCULATORY SYSTEM

Z84.81 FAMILY HISTORY OF CARRIER OF GENETIC DISEASE

This letter is regarding my patient and your subscriber, referenced above, to request full coverage of medically indicated genetic testing for **inherited thoracic aortic aneurysms and dissections (TAAD)** to be performed by Ambry Genetics Corporation.

Thoracic aortic aneurysm (TAA) is caused by an abnormal, usually progressive widening of one or multiple segments of the aorta due to weakening of the vessel wall. Most patients with TAA are asymptomatic and are identified incidentally during imaging studies for other purposes or upon screening of at-risk relatives. Patients with TAA are more likely to develop aneurysms elsewhere in the arterial tree, such as in the abdomen or crania. **Left undiagnosed or untreated, these aortic vessels can also rupture, leading to sudden death**.1

TAA has a strong genetic component and is associated with mutations in multiple genes.  TAA can either be syndromic or non-syndromic.  Syndromic TAA are multisystem disorders with autosomal dominant, autosomal recessive, or X-linked inheritance depending on the causative gene.  Non-syndromic TAA is typically inherited in an autosomal dominant manner.2 Both syndromic and non-syndromic TAA can be seen with or without a positive family history.

**Significant aspects of my patient’s personal and/or family medical history that suggest a reasonable probability of inherited TAAD are below:** [check all that apply]

* Clinical/suspected diagnosis of TAAD
* Known or suspected diagnosis of a connective tissue disorder such as Ehlers-Danlos, Loeys-Dietz , Marfan or Shprintzen-Golderg syndrome
* Family history of TAAD
* Family history of a TAAD-related syndrome
* Other: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

The American College of Cardiology Foundation (ACCF), American Heart Association (AHA), American Association for Thoracic Surgery (AATS), American College of Radiology (ACR), American Stroke Association (ASA), Society of Cardiovascular Anesthesiologists (SCA), Society for Cardiovascular Angiography and Interventions (SCAI), Society of Interventional Radiology (SIR), Society of Thoracic Surgeons (STS) and Society for Vascular Medicine (SVM) **have all recognized the clinical utility of genetic testing for TAAD and support it as standard of care**. 2,3,5

Identification of a mutation in a TAAD-related gene through genetic testing confirms a diagnosis of inherited TAAD or a predisposition to TAAD. Genetic testing also informs prognosis, screening and treatment options, prevention efforts and genetic counseling, which can vary depending on the specific gene implicated in the disease. 1,2,3,4,6 Examples of this include:

* Patients with mutations identified in genes causing broader syndromes (such as Marfan, Loeys-Dietz, Ehlers-Danlos, or Shprintzen-Golderg syndrome) would require additional specialty visits for the evaluation of the extra-cardiac manifestations of the disorder. 1,2,3
* *TGFBR1, TGFBR2,* and SMAD3 mutations are associated with a very high risk of acute aortic dissection; therefore, surgical repair should be considered when the aortic root or ascending aorta reaches a maximum diameter of 4.0 cm.6
* *ACTA2, MYH11, MYLK, PRKG1,* and *TGFB2* mutations are associated with a high risk of acute aortic dissection; therefore, surgical repair should be considered when the aortic root or ascending aorta reaches a maximum diameter of 4.5 cm.4,6
* In individuals with *FBN1* or *COL3A1*mutations, the aortic root can be monitored to 5 cm unless there is a family history of dissection at smaller diameters, rapid enlargement (i.e., greater than 0.5 cm/year), or significant aortic regurgitation.3,6

Specifically for this patient, the impact of testing may include: [check all that apply]

* Genetic testing could allow immediate management, guiding surgical decisions and treatment to anticipate and control common clinical findings based on the results of the testing
* Genetic testing could inform lifestyle modifications for the patient
* Genetic testing could assist in long-term management and monitoring of suspected disease progression based on the results of the testing
* Genetic testing could lead to changes in diagnostic procedures such that more potentially invasive alternative procedures could be avoided, reducing unnecessary tests and cost
* Genetic testing will lead to informed decisions for other family members with similar conditions, or that may be at risk for similar conditions
* Genetic testing could alleviate the need for long-term clinical surveillance in individuals who test negative for any disease-causing variants found in my patient
* Other: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Based on the screening, lifestyle, and treatment modifications indicated above, this test has clinical utility for my patient. Due to the risk of acute aortic dissection and sudden death associated with these mutations and the interventions available to reduce these risks, **I am requesting coverage for this testing as medically necessary care and affirm that my patient has provided informed consent for genetic testing.** I recommend that you support this request for coverage of genetic testing for TAAD in my patient.

Thank you for your time and please don’t hesitate to contact me with any questions.

Sincerely,

Ordering Clinician Name (Signature Provided on Test Requisition Form)

(MD/DO, Clinical Nurse Specialist, Nurse-Midwives, Nurse Practitioner, Physician Assistant, Genetic Counselor\*)

\*Authorized clinician requirements vary by state

**Test Details**

Test Name: TAADNext

CPT codes: 81410, 81411

Laboratory: Ambry Genetics Corporation (TIN 33-0892453 / NPI 1861568784), a CAP-accredited and CLIA-certified laboratory located at 7 Argonaut, Aliso Viejo, CA 92656

**References**

1. Verhagen JMA, et al. Expert consensus recommendations on the cardiogenetic care for patients with thoracic aortic disease and their first-degree relatives.  [Int J Cardiol.](https://www.ncbi.nlm.nih.gov/pubmed/?term=29452988) 2018 May 1;258:243-248.
2. Verstraeten A, et al. Aetiology and management of hereditary aortopathy.  [Nat Rev Cardiol.](https://www.ncbi.nlm.nih.gov/pubmed/28102232) 2017 Apr;14(4):197-208.
3. Hiratzka LF, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with Thoracic Aortic Disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. [Circulation.](https://www.ncbi.nlm.nih.gov/pubmed/?term=20233780) 2010 Apr 6;121(13):e266-369.
4. Regalado ES, et al. Aortic disease presentation and outcome associated with ACTA2 mutations. [Circ Cardiovasc Genet.](https://www.ncbi.nlm.nih.gov/pubmed/25759435) 2015 Jun;8(3):457-64.
5. Musunuru K, et al. Genetic Testing for Inherited Cardiovascular Diseases: A Scientific Statement From the American Heart Association. Circ Genom Precis Med*.* 2020 Aug;13(4):e000067
6. Faggion Vinholo T, et al. Genes Associated with Thoracic Aortic Aneurysm and Dissection: 2019 Update and Clinical Implications. Aorta (Stamford). 2019;7(4):99-107. doi:10.1055/s-0039-3400233