

# Clinical Policy: Genetic Testing: Aortopathies and Connective Tissue Disorders

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[Coding Implications](#)

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

## Description

Hereditary connective tissue disorders are a group of disorders that affect the connective tissues that support the skin, bones, joints, heart, blood vessels, eyes, and other organs. While specific features vary by type, an unusually large range of joint movement (hypermobility) and cardiovascular disease (such as thoracic aortic aneurysms and dissections) are features that are present in many hereditary connective tissue disorders. Medical management may differ based on the underlying genetic etiology. A diagnosis may be made based on clinical examination; however, it can be difficult to reliably diagnose a hereditary connective tissue disorder based on clinical and family history alone.

Accurate diagnosis of a hereditary connective tissue disorder can lead to changes in clinical management, including surveillance of the aorta, surgical repair of the aorta, when necessary, pharmacologic management, as well as surveillance for multisystem involvement in syndromic conditions with risk for thoracic aortic aneurysms and dissection.

CPT® Codes	Example Tests (Labs)	Criteria Section	Common ICD Codes
81403	Targeted Mutation Analysis for a Known Familial Variant	<a href="#">Known Familial Variant Analysis</a>	N/A
81408	FBN1 Sequencing and/or Deletion/Duplication Analysis	<a href="#">FBN1 Sequencing and/or Deletion/Duplication Analysis</a>	I71.00-I71.9, Q12.1, Q87.40- Q87.43
81479	FBN1 Deletion/Duplication Analysis	<a href="#">FBN1 Sequencing and/or Deletion/Duplication Analysis</a>	I71.00-I71.9, Q12.1, Q87.40- Q87.43
81405,81408, 81479	Loeys-Dietz Syndrome Panel (Prevention Genetics)  Loeys-Dietz Syndrome NGS Panel (CTGT)  Loeys-Dietz Syndrome NGS Panel (Sequencing & Deletion/Duplication) (Fulgent Genetics)	<a href="#">Loeys-Dietz Syndrome Multigene Panel</a>	I71.00-I71.9
81405,81406, 81479	Thoracic Aortic Aneurysm Panel (Cincinnati Children’s Hospital Medical Center-	<a href="#">Familial Thoracic Aortic Aneurysm and Dissection (TAAD) Multigene Panel</a>	I71.00-I71.9, Q87.5

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CPT® Codes	Example Tests (Labs)	Criteria Section	Common ICD Codes
	Molecular Genetics and Cytogenetics Laboratories)		
81410,81411	<p>TAAD Panel Next Generation Sequencing (DDC Clinic Laboratory)</p> <p>TAADNext (Ambry Genetics) Marfan syndrome, Loeys-Dietz syndrome, Familial thoracic aortic aneurysms &amp; dissections, and Related disorders NGS Panel - Comprehensive (CTGT)</p> <p>Marfan Syndrome and Thoracic Aortic Aneurysm and Dissection NGS Panel (Sequencing &amp; Deletion/Duplication) (Fulgent Genetics)</p> <p>Marfan/TAAD Panel (GeneDx)</p> <p>Invitae Aortopathy Comprehensive Panel – Primary Genes Only (Invitae)</p>	<p><a href="#">Familial Thoracic Aortic Aneurysm and Dissection (TAAD) Multigene Panel</a></p>	
81479	<p>Ehlers-Danlos syndrome, classic type NGS Panel (CTGT)</p> <p>Ehlers-Danlos syndrome type 1 and 2 (sequence analysis of COL5A1 and COL5A2 genes) (CGC Genetics USA)</p>	<p><a href="#">Classic Ehlers-Danlos Syndrome (cEDS)</a> <i>COL5A1</i>, <i>COL5A2</i>, and <i>COL1A1</i> Sequencing and/or Deletion/Duplication Analysis or Targeted Multigene Panel</p>	M35.7, Q79.61- Q79.62
81479	<p>COL3A1 Sequencing Analysis COL3A1 Deletion/Duplication Analysis</p>	<p><a href="#">Vascular Ehlers-Danlos Syndrome (vEDS)</a> <i>COL3A1</i> Sequencing and/or Deletion/Duplication Analysis</p>	Q79.63

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CPT® Codes	Example Tests (Labs)	Criteria Section	Common ICD Codes
81479	Ehlers-Danlos Syndrome Panel (BluePrint)  Ehlers-Danlos syndrome NGS Panel – Dominant & Recessive – Comprehensive (CTGT)  Ehlers-Danlos Syndrome NGS Panel (Sequencing & Deletion/Duplication) (Fulgent Genetics)  Invitae Ehlers-Danlos Syndrome Panel (Invitae)	<a href="#">Comprehensive Ehlers-Danlos Syndrome Multigene Panels</a>	Q79.63
81400-81408	Other Covered Connective Tissue Disorders	<a href="#">Other Covered Connective Tissue Disorders</a>	

**OTHER RELATED POLICIES**

This policy document provides criteria for genetic testing for cardiovascular disorders. Please refer to:

- **CP.MP.216 Genetic Testing: Cardiac Disorders** for criteria related to arrhythmias and cardiomyopathies.
- **CP.MP.230 Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay** for criteria related to genetic disorders that affect multiple organ systems.
- **CP.MP.235 Genetic Testing: Prenatal Diagnosis (via amniocentesis, CVS, or PUBS) and Pregnancy Loss** for related to prenatal and pregnancy loss diagnostic genetic testing.
- **CP.MP.233 Genetic Testing: Preimplantation Genetic Testing** for criteria related to genetic testing of embryos prior to in vitro fertilization.
- **CP.MP.222 Genetic Testing: General Approach to Genetic Testing** for criteria related to aortopathies and connective tissue disorders not specifically discussed in this or another non-general policy.

**Policy/Criteria**

Known Familial Variant Analysis for Aortopathies and Connective Tissue Disorders

- I. Targeted mutation analysis for a known familial variant (81403) for an aortopathies and connective tissue disorder is considered **medically necessary** when:
  - A. The member/enrollee has a [close relative](#)<sup>1</sup> with a known pathogenic or likely pathogenic variant causing the condition.

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- II. Current evidence does not support targeted mutation analysis for a known familial variant (81403) for an aortopathies and connective tissue disorders for all other indications.

#### Marfan Syndrome

##### FBNI Sequencing and/or Deletion/Duplication Analysis

- I. *FBNI* sequencing and/or deletion/duplication analysis (81408, 81479) to establish or confirm a diagnosis of Marfan syndrome is considered **medically necessary** when:

A. The member/enrollee has at least one of the following:

1. Aortic root enlargement (Z-score  $\geq 2.0$ ) or dissection;
2. Ectopia lentis;
3. A systemic score of  $\geq 7$ , as demonstrated by the following clinical features and associated scores\*:
  - a) Wrist and thumb sign (3)
  - b) Wrist or thumb sign (1)
  - c) Pectus carinatum deformity (2)
  - d) Pectus excavatum or chest asymmetry (1)
  - e) Hindfoot deformity (2)
  - f) Plain flat foot (pes planus) (1)
  - g) Pneumothorax (2)
  - h) Dural ectasia (2)
  - i) Protrusio acetabulae (2)
  - j) Reduced upper segment / lower segment and increased arm span/height ratios (1)
  - k) Scoliosis or thoracolumbar kyphosis (1)
  - l) Reduced elbow extension (1)
  - m) 3 of 5 facial features (dolichocephaly, downward slanting palpebral fissures, enophthalmos, retrognathia, malar hypoplasia) (1)
  - n) Skin striae (1)
  - o) Myopia (1)
  - p) Mitral valve prolapse (1)
4. The member/enrollee has a [close relative<sup>1</sup>](#) with a clinical diagnosis of Marfan syndrome.

- II. Current evidence does not support *FBNI* sequencing and/or deletion/duplication analysis (81408, 81479) to establish or confirm a diagnosis of Marfan syndrome for all other indications.

\*Full explanation of each feature and calculation can be found at <https://www.marfan.org/dx/score>

#### Loeys-Dietz Syndrome

##### Loeys-Dietz Syndrome Multigene Panel

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- I. Loeys-Dietz syndrome (LDS) multigene panel analysis (81405, 81408, 81479) to establish or confirm a diagnosis of Loeys-Dietz syndrome is considered **medically necessary** when meeting both of the following:
  - A. The member/enrollee meets at least two of the following:
    1. Aortic root enlargement (Z-score  $\geq 2.0$ );
    2. Type A aortic dissection;
    3. At least one cutaneous finding: soft and velvety skin, easy bruising, translucent skin with easily visible underlying veins, dystrophic scars, milia on the face;
    4. At least one LDS craniofacial finding: widely spaced eyes, bifid uvula/cleft palate, craniosynostosis;
    5. At least one skeletal finding: pectus excavatum or pectus carinatum, scoliosis, joint laxity or contracture, arachnodactyly, talipes equinovarus, cervical spine malformation and/or instability, osteoarthritis;
    6. The member/enrollee has a [close relative](#)<sup>1</sup> with a clinical diagnosis of LDS
  - B. The panel includes, at a minimum, the following genes\*: *TGFBR1* and *TGFBR2*.
- II. Current evidence does not support Loeys-Dietz syndrome (LDS) multigene panel analysis (81405, 81408, 81479) to establish or confirm a diagnosis of Loeys-Dietz syndrome for all other indications.

\* If the member/enrollee has both aortic root enlargement and ectopia lentis, *FBN1* should either be included in the panel or should have been previously performed and the results were negative.

**Familial Thoracic Aortic Aneurysm and Dissection (TAAD)****Familial Thoracic Aortic Aneurysm and Dissection (TAAD) Multigene Panel**

- I. Familial thoracic aortic aneurysm and dissection (TAAD) multigene panel analysis (81405, 81408, 81410, 81411, 81479) to establish a genetic diagnosis for TAAD is considered **medically necessary** when meeting both of the following:
  - A. The member/enrollee has aortic root enlargement (Z-score  $\geq 2.0$ ) or has had a type A or type B aortic dissection;
  - B. The panel includes, at a minimum, the following genes: *ACTA2*, *FBN1*, *MYH11*, *SMAD3*, *TGFBR1*, *TGFBR2*.
- II. Current evidence does not support thoracic aortic aneurysm and dissection (TAAD) multigene panel analysis (81405, 81408, 81410, 81411, 81479) to establish a genetic diagnosis for TAAD for all other indications.

\*If a panel is performed, the appropriate panel code should be used

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#### Ehlers-Danlos Syndrome

##### Classic Ehlers-Danlos Syndrome (cEDS)

##### Classic Ehlers-Danlos Syndrome Multigene Panel

- I. Classic Ehlers-Danlos syndrome multigene panel analysis (81479) to establish or confirm a diagnosis of cEDS is considered **medically necessary** when meeting all of the following:
  - A. The member/enrollee has skin hyperextensibility and atrophic scarring;
  - B. The member/enrollee meets at least one of the following:
    1. Generalized joint hypermobility;
    2. At least three of the following:
      - a) Easy bruising
      - b) Soft, doughy skin
      - c) Skin fragility (or traumatic splitting)
      - d) Molluscoid pseudotumors
      - e) Subcutaneous spheroids
      - f) Hernia
      - g) Epicanthal folds
      - h) Complications of joint hypermobility (e.g., sprains, luxation/subluxation, pain, flexible flatfoot)
      - i) Family history of a [first-degree<sup>1a</sup> relative](#) that has a clinical diagnosis of cEDS
  - C. The panel is limited to the following genes: *COL5A1*, *COL5A2*, and *COL1A1*.
- II. Current evidence does not support Classic Ehlers-Danlos syndrome multigene panel analysis (81479) to establish or confirm a diagnosis of cEDS for all other indications.

#### Vascular Ehlers-Danlos Syndrome (vEDS)

##### COL3A1 Sequencing and/or Deletion/Duplication Analysis

- I. *COL3A1* sequencing and/or deletion/duplication analysis (81479) to establish or confirm a diagnosis of vEDS is considered **medically necessary** when:
  - A. The member/enrollee meets any of the following:
    1. Arterial rupture under the age of 40;
    2. Spontaneous sigmoid colon perforation in the absence of known diverticular disease or other bowel pathology;
    3. Uterine rupture during the third trimester in the absence of previous C-section and/or severe peripartum perineum tears;
    4. Carotid-cavernous sinus fistula (CCSF) formation in the absence of trauma;

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5. The member/enrollee has a [close relative](#)<sup>1</sup> that has a clinical diagnosis of vEDS;
  6. The member/enrollee has at least two of the following minor criteria:
    - a) Bruising unrelated to identified trauma and/or in unusual sites such as cheeks and back
    - b) Thin, translucent skin with increased venous visibility
    - c) Characteristic facial appearance
    - d) Spontaneous pneumothorax
    - e) Acrogeria
    - f) Talipes equinovarus
    - g) Congenital hip dislocation
    - h) Hypermobility of small joints
    - i) Tendon and muscle rupture
    - j) Keratoconus
    - k) Gingival recession and gingival fragility
    - l) Early onset varicose veins (under the age of 30 and nulliparous if females)
- II. Current evidence does not support *COL3A1* sequencing and/or deletion/duplication analysis (81479) to establish or confirm a diagnosis of vEDS for all other indications.

#### Comprehensive Ehlers-Danlos Syndrome Multigene Panels

- I. Current evidence does not support Comprehensive Ehlers-Danlos syndrome (EDS) multigene panel analysis (81479) for all indications, including hypermobile EDS.

#### Other Covered Connective Tissue Disorders\*

The following is a list of conditions that have a known genetic association. Due to their relative rareness, these genetic tests may be appropriate to establish or confirm a diagnosis.

- I. Genetic testing to establish or confirm one of the following connective tissue disorders to guide management is considered **medically necessary** when the member/enrollee demonstrates clinical features\* consistent with the disorder (the list is not meant to be comprehensive, see II below):
  - A. Arthrochalasia EDS (*COL1A1, COL1A2*)
  - B. Brittle cornea syndrome (*ZNF469, PRDM5*)
  - C. Cardiac-valvular EDS (*COL1A2*)
  - D. Classical-like EDS (*TNXB*)
  - E. Dermatosparaxis EDS (*ADAMTS2*)
  - F. [Epidermolysis Bullosa](#)
  - G. [Kyphoscoliotic EDS](#) (*PLOD1, FKBP14*)
  - H. Musculocontractural EDS (*CHST14, DSE*)
  - I. Myopathic EDS (*COL12A1*)
  - J. [Osteogenesis Imperfecta](#)
  - K. Periodontal EDS (*CIR, CIS*)
  - L. Spondylodysplastic EDS (*B4GALT7, B3GALT6, SLC9A13*)

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- II. Genetic testing to establish or confirm the diagnosis of all other connective tissue disorders not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Genetic Testing* (see policy for criteria).

\*Clinical features for a specific disorder may be outlined in resources such as [GeneReviews](#), [OMIM](#), [National Library of Medicine, Genetics Home Reference](#), or other scholarly source.

#### Notes and Definitions

1. Close relatives include first, second, and third degree **blood** relatives:
  - a. **First-degree relatives** are parents, siblings, and children
  - b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
  - c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

#### Background

*American College of Medical Genetics and Genomics*

American College of Medical Genetics and Genomics (2012) issued guidelines on the evaluation of adolescents or adults with some features of Marfan syndrome (MFS), which recommendations included the following:

- If there is no family history of MFS, then the subject has the condition under any of the following four situations:
  - A dilated aortic root (defined as greater than or equal to two standard deviations above the mean for age, sex, and body surface area) and ectopia lentis
  - A dilated aortic root and a mutation [pathogenic variant] in FBN1 that is clearly pathologic
  - A dilated aortic root and multiple systemic features or
  - Ectopia lentis and a mutation [pathogenic variant] in FBN1 that has previously been associated with aortic disease.
- If there is a positive family history of MFS (independently ascertained with these criteria), then the subject has the condition under any of the following three situations:
  - Ectopia lentis
  - Multiple systemic features or
  - A dilated aortic root (if over 20 years, greater than two standard deviations; if younger than 20, greater than three standard deviations)

*American College of Cardiology Foundation, et. al.*

American College of Cardiology Foundation and 9 other medical associations published joint evidence-based guidelines (2010) for the diagnosis and management of thoracic aortic disease, including Marfan syndrome, which included the following guidelines regarding genetic testing:

- If the mutant gene (FBN1, TGFBR1, TGFBR2, COL3A1, ACTA2, MYH11) associated with aortic aneurysm and/or dissection is identified in a patient, first-degree relatives should undergo counseling and testing. Then, only the relatives with the genetic mutation [pathogenic variant] should undergo aortic imaging. [class 1, level of evidence C.]



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- The criteria for Marfan syndrome is based primarily on clinical findings in the various organ systems affected in the Marfan syndrome, along with family history and FBN1 mutations [pathogenic variants] status.

#### *2017 International Classification of the Ehlers-Danlos Syndromes*

The 2017 International Classification of the Ehlers-Danlos Syndromes included the following clinical features for the associated conditions:

Classical EDS (cEDS):

Major criteria

1. Skin hyperextensibility and atrophic scarring
2. Generalized joint hypermobility (GJH)

Minor criteria

1. Easy bruising
2. Soft, doughy skin
3. Skin fragility (or traumatic splitting)
4. Molluscoid pseudotumors
5. Subcutaneous spheroids
6. Hernia (or history thereof)
7. Epicanthal folds
8. Complications of joint hypermobility (e.g., sprains, luxation/subluxation, pain, flexible flatfoot)
9. Family history of a first degree relative who meets clinical criteria

Minimal Criteria suggestive for cEDS:

- Major criterion (1): skin hyperextensibility and atrophic scarring  
Plus
- Either major criterion (2): GJH
- And/or: at least three minor criteria

Confirmatory molecular testing is obligatory to reach a final diagnosis.

Vascular EDS (vEDS)

Major criteria

1. Family history of vEDS with documented causative variant in COL3A1
2. Arterial rupture at a young age
3. Spontaneous sigmoid colon perforation in the absence of known diverticular disease or other bowel pathology
4. Uterine rupture during the third trimester in the absence of previous C-section and/or severe peripartum perineum tears
5. Carotid-cavernous sinus fistula (CCSF) Formation in the absence of trauma

Minor criteria

1. Bruising unrelated to identified trauma and/or in unusual sites such as cheeks and back
2. Thin, translucent skin with increased venous visibility
3. Characteristic facial appearance
4. Spontaneous pneumothorax
5. Acrogeria
6. Talipes equinovarus
7. Congenital hip dislocation
8. Hypermobility of small joints

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9. Tendon and muscle rupture
10. Keratoconus
11. Gingival recession and gingival fragility
12. Early onset varicose veins (under age 30 and nulliparous if female)

Minimal criteria suggestive for vEDS:

- A family history of the disorder, arterial rupture or dissection in individuals less than 40 years of age, unexplained sigmoid colon rupture, or spontaneous pneumothorax in the presence of other features consistent with vEDS should all lead to diagnostic studies to determine if the individual has vEDS. Testing for vEDS should also be considered in the presence of a combination of the other “minor” clinical features listed above. Even for experienced clinicians the clinical diagnosis of vEDS may be difficult. Because of implications for treatment, natural history, and recurrence risk, the diagnosis of vEDS rests on the identification of a causative variant in one allele of COL3A1.

*CSANZ Cardiovascular Genetic Diseases Council*

CSANZ Cardiovascular Genetic Diseases Council (2017) published a position statement with updates on the diagnosis and management of inherited aortopathies, including Marfan syndrome, that stated the following key points:

1. A number of inherited conditions can predispose the aorta, and less commonly other blood vessels, to dilatation and/ or rupture.
2. Broadly speaking, these conditions are recognized as syndromic when accompanied by a number of systemic features or non-syndromic when the aortic dilatation appears to exist in isolation.
3. The commonest syndromic aortopathy is Marfan syndrome and the commonest non-syndromic aortopathy is that which accompanies congenital bicuspid aortic valve.
4. Mutations in a number of genes have been identified, particularly in syndromic aortopathy.
5. Although genotype-phenotype relationships exist, the phenotypes of the syndromic aortopathies may have significant overlap.
6. When a syndromic aortopathy is suspected, review by a clinical geneticist is instrumental in characterizing the clinical signs and the family history.
7. Confirmation of a diagnosis (either clinically or by gene testing) allows identification of individuals at increased risk of aortic sequelae who will benefit from active medical management.
8. Medical management is usually undertaken by a cardiologist with referral to other specialists (egg cardiothoracic surgeons) as appropriate.
9. At risk family members should be offered predictive testing if a mutation is identified, and should otherwise be screened in keeping with the presumptive clinical diagnosis and assessment of risk.
10. Pregnancy and the post-partum period confer a higher risk for aortic complications:
  - a. Women with a personal or family history of aortopathy need appropriate pre-conception screening and counselling.
  - b. Intervention may be required pre-conception and they should be managed closely throughout pregnancy, ideally in a high-risk obstetric clinic, with joint management by an obstetrician and a cardiologist.

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- c. Management may include appropriate cessation and commencement/continuation of medication ((ACE inhibitors and ARB are teratogenic and contraindicated in pregnancy, beta blockers can be used in pregnancy) and should include involvement of a cardiologist in the management during pregnancy and decision making for delivery.
11. A clinical diagnosis of an inherited aortopathy can be made in the absence of a positive genetic test if the systemic features are consistent with a specific syndromic aortopathy. A familial history of aortic dissection in the absence of both a positive gene test and systemic examination findings may be more difficult to manage without a working clinical diagnosis. However, an inherited risk of dissection should nonetheless be considered in this setting, particularly if the process has affected young individuals and/or in the absence of traditional risk factors.

**Coding Implications**

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Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed	02/22	02/22

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#### **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. The Health Plan 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. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees 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 the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members/enrollees 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/enrollees and their representatives agree to be bound by such terms and conditions by providing services to members/enrollees and/or submitting claims for payment for such services.

**Note: For Medicaid members/enrollees**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

## CLINICAL POLICY

### Genetic Testing Aortopathies and Connective Tissue Disorders

**Note: For Medicare members/enrollees**, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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