GENETIC TESTING: AORTOPATHIES AND CONNECTIVE TISSUE DISORDERS (REQUIRES PREAUTHORIZATION

V.73

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DESCRIPTION

Hereditary connective tissue disorders are a group of disorders that affect the connective tissues that support the skin, bones, joints, hear, blood vessles, eyes, and other organs. While specific features vary by type, an unusually large range of joint movement 9hypermobility) and cardiovascular disease (such as thoracic aortic aneurysms and dissections) are features that are present in many hereditary connective tissues disorders. Medical management may differ based on the underlying genetic etiology. A diagnosis may be made based on clinical examination: howver, it can be difficult to reliability diagnose a hereditary connective tissue disorder based on clinical and family history alone.

Accurate diagnosis of a hereditary connective tissue disorder can lead to change in clinical maagement, 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 dissections.

Of note, per GeneReviews, hypermobile Ehlers-Danlos syndrome (hEDS) is based entirely on clinical evaluation and family history and not genetic testing, as the gene(s) associated with hEDS are currently unknown. Therefore, clinical genetic testing for the sole purpose of evaluating for hEDS is not appropriate at this time. Genetic evaluation for other types of EDS are addressed within this policy.

Dates

08-07-2024
Next Review
08-10-2025

REFERENCE TABLE

The tests and associated laboratories and CPT codes contained within this document serve only as examples to help users navigate claims and corresponding coverage criteria; as such, they are not comprehensive and are not a guarantee of coverage or non-coverage. Please see the Concert Genetics Platform for a comprehensive list of registered tests.

Coverage Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	
Connective Tissue Disorders				
Comprehensive Connective Tissue Disorders Multigene Panel	Heritable Disorders of Connective Tissue Panel (GeneDx)	81410, 81411	I71.00-I71.9, M35.7, Q79.60, Q79.61, Q79.63, Q79.69, Q12.1, Q87.4, Q87.5	
	Invitae Connective Tissue Disorders Panel (Invitae)			
Marfan Syndrome				
FBN1 Sequencing and/or Deletion/Duplication Analysis	FBN1 Full Gene Sequencing and Deletion/Duplication (Invitae)	81408, 81479	I71.00-I71.9, Q12.1, Q87.40-Q87.43	
	Marfan Syndrome via FBN1 Gene (PreventionGenetics, part of Exact Sciences)			
Loeys-Dietz Syndrome				
Loeys-Dietz Syndrome Multigene Panel	Loeys-Dietz Syndrome Panel (PreventionGenetics, part of Exact Sciences)	81405, 81408, 81479	I71.00-I71.9	
	Loeys-Dietz Syndrome Panel (Invitae)			
Familial Thoracic Aortic Aneurysm and Dissection (TAAD)				
Familial Thoracic Aortic Aneurysm and Dissection	Thoracic Aortic Aneurysm Panel (Cincinnati Children's Hospital	81405, 81406, 81408, 81479	I71.00-I71.9, Q87.5	

	Sequencing (DDC Clinic Laboratory)			
	TAADNext (Ambry Genetics)			
	Marfan syndrome, Loeys-Dietz syndrome, Familial thoracic aortic aneurysms & dissections, and Related disorders NGS Panel - Comprehensive (CTGT)			
	Marfan Syndrome and Thoracic Aortic Aneurysm and Dissection NGS Panel (Sequencing & Deletion/Duplication) (Fulgent Genetics)			
	Marfan/TAAD Panel (GeneDx)			
	Aortopathy Comprehensive Panel (Invitae)			
Ehlers-Danlos Syndrome				
Classic Ehlers-Danlos Syndrome (cEDS)				
Classic Ehlers-Danlos Syndrome (cEDS) Multigene Panel	Ehlers Danlos Panel (GeneDx)	81408, 81479	M35.7, Q79.61, Q79.63, Q79.69	
	Ehlers-Danlos Syndrome Panel (Revvity)			
	Ehlers-Danlos syndrome, classic type NGS panel (CTGT)			
Vascular Ehlers-Danlos Syndrome (vEDS)				
COL3A1 Sequencing and/or Deletion/Duplication Analysis	COL3A1 Full Gene Sequencing and Deletion/Duplication (Invitae)	81479	Q79.63	
Other Covered Connective Tissue Disorders				
Other Covered Connective Tissue Disorders	See list below	81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408		

- V.66 - Genetic Testing: Cardiac Disorders for coverage criteria related to arrhythmias and cardiomyopathies
- V.62 - Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay for coverage criteria related to genetic disorders that affect multiple organ systems
- V.30 - Genetic Testing: Prenatal Diagnosis (via amniocentesis, CVS, or PUBS) and Pregnancy Loss for coverage related to prenatal and pregnancy loss diagnostic genetic testing
- V.75 - Genetic Testing: Preimplantation Genetic Testing for coverage criteria related to genetic testing of embryos to in-vitro fertilization
- V.74 - Genetic Testing: General Approach to Genetic and Molecular Testing for coverage criteria related to aortopathies and connective tissue disorders not specifically discussed in this or another non-general policy, including known familial variant testing.

POLICY

CONNECTIVE TISSUE DISORDERS

I. Comprehensive connective tissue disorders multigene panel analysis (81410, 81411) is considered **medically necessary** when:

A. The member meets criteria for at least one of the following (see specific coverage criteria sections below):

1. Marfan Syndrome
2. Loeys-Dietz Syndrome
3. Classic Ehlers-Danlos Syndrome
4. Vascular Ehlers-Danlos Syndrome (vEDS)

II. Comprehensive connective tissue disorders multigene panel analysis (81410, 81411) is considered **investigational** for all other indications, including isolated hypermobility and hypermobile Ehlers-Danlos syndrome (hEDS).

NOTE: If a panel is performed, the appropriate panel code should be used

MARFAN SYNDROME

81479) to confirm a diagnosis of Marfan syndrome is considered **medically necessary** when:

A. The member has one of the following:

1. Aortic root enlargement (Z-score of 2 or greater) or dissection, **OR**

2. Ectopia lentis, **OR**

B. The member has a systemic score of 7 or higher using the list of symptoms below (point values in parentheses):

1. Wrist AND thumb sign (3)
2. Wrist OR thumb sign (1)
3. Pectus carinatum deformity (2)
4. Pectus excavatum or chest asymmetry (1)
5. Hindfoot deformity (2)
6. Plain flat foot (pes planus) (1)
7. Pneumothorax (2)
8. Dural ectasia (2)
9. Protrusio acetabulae (2)
10. Reduced upper segment / lower segment AND increased arm span/height ratios (1)
11. Scoliosis or thoracolumbar kyphosis (1)
12. Reduced elbow extension (1)
13. 3 of 5 facial features (dolichocephaly, downward slanting palpebral fissures, enophthalmos, retrognathia, malar hypoplasia) (1)
14. Skin striae (1)
15. Myopia (1)
16. Mitral valve prolapse (1).

II .*FBN1* sequencing and/or deletion/duplication analysis (81408, 81479) to establish or confirm a molecular diagnosis of Marfan syndrome is considered **investigational** for all other indications.

NOTE: 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

I.Loeys-Dietz syndrome (LDS) multigene panel analysis (81405, 81408, 81479)* to establish or confirm a diagnosis of Loeys-Dietz

1.Characteristic facial features, including widely spaced eyes and craniosynostosis, **OR**

2.Bifid uvula or cleft palate, **OR**

3.Tortuosity of the aorta and its branches, **OR**

4.Aortic dilatation and dissection, **OR**

5.Joint hypermobility, **OR**

6.The member has a first-degree relative with a clinical diagnosis of LDS.

II.Loeys-Dietz syndrome (LDS) analysis (81405, 81408, 81479) to establish or confirm a diagnosis of Loeys-Dietz syndrome is considered **investigational** for all other indications.

NOTE: If a panel is performed, the appropriate panel code should be used

NOTE**:** If the member 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, 81406, 81408, 81410, 81411, 81479) to establish a genetic diagnosis for TAAD is considered **medically necessary** when:

A. The member has a history of any of the following:

1. Aortic root enlargement, **OR**

2. Thoracic aneurysm, **OR**

3. Type A or type B aortic dissection, **AND**

C. The member has a family history of dilation of dissection of the aortic root, consistent with autosomal dominant inheritance.

II. Thoracic aortic aneurysm and dissection (TAAD) multigene panel analysis (81405, 81406, 81408, 81410, 81411, 81479) to establish a genetic diagnosis for TAAD is considered **investigational** for all other indications.

NOTE: If a panel is performed, the appropriate panel code should be used

EHLERS-DANLOS SYNDROME

Classic Ehlers-Danlos Syndrome (cEDS) Multigene Panel

I. Classic Ehlers-Danlos syndrome multigene panel analysis (81408, 81479) to establish or confirm a diagnosis of cEDS is considered **medically necessary** when:

A. The member has skin hyperextensibility and atrophic scarring, **AND**

B. The member meets at least one of the following:

1. Generalized joint hypermobility, **OR**

2. At least three of the following:

a. Easy bruising, **OR**
b. Soft, doughy skin, **OR**
c. Skin fragility (or traumatic splitting), **OR**
d. Molluscoid pseudotumors, **OR**
e. Subcutaneous spheroids, **OR**
f. Hernia, **OR**
g. Epicanthal folds, **OR**
h. Complications of joint hypermobility (e.g., sprains, luxation/subluxation, pain, flexible flatfoot), **OR**
i. Family history of a first-degree relative that has a clinical diagnosis of cEDS, **AND**

C. The panel includes, at a minimum, the following genes: *COL5A1* and *COL5A2*.

II. Classic Ehlers-Danlos syndrome multigene panel analysis (81408, 81479) to establish or confirm a diagnosis of cEDS is considered **investigational** for all other indications, including

BlueCross BlueShield Nebraska

NOTE: Per GeneReviews, hypermobile Ehlers-Danlos syndrome (hEDS) is based entirely on clinical evaluation and family history and not genetic testing, as the gene(s) associated with hEDS are currently unknown. Therefore, clinical genetic testing for the sole purpose of evaluating for hEDS is not appropriate at this time.

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 meets any of the following:

1. Arterial rupture or dissection under the age of 40, **OR**

2. Spontaneous sigmoid colon perforation in the absence of known diverticular disease or other bowel pathology, **OR**

3. Uterine rupture during the third trimester in the absence of previous C-section and/or severe peripartum perineum tears, **OR**

4. Carotid-cavernous sinus fistula (CCSF) formation in the absence of trauma, **OR**

5. The member has a close relative with a clinical diagnosis of vEDS, **OR**

6. The member 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, **OR**
b. Thin, translucent skin with increased venous visibility, **OR**
c. Characteristic facial appearance, **OR**
d. Spontaneous pneumothorax, **OR**
e. Acrogeria, **OR**
f. Talipes equinovarus, **OR**
g. Congenital hip dislocation, **OR**

k. Gingival recession and gingival fragility,
OR
l. Early onset varicose veins (under the age of 30 and nulliparous if female).

II. *COL3A1* sequencing and/or deletion/duplication analysis (81479) to establish or confirm a diagnosis of vEDS is considered **investigational** for all other indications, including isolated hypermobility and hypermobile Ehlers-Danlos syndrome (hEDS).

NOTE: Per GeneReviews, hypermobile Ehlers-Danlos syndrome (hEDS) is based entirely on clinical evaluation and family history and not genetic testing, as the gene(s) associated with hEDS are currently unknown. Therefore, clinical genetic testing for the sole purpose of evaluating for hEDS is not appropriate at this time.

OTHER COVERED CONNECTIVE TISSUE DISORDERS

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

I. Genetic testing to establish or confirm one of the following connective tissue disorders (81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408) to guide management is considered **medically necessary** when the member 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. Kyphoscoliotic EDS (*PLOD1, FKBP14*)
G. Musculocontractural EDS (*CHST14*, *DSE*)
H. Myopathic EDS (*COL12A1*)
I. Periodontal EDS (*C1R*, *C1S*)
J. Spondylodysplastic EDS (*B4GALT7*, *B3GALT6*, *SLC39A13*)

II. Genetic testing to establish or confirm the diagnosis of all other connective tissue disorders (81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408) not specifically discussed within this or

NOTE: 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.

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
2. **Type A aortic dissections** occur at the ascending part of the aorta, just as it branches off the heart. **Type B aortic dissections** occur at the descending part of the aorta, and may extend into the abdomen.

BACKGROUND

Comprehensive Connective Tissue Disorders Multigene Panel

GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online.

GeneReviews: Classic Ehlers-Danlos Syndrome

The GeneReviews for Ehlers-Danlos Syndrome (EDS) states that "Sequence analysis of *COL5A1* and *COL5A2* (multigene targeted panels may also include *COL1A1* and other EDS-related genes…) is performed first to detect missense, nonsense, and splice site variants and small intragenic deletions/insertions…"

GeneReviews: Hypermobile Ehlers-Danlos Syndrome

Per the Hypermobile Ehlers-Danlos Syndrome (EDS) GeneReviews, "if an individual's personal or family history is suggestive of one of the other types of EDS or another hereditary disorder of connective tissue or

GeneReviews: FBN1-Related Marfan Syndrome

Per the *FBN1*-Related Marfan Syndrome Gene Reviews, “molecular genetic testing approaches can include a combination of gene-targeted testing (single-gene testing, multigene panel) and comprehensive genomic testing (exome sequencing, genome sequencing) depending on the phenotype. A Marfan syndrome/Loeys-Dietz syndrome/familial thoracic aortic aneurysms and dissections multigene panel that includes *FBN1* and other genes of interest is most likely to identify the genetic cause of the condition while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype.”

GeneReviews: Loeys-Dietz Syndrome

Per the Loeys-Dietz Syndrome (LDS) GeneReviews, “When the clinical findings suggest the diagnosis of LDS, molecular genetic testing approaches can include serial single-gene testing or use of a multigene panel. A multigene Marfan syndrome/Loeys-Dietz syndrome/familial thoracic aortic aneurysms and dissections panel that includes *SMAD2*, *SMAD3*, *TGFB2*, *TGFB3*, *TGFBR1*, and *TGFBR2* as well as a number of other genes associated with disorders that include aortic aneurysms and dissections may be offered by clinical laboratories.”

FBN1 Sequencing and/or Deletion/Duplication Analysis

GeneReviews: FBN1-Related Marfan Syndrome

GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online.

Marfan syndrome should be suspected in individuals with the following clinical findings and family history:

-Aortic root enlargement (Z-score ≥2.0). Note: Aortic size must be standardized to age and body size for accurate interpretation. A Z-score ≥2.0 indicates a value at or above the 95th percentile, while a Z-score ≥3.0 indicates a value at or above the 99th percentile. References and calculators for this determination are available at the Marfan Foundation website.
-Ectopia lentis; most reliably diagnosed by slit-lamp examination after maximal pupillary dilatation
-A systemic score ≥7

to be associated with Marfan syndrome and EITHER of the following [Loeys et al 2010]:

-Aortic root enlargement (Z-score >2.0)
-Ectopia lentis

Loeys-Dietz Syndrome Multigene Panel

American College of Medical Genetics and Genomics (ACMG)

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

Genetic testing for Loeys-Dietz Syndrome (LDS) can aid in the diagnosis of LDS in addition to physical exam, echocardiography, dilated eye exam and MRI of the head, neck, thorax, abdomen and pelvis. Features of LDS include characteristic facial features, craniosynostosis, bifid uvula or cleft palate, tortuosity of the aorta and its branches, aortic dilatation and dissection, and joint hypermobility.

Patients have had mutations in one or another of the receptors for TGFβ. In a patient found to have consistent facial features, bifid uvula, and arterial tortuosity, the diagnosis can be confirmed with molecular testing. Tortuosity can sometimes be isolated (e.g., found only in the head and neck). (p. 175)

Familial Thoracic Aortic Aneurysm and Dissection (TAAD) Multigene Panel

American College of Medical Genetics and Genomics (ACMG)

American College of Medical Genetics and Genomics (2012) issued guidelines on the evaluation of adolescents or adults with some features of Marfan syndrome (MFS) (including TAAD), which recommendations included the following (p. 174-175):

Genetic testing for TAAD can aid in the diagnosis in addition to physical exam, family history, dilated eye exam, echocardiography and vasculature imaging. Diagnostic criteria for TAAD include autosomal dominant history of dilatation or dissection of the aortic root, ascending aorta or descending aorta in the absence of major criteria for the diagnosis of Marfan syndrome or other connective tissue disease.

testing is recommended for patients with aortic root/ascending aortic aneurysms or aortic dissection and risk factors for hereditary thoracic aortic disease (strong recommendation, moderate quality of evidence). These risk factors include:

-Thoracic aortic disease (TAD) and syndromic features of Marfan, Loeys-Dietz or vascular Ehlers-Danlos syndrome
-TAD presentation under 60 years of age
-Family history of either TAD or peripheral/intracranial aneurysms in first or second degree relative
-History of unexplained sudden death at a relatively young age in first or second degree relative. (p. e361)
-A multigene panel comprising all genes suspected to cause HTAD [heritable thoracic aortic disease] is the most cost-effective and clinically useful approach to testing. (p. e362)

GeneReviews: Heritable Thoracic Aortic Disease Overview

GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online.

Per the Heritable Thoracic Aortic Disease GeneReviews article, “A multigene panel that includes genes associated with HTAD [heritable thoracic aortic disease] is recommended.” Per Table 1 of this article, these genes include: *ACTA2, COL3A, FBN1, MYH11, MYLK, SMAD3, TGFB2, TGFBR1, TGFBR2, LOX, PRKG1, EFEMP2, FOXE3, MFAP5, SMAD2, BGN, CBS, COL4A5, ELN, FBN2, FLNA, HCN4, NOTCH1, MAT2A, PKD1, PKD2, SKI, SLC2A10, SMAD4, TGFB3*.

EHLERS-DANLOS SYNDROME

Classic Ehlers-Danlos Syndrome (cEDS) Multigene Panel

International EDS Consortium

The 2017 International Classification of the Ehlers-Danlos Syndromes (p. 11 and 13) included the following clinical features for the associated conditions. Confirmatory molecular testing is needed to reach a final diagnosis.

Classical EDS (cEDS):

Major criteria
1.Skin hyperextensibility and atrophic scarring

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

More than 90% of cEDS patients harbor a heterozygous mutation in one of the genes encoding type V collagen (*COL5A1* and *COL5A2*). (p. 13)

GeneReviews: Classic Ehlers-Danlos Syndrome

GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online.

“Sequencing analysis of *COL5A1* and *COL5A2*…is performed first to detect missense, nonsense, and splice site variants and small intragenic deletions/insertions.”

Vascular Ehlers-Danlos Syndrome (vEDS) – COL3A1 Sequencing and/or Deletion/Duplication Analysis

International EDS Consortium

The 2017 International Classification of the Ehlers-Danlos Syndromes (Malfait et al, 2017, p. 16) included the following clinical features for the associated conditions:

Vascular EDS (vEDS)

Major criteria

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
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*.

Patients with vEDS typically harbor a heterozygous variant in the *COL3A1* gene, encoding type III collagen, with the rare exception of specific heterozygous variants in *COL1A1*. Verification of clinical diagnosis via Molecular

approach should be complemented with a CNV detection strategy to identify large deletions or duplications.

Quick Code Search

Use this feature to find out if a procedure and diagnosis code pair will be approved, denied or held for review. Simply put in the procedure code, then the diagnosis code, then click "Add Code Pair". If the codes are listed in this policy, we will help you by showing a dropdown to help you.

Procedure

Please type a procedure code

Enter at least the first 3 characters of the code

Diagnosis

Please type a diagnosis code

Enter at least the first 3 characters of the code

Add

CODES

+ **CPT4**

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REVISIONS

01-01-2024
Updated Background. Minor updates to policy.

09-29-2023
Removed "medically necessary" and replaced with "scientifically validated" and also added "iinvestigational when the above criteria is not met and for all other indications"

06-13-2023
Updating format and references for 07/01/2023

01-01-2023
Updated table and minor changes in policy wording. References and background updated.

12-20-2021
Added indications to "Other Covered Connective Tissue Disorders"