Medical Policy

PARAMOUNT

HMO AND PPO
ELITE (MEDICARE ADVANTAGE)
MARKETPLACE

Genetic Testing for Cardiac Conditions

Policy Number: PG0280
Last Review: 03/10/2023

GUIDELINES:

- This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder terms, conditions, exclusions, and limitations contract. It does not constitute a contract or guarantee regarding coverage or reimbursement/payment. Self-Insured group specific policy will supersede this general policy when group supplementary plan document or individual plan decision directs otherwise.
- Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards.
- This medical policy is solely for guiding medical necessity and explaining correct procedure reporting used to assist in making coverage decisions and administering benefits.

SCOPE:

X Professional
X Facility

DESCRIPTION:

Cardiomyopathy is a chronic disease of the heart muscle (myocardium). The heart muscle becomes enlarged, thick, or rigid resulting in a failure to pump blood effectively, irregular heartbeats (arrhythmias) and possibly heart failure. Cardiomyopathy can be acquired or inherited. Hypertrophic cardiomyopathy (HCM) is one of the main types of cardiomyopathies. Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is another type of cardiomyopathy characterized by fatty and fibro-fatty infiltration of the right ventricle with resultant myocardial cell atrophy, cell death and ventricular arrhythmias ranging from frequent premature ventricular contractions to ventricular tachycardia. Inherited arrhythmias, which may be life-threatening, often begin in childhood and adolescence.

Cardiac ion channelopathies are a group of diseases that develop due to defects in ion channels and can be caused by either genetic or acquired factors. Genetic testing may be used to detect mutations believed to be linked to inherited cardiomyopathies and channelopathies to assist with diagnosis, determine prognosis and identify susceptibility in at-risk asymptomatic family members.

Long QT Syndrome (LQTS) is a genetic cardiac channelopathy where the heart muscle takes more time than usual to recharge between beats. This shows as a prolonged QT interval on an electrocardiogram (EKG). This abnormal heartbeat pattern can lead to episodes of dizziness/fainting, cardiac arrest, and sudden cardiac death (SCD) in affected individuals.

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) is a genetic cardiac channelopathy characterized by an extremely fast and irregular heartbeat in response to exercise or emotional stress. CPVT may cause syncope (fainting), cardiac arrest, or sudden cardiac death (SCD).

Short QT Syndrome (SQTS) is an autosomal dominant channelopathy where the heart muscle takes less time than usual to recharge between beats. This shows as a shortened QT interval on an electrocardiogram (EKG). This abnormal heartbeat pattern may cause symptoms of dizziness/fainting and may increase the risk for adverse cardiac events. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Brugada syndrome is characterized by cardiac conduction abnormalities that increase the risk of syncope, ventricular arrhythmia, and sudden cardiac death. The disorder primarily manifests during adulthood, although

ages between 2 days and 85 years have been reported. Males are more likely to be affected than females (approximately an 8:1 ratio). There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Familial Hypercholesteremia (FH) is a genetic condition in which affected individuals have significantly elevated low-density lipoprotein cholesterol (LDL-C). This results in atherosclerotic plaque deposition in the coronary arteries and proximal aorta at a young age and increases the risk of premature cardiovascular events like angina and myocardial infarction. Stroke occurs more rarely in FH. Additionally, individuals with FH may develop xanthomas and xanthelasmas as well as corneal arcus (typically at a younger age than individuals without FH). Individuals who have biallelic mutations in FH-related genes may develop a more severe phenotype including very significant elevations in LDL-C (>500 mg/dL), coronary artery disease presenting in childhood for some, and calcific aortic valve disease.

Familial thoracic aortic aneurysms and aortic dissections (TAAD) is a condition in which individuals may experience a permanent, localized dilation in their thoracic aorta (upper part of the aorta, close to the heart). Thoracic aortic aneurysms often are asymptomatic and increase in size over time, which if undiagnosed/untreated can cause aortic dissections. Aortic dissections are a tear in the inner wall of the aorta, which leads to bleeding to occur between the inner and outer walls of the aorta.

Thoracic aortic aneurysms and aortic dissections (TAAD) can be related to a gene mutation that confers a high risk for TAAD (heritable thoracic aortic disease/HTAD). It is estimated that 20% of TAAD are related to a genetic mutation (i.e. HTAD). Multi-gene panels related to TAAD should include the following genes that convey a highly penetrant risk: FBN1, LOX, COL3A1, TGFBR1, TGFBR2, SMAD3, TGFB2, ACTA2, MYH11, MYLK, and PRKG1. These genes can also be associated with systemic features and can overlap with Marfan syndrome, Loeys-Dietz syndrome, as well as Ehlers-Danlos syndrome.

POLICY:

Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans

- **Genetic testing for cardiac conditions (81413, 81414, 81439, 81479, S3865, S3866) requires prior authorization.**

Medicare Advantage Plans

- **Genetic testing for cardiac conditions (81413, 81414, 81439, 81479) requires prior authorization.**
- **Procedure codes S3865 and S3866 are non-covered**

Paramount Commercial Insurance Plans, Medicare Advantage Plans and Paramount Medicaid Advantage

- **Procedure code S3861 is non-covered.**

Genetic testing may be excluded by contract. Please consult the member's individual contract regarding coverage.

COVERAGE CRITERIA:

Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans

General Criteria for Genetic Tests

Paramount members may be eligible for genetic testing when ALL the following criteria are met:

- Individual has not previously received genetic testing for the disorder. Note: In general, genetic testing for a particular disorder should be performed once per lifetime; however, there are rare instances in which testing may be performed more than once in a lifetime (e.g., previous testing methodology is inaccurate, a new discovery has added significant relevant mutations for a disease, significant changes in technology or treatments indicate that test results or outcomes may change as a result of repeat testing)
- Laboratory or clinical tests to definitively diagnose the genetic disorder are unavailable or results are equivocal

- Panels including, but may not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/method is clinically available, may be covered ONLY for the number of genes or tests deemed medically necessary to establish a diagnosis
- Results of genetic testing will directly impact and change clinical management of the individual being tested who is a covered member
- Technical and clinical performance of the genetic test is supported by published peer-reviewed medical literature

The following genetic tests must meet the above General Criteria for Genetic Tests, as indicated above, in addition to the individual criteria outlined below for each test.

Hereditary Cardiomyopathy and Arrhythmia syndromes
Genetic testing for hereditary cardiomyopathy or arrhythmia syndromes is medically necessary in individuals with a confirmed or suspected diagnosis of one of the following conditions:

- Arrhythmogenic right ventricular cardiomyopathy; or
- Brugada syndrome; or
- Catecholaminergic polymorphic ventricular tachycardia (CPVT); or
- Dilated cardiomyopathy
- Hypertrophic cardiomyopathy
- Left ventricular non-compaction cardiomyopathy
- Long QT syndrome
- Restrictive cardiomyopathy

AND when testing is targeted to a subset of genes associated with the individual's suspected or diagnosed condition.

Genetic testing with broad multi-gene panel testing is considered not medically necessary when a specific cardiac phenotype has been identified.

Genetic testing of asymptomatic individuals who have a first or second degree relative with a known mutation related to one of the previously mentioned hereditary cardiomyopathy or arrhythmia syndromes is medically necessary (Note: Test for the known familial mutation).

Familial Hypercholesterolemia (APOB, LDLR, LDLRAP1 [ARH] and PCSK9 Genes)
Paramount members may be eligible for genetic testing for Familial Hypercholesterolemia when one of the following criteria are met:

- Adults (untreated): Low-density lipoprotein cholesterol (LDL-C) levels >190 mg/dL (>4.9 mmol/L) (without an apparent secondary cause of hypercholesterolemia)
- Children/adolescents (untreated): LDL-C levels >160 mg/dL (without an apparent secondary cause of hypercholesterolemia); or with an LDL-C level ≥190 mg/dl in ≥1 parent
- Personal history of premature coronary artery disease such as myocardial infarction or obstructive CAD requiring intervention or other cardiovascular disease (e.g., ischemic stroke, peripheral vascular disease) diagnosed before age 55 in males and age 65 in females
- Individual with physical findings concerning for FH such as xanthomas, xanthelasmas, or corneal arcus (particularly when the individual is younger than 45)
- Family history of a known FH-related mutation in a first or second degree relative (Note: Test for the known familial mutation)

Exclusions:

- Genetic testing to confirm a diagnosis of Familial Hypercholesterolemia does not meet coverage criteria in all other situations
- Genetic testing for the sole purpose of treatment decisions (i.e., PCSK9 inhibitors) in the absence of a clinical suspicion supported

Heritable Thoracic Aortic Disease

Paramount members may be eligible for genetic testing for Heritable Thoracic Aortic Disease when the following criteria are met:

- Multi-gene panel testing for individuals with a confirmed or suspected diagnosis of heritable thoracic aortic disease is medically necessary; or
- Asymptomatic persons with an affected first-degree blood relative (i.e., parent, full-sibling, child) with a known deleterious or suspected deleterious mutation in a gene known to cause familial thoracic aortic aneurysms and dissections.

Exclusions:

- Genetic testing for thoracic aortic aneurysms and dissections (TAAD) is considered experimental and investigational for any other indication, including but not limited to persons clinically diagnosed with TAAD, with a positive family history of the disorder, and for whom a genetic syndrome has been excluded.

Paramount does not cover genetic testing for atrial fibrillation or Short QT syndrome because it is considered not medically necessary.

Paramount does not cover genetic testing for hereditary cardiac conditions in the general population because such screening is considered not medically necessary.

Elite (Medicare Advantage) Plans

Genetic testing for hereditary cardiovascular disease will be considered medically reasonable and necessary if:

- The patient has rigorous disease-appropriate phenotyping to establish clinical diagnosis or suspected diagnosis for which the test results would directly impact the management of the patient's condition, prior to ordering the test AND
- The evidence for the gene-disease association is evaluated by the evidence-based, transparent, peer-reviewed process of the National Institutes of Health (NIH) sponsored Clinical Genome Resource (ClinGen) and is determined to demonstrate action ability in clinical decision making, meeting all bulleted metrics:
    - Disease severity of sudden death, possible death or major morbidity, modest morbidity
    - Substantial or moderate evidence of a >40% likelihood of disease
    - Substantial or moderate evidence of a highly effective or moderately effective intervention
    - The nature of intervention is either low risk/medically acceptable/low intensity intervention or moderately acceptable/risk/intensive interventions, AND
- Clinical validity and qualitative descriptors from Moderate, Strong & Definitive with contradictory evidence NOT being reported as disputed or refuted.

Limitations

The following are considered not medically reasonable and necessary:

- A genetic test where either analytical validity, clinical validity, or clinical utility has not been established.
- Genetic testing in patients who do not demonstrate the disease-appropriate phenotype of the gene-disease association.
- Genetic testing of asymptomatic patients.
- Genetic testing solely for purposes of proband identification.
- Genetic testing with family history as the only indication.
- Gene tests for cardiovascular disease are considered germline testing, and therefore only permitted once per member's lifecycle.

Provider Qualifications

The ordering provider of a genetic test for a patient with a cardiovascular disease-appropriate phenotype:

- Must be the treating clinician who is responsible for the cardiovascular disease management of the patient's condition; and,

- Understands how the test result will impact the patient's condition; and,
- Has presented this information to the patient eliciting patient understanding.

Reference:
First-degree relatives are parents, full siblings, and children. Second-degree relatives are grandparents, grandchildren, aunts, uncles, nephews, nieces, and half-siblings

CODING/BILLING INFORMATION:
The appearance of a code in this section does not necessarily indicate coverage. Codes that are covered may have selection criteria that must be met. Payment for supplies may be included in payment for other services rendered.

CPT CODES	
81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat) [APOB Targeted Mutation Analysis}
81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons) [LDLR Known Familial Mutation Analysis]
81404	Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
81405	Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis) [LDLR Deletion/Duplication Analysis]
81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons) [LDLR Sequence Analysis][PCSK9 Sequence Analysis]
81407	Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform) [APOB Sequence Analysis]
81408	Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis)
81413	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A
81414	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); duplication/deletion gene analysis panel, must include analysis of at least 2 genes, including KCNH2 and KCNQ1
81439	Inherited cardiomyopathy (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy) genomic sequence analysis panel, must include sequencing of at least 5 genes, including DSG2, MYBPC3, MYH7, PKP2, and TTN
81479	Unlisted molecular pathology procedure
HCPCS CODES	
S3861	Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada Syndrome
S3865	Comprehensive gene sequence analysis for hypertrophic cardiomyopathy
S3866	Genetic analysis for a specific gene mutation for hypertrophic cardiomyopathy (HCM) in an individual with a known HCM mutation in the family

REVISION HISTORY EXPLANATION: ORIGINAL EFFECTIVE DATE: 01/15/2010

Date	Explanation & Changes
01/01/2011	• No change
07/12/2012	• Revision to match U/CM Benefit Description and Limitations of Coverage

09/09/2014	• Removed deleted codes 83891, 83892, 83894, 83898, 83904, 83909, 83912, S3860, & S3862 • Added new codes 81280, 81281, 81282, & 81406 • Policy reviewed and updated to reflect most current clinical evidence per Medical Policy Steering Committee
03/24/2017	• Changed title from Long QT Syndrome (LQTS) Genetic Testing to Genetic Testing for Cardiac Conditions • Deleted effective 12/31/16 CPT codes 81280-81282 • Added effective 01/01/17 new CPT codes 81413, 81414, & 81439 requiring prior authorization • Added codes 81403-81405, 81407-81408, & S3861-S3866 • Code S3861 is non-covered for all product lines • Codes 81403-81405, 81407-81408, & S3865, S3866 require prior authorization • Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
03/22/2018	• Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
12/18/2020	• Medical policy placed on the new Paramount Medical Policy Format
02/16/2023	• Medical Policy updated to reflect Medicaid coverage to Anthem as of 02/01/2023
03/10/2023	• Policy reviewed and updated to reflect most current clinical evidence • Added coverage criteria for genetic testing for Familial Hypercholesterolemia (FH) for the Paramount Commercial Insurance Plans and • Added coverage criteria for genetic testing for Heritable Thoracic Aortic Disease for the Paramount Commercial Insurance Plans. • Updated the coverage criteria for the Medicare Advantage Plans based upon most recent coverage determination, L39082 • Removed deleted codes 81280, 81281 and 81282
03/06/2024	• Medical policy placed on the new Paramount Medical Policy Format

Paramount reserves the right to review and revise our policies periodically when necessary. When there is an update, we will publish the most current policy to https://www.paramounthealthcare.com/providers/medical-policies/policy-library

REFERENCES/RESOURCES

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Internet-Only-Manuals-IOMs

American Medical Association, *Current Procedural Terminology (CPT®)* and associated publications and services https://www.ama-assn.org/amaone/cpt-current-procedural-terminology

Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets https://www.cms.gov/Medicare/Coding/HCPCSReleaseCodeSets/HCPCS-Quarterly-Update

U.S. Preventive Services Task Force, https://www.uspreventiveservicestaskforce.org/uspstf/
Industry Standard Review

Hayes, Inc., https://www.hayesinc.com/

Industry Standard Review