Genetic Testing for Cardiac Conditions

INDEPENDENT CARE HEALTH PLAN

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Medicare Advantage Medical Coverage Policy

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Related Documents

Please refer to CMS website for the most current applicable National Coverage Determination (NCD)/ Local Coverage Determination (LCD)/Local Coverage Article (LCA)/CMS Online Manual System/Transmittals.

Type	Title	ID Number	Jurisdiction Medicare Administrative Contractors (MACs)	Applicable States/Territories
LCD	Biomarkers Overview	L35062	JH, JL - Novitas Solutions, Inc.	AR, CO, DE, MD, NJ, NM, OK, PA, TX, LA, MS, D.C.
LCD	Genetic Testing for Cardiovascular Disease	L39082		
LCD	Genetic Testing for Cardiovascular Disease	L39084	JN - First Coast Service Options, Inc. (Part A/B MAC)	FL, PR, U.S. VI
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36523	J5, J8 - Wisconsin Physicians Service Insurance Corporation	IA, IN, KS, MI, MO, NE
LCD	MolDX: Genetic Testing for Hypercoagulability/Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L36400		
LCD	MolDX: Molecular Diagnostic Tests (MDT)	L36807		
LCA	MolDX: ApoE Genotype	A55141		
LCA	MolDX 4q25-AF Risk Genotype Testing	A55137		
LCA	MolDX: 9p21 Genotype Test	A55138		
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36139	J15 - CGS Administrators, LLC	KY, OH
LCD	MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L35984		
LCD	MolDX: Molecular Diagnostic Tests (MDT)	L36021		
LCA		A54241		

LCA	MolDX 4q25-AF Risk Genotype Testing	A54242		
LCA	MolDX: 9p21 Genotype Test	A54244		
	MolDX: ApoE Genotype			
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36358		
LCD	MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L36155	JE - Noridian Healthcare Solutions, LLC	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
LCA	MolDX: 4q25-AF Risk Genotype	A55090		
LCA	MolDX: 9p21 Genotype Test	A55092		
LCA	MolDX: ApoE Genotype	A55094		
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36362		
LCD	MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L36159	JF - Noridian Healthcare Solutions, LLC	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
LCA	MolDX: 4q25-AF Risk Genotype	A55091		
LCA	MolDX: 9p21 Genotype Test	A55093		
LCA	MolDX: ApoE Genotype	A55095		
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36129		
LCD	MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L36089	JJ, JM - Palmetto GBA	AL, GA, NC, SC, TN, VA, WV
LCA	MolDX: 4q25-AF Risk Genotype	A53457		

LCA LCA	MolDX: 9p21 Genotype Test MolDX: ApoE Genotype	A53657 A53652		
LCD	Molecular Pathology Procedures	L35000	J6, JK - National Government Services, Inc.	CT, IL, ME, MA, MN, NH, NY, RI, VT, WI

Description

Cardiovascular Disease Genetic Markers

Cardiovascular disease (CVD) risk testing is performed to help determine an individual's risk of having a cardiovascular event such as a heart attack or stroke. The most common test used to determine CVD risk is the lipid profile, which measures cholesterol, triglycerides, high density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C).

Panels beyond the basic lipid profile are commercially available and may include analysis of genetic markers for CVD risk including single nucleotide polymorphism (SNPs) genotyping and often pharmacogenomics tests. SNP genotype testing has been proposed to identify an individual at risk for atrial fibrillation (AF), coronary artery disease and early myocardial infarction (MI). Examples of genotyping tests include but may not be limited to:

- 4q25 (eg, 4q25-AF Risk Genotype Test, Cardio IQ 4q25-AF Risk Genotype Test)
- 9p21 (eg, Cardio IQ 9p21 Genotype Test)
- LPA Intron-25 (eg, Cardio IQ LPA Intron-25 Genotype Test, LPA-Intron 25 Genotype Test)
- ST2 (growth stimulation expressed gene 2) (eg, Cardio IQ ST2)

CVD risk panels may also include genetic tests to determine an individual's susceptibility for hypercoagulation or thrombosis, which has been proposed as a risk factor for CVD. Testing may include factor II (ie, *F2* gene), factor V (ie, *F5* gene) or plasminogen activator inhibitor (PAI-1).

Inherited Cardiomyopathies and Channelopathies

Cardiomyopathy is a chronic disease of the myocardium (heart muscle). The heart muscle becomes enlarged, thick or rigid, resulting in a failure to pump blood effectively, which can lead to arrhythmias (irregular heartbeats) and possible heart failure. Cardiomyopathy can be acquired or inherited. Hypertrophic cardiomyopathy (HCM) is one of the main types of cardiomyopathies.

Cardiac ion channelopathies are a group of diseases that develop due to defects in ion channels and can be caused by either genetic (germline) or acquired factors. Inherited cardiac channelopathies include, but are not limited to, Brugada syndrome (BrS), catecholaminergic polymorphic ventricular tachycardia (CPVT) and long QT syndrome (LQTS).

Genetic testing may be used to detect variants believed to be linked to inherited cardiomyopathies and channelopathies to assist with diagnosis, determine prognosis and identify susceptibility in at-risk, unaffected family members.

Multigene (or expanded) panels analyze a broad set of genes simultaneously (as opposed to single gene testing that searches for variants in one specific gene) and have been proposed to evaluate the DNA of an individual with a personal and/or family history of more than one hereditary condition or syndrome or hereditary conditions/syndromes associated with more than one gene. Panels often include medically actionable genes but may also include those with unclear medical management. **Targeted (or focused) multigene panels** analyze a limited number of genes targeted to a specific condition.

Multicondition multigene panels are also available to analyze a broader range of genes associated with a group of diseases (eg, inherited channelopathies). In this example the panel may target genes for all inherited channelopathies including BrS, CPVT and LQTS.

Finally, what can be termed as **comprehensive multigene panels** offer analysis of an even broader range of genes and include those associated with both inherited cardiomyopathies and channelopathies.

Examples of multicondition and comprehensive multigene panels include, but may not be limited to:

- AtheroGxOne
- CardioNext
- CMNext
- DCMNext
- Genomic Unity Cardiac Ion Channelopathies Analysis
- HCMNext
- LongQTNext
- Pan Cardiomyopathy Panel
- RhythmNext

Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is a genetic (germline, autosomal dominant) disorder. Gene variants can inhibit the liver from metabolizing excess low density lipoprotein cholesterol (LDL-C), resulting in lifelong exposure to elevated LDL-C levels which contributes to premature atherosclerotic cardiovascular disease.

There are two forms of FH including heterozygous FH (HeFH) (single gene variant received from one parent) and homozygous FH (HoFH) (more than one variant received from one or both parents). HeFH is the most common form and is found in approximately 1:250 individuals. HoFH is rare, occurring in approximately 1:350,000 individuals, but can have an earlier onset with more severe outcomes.[105]

Marfan Syndrome

Marfan syndrome is a genetic (germline, autosomal dominant) disorder in which the body's connective tissue is abnormal. The disorder affects many parts of the body; primarily, blood vessels, bones, connective

tissue of the heart, covering of the spinal cord, eyes and lungs. Marfan syndrome diagnosis relies on a set of strict major and minor criteria known as the Ghent nosology, a scoring system developed to aid in the clinical diagnosis of Marfan syndrome.[72] Two fundamental features of the Ghent nosology are aortic root dilatation and ectopia lentis. In the absence of a family history of Marfan syndrome, the presence of aortic root dilatation and ectopia lentis are sufficient to diagnose Marfan syndrome. Without these two conditions or a combination of systemic features described in the Ghent nosology, genetic testing may be required to confirm a diagnosis. Even with the availability of genetic testing, establishing a diagnosis of Marfan syndrome depends heavily upon significant clinical findings.

Coverage Determination

iCare follows the CMS requirement that only allows coverage and payment for services that are reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member except as specifically allowed by Medicare.

Genetic tests must demonstrate clinical utility, analytical and clinical validity and fulfill the CMS "reasonable and necessary" criteria. Analytic validity (test accurately identifies the gene variant), clinical validity (test identifies or predicts the clinically defined disorder) and clinical utility (test measurably improves clinical outcomes) of the genetic test is supported by generally accepted standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, specialty society recommendations, and views of physicians practicing in relevant clinical areas. The test must be ordered by a physician who is treating the beneficiary and the results will be used in the management of a beneficiary's specific medical problem.

For jurisdictions with no Medicare guidance for a particular test, iCare will utilize the MolDX program and Technical Assessments for molecular assays as the standard to evaluate clinical utility, analytical and clinical validity in conjunction with adhering to Medicare's reasonable and necessary requirement.

In interpreting or supplementing the criteria above and in order to determine medical necessity consistently, iCare may consider the following criteria:

General Criteria for Cardiac Conditions

Apply general criteria for genetic testing for cardiac conditions when disease- or gene-specific criteria are not available in this medical coverage policy.

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

- Analytic validity (test accurately identifies the gene variant), clinical validity (test identifies or predicts the clinically defined disorder) and clinical utility (test measurably improves clinical outcomes) of the genetic test is supported by the MolDX Program or by generally accepted standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the

relevant medical community, specialty society recommendations and views of physicians practicing in relevant clinical areas; **AND**

- Alternative laboratory or clinical tests to definitively diagnose the disorder/identify the condition are unavailable or results are clearly equivocal; **AND**

- Individual has a rigorous disease-appropriate phenotyping to establish clinical diagnosis or suspected diagnosis for which the test results would directly impact the management of the condition, prior to ordering the test; **AND**

- Evidence for the gene-disease association demonstrates actionability in clinical decision making including all of the following:

  - Disease severity of sudden death, possible death or major morbidity, modest morbidity; **AND**
  - Substantial or moderate evidence of a greater than 40% likelihood of disease; **AND**
  - Substantial or moderate evidence of a highly effective or moderately effective intervention; **AND**
  - The nature of intervention is either low risk/medically acceptable/low intensity intervention or moderately acceptable/risk/intensive interventions, **AND**

- Results of the genetic testing must directly impact treatment or management of the Medicare beneficiary

Criteria for Specific Cardiac Conditions:

GERMLINE (HEREDITARY) TESTING:

Catecholaminergic Polymorphic Ventricular Tachycardia (*CALM1, CALM2, CALM3, CASQ2, KCNJ2, RYR2, TECRL and TRDN* Genes)
Genetic testing for catecholaminergic polymorphic ventricular tachycardia (CPVT) will be considered medically reasonable and necessary when the following requirements are met:

- Individual to be tested is affected and has an affected first-degree relative with a pathogenic or likely pathogenic CPVT variant (**genetic testing should be limited to known familial variant [KFV]**)

- Individual to be tested exhibits clinical features suggestive of CPVT including unexplained exercise- or catecholamine-induced polymorphic ventricular arrhythmias and syncope during physical activity or acute emotion occurring in a structurally normal heart; **OR**

  CPVT Testing Strategy: perform single gene sequencing and/or deletion/duplication analysis or targeted multigene panel that includes *CALM1, CALM2, CALM3, CASQ2, KCNJ2, RYR2, TECRL, TRDN* genes.[84]

Familial Hypercholesterolemia (*APOB, LDLR, LDLRAP1* [*ARH*] and *PCSK9 Genes*)

Genetic testing for familial hypercholesterolemia (FH) will be considered medically reasonable and necessary when the following requirements are met:

- Acquired and secondary causes of hypercholesterolemia (eg, diet and medication-induced hypercholesterolemia, endocrine, hepatic and renal disease) have been excluded by standard diagnostic evaluation; **AND**

  - Individual to be tested is affected and has an affected first- or second-degree relative with a pathogenic or likely pathogenic variant of an FH associated gene (**genetic testing should be limited to KFV**); **OR**

  - Individual to be tested has a persistent LDL-C level***** greater than 190 mg/dL (18 years of age or older) or 160 mg/dL (17 years of age or younger); **OR**

  - Individual to be tested has diagnosis of premature atherosclerotic cardiovascular disease (before 55 years of age in males; before 60 years of age in females)

  Testing Strategy: perform single gene sequencing and/or deletion/duplication analysis or targeted multigene panel that includes *APOB*, *LDLR*, *LDLRAP1* and *PCSK9* genes.[86]

*****Two or more measurements, including assessment after intensive lifestyle modification.[51]

Hypertrophic Cardiomyopathy – Nonsyndromic (*ACTC1*, *MYBPC3*, *MYH7*, *MYL2*, *MYL3*, *TNNI3*, *TNNT2* and *TPMI* Genes)

Genetic testing for hypertrophic cardiomyopathy (HCM) will be considered medically reasonable and necessary when the following requirements are met:

- Individual to be tested is affected and has an affected first-degree relative in whom a pathogenic or likely pathogenic HCM variant has been identified (**test for KVF**); **OR**

- Individual to be tested has been diagnosed with left ventricular hypertrophy (LVH) using noninvasive cardiac imaging (eg, electrocardiogram [ECG], echocardiography and/or cardiac magnetic resonance imaging [MRI]) and no identifiable cause (eg, valvular disease, hypertension, infiltrative or neuromuscular disorder) has been identified

  Testing Strategy: perform targeted multigene analysis for pathogenic or likely pathogenic variant that includes *ACTC1, MYBPC3*, *MYH7*, *MYL2*, *MYL3, TNNI3*, *TNNT2* and *TPMI* genes.[88]

Long QT Syndrome (*KCNH2, KCNQ1* and *SCN5A* Genes)

Genetic testing for long QT syndrome (LQTS) will be considered medically reasonable and necessary when the following requirements are met:

- Individual to be tested is affected and has an affected first-degree relative in whom a pathogenic or likely pathogenic LQTS variant has been identified (**genetic testing should be limited to KFV**); **OR**

- Individual to be tested has prolonged QT interval on ECG in whom an acquired cause of QT interval prolongation has been ruled out (eg, bradycardia, electrolyte imbalances, heart failure or medications); **OR**

  Testing Strategy for LTQS: perform single gene sequencing and/or deletion/duplication analysis or targeted multigene panel that includes *KCNH2, KCNQ1* and *SCN5A* gene.[89]

Marfan Syndrome – *FBN1* Gene
***FBN1* gene testing for Marfan syndrome** will be considered medically reasonable and necessary when the following requirements are met:

- Individual to be tested is affected and has an affected first-degree relative with a known pathogenic or likely pathogenic variant (**genetic testing should be limited to KFV**); **OR**

- Individual to be tested does not meet Clinical Diagnostic Criteria for Marfan Syndrome but diagnosis is highly suspected

  Testing strategy: perform *FBN1* gene sequencing. If negative, proceed to *FBN1* gene deletion/duplication analysis.[50,87]

The use of the criteria in this Medicare Advantage Medical Coverage Policy provides clinical benefits highly likely to outweigh any clinical harms. Services that do not meet the criteria above are not medically necessary and thus do not provide a clinical benefit. Medically unnecessary services carry risks of adverse outcomes and may interfere with the pursuit of other treatments which have demonstrated efficacy.

Coverage Limitations

US Government Publishing Office. Electronic code of federal regulations: part 411 – 42 CFR § 411.15 - Particular services excluded from coverage

The following tests may not be considered a benefit (statutory exclusion):

- Apolipoprotein E (*APOE*) genotype testing[30,31,32,33]

- Cardiovascular disease (CVD) risk markers, alone or within panels

  - 4q25 genotype testing (eg, 4q25-AF Risk Genotype, Cardio IQ 4q25-AF Risk Genotype)[20,21,22,23,24]

  - 9p21 genotype testing (eg, 9p21 Genotype)[25,26,27,28,29]

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  - LPA Intron-25 (eg, Cardio IQ LPA Intron-25 Genotype Test, LPA-Intron 25 Genotype Test)[35]
  - CARDIO inCode-Score (0401U)[36,37,48,49]

- Hypercoagulation, prothrombin or thrombophilia genetic testing in nonpregnant individuals including, but not limited to:
  - Factor II (thrombin) (*F2* gene)[43,44,45,46,47]
  - Factor V Leiden (*F5* gene)[43,44,45,46,47]
  - Plasminogen activator inhibitor (PAI-1)[38,39,40,41,42]
- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law;[91] **OR**
- Tests that confirm a diagnosis or known information;[91] **OR**
- Tests that investigate the same germline genetic content, for the same genetic information, that has already been tested in the same individual; **OR**
- Tests to determine risk for developing a disease or condition;[91] **OR**
- Tests performed to measure the quality of a process;[91] **OR**
- Tests without diagnosis specific indications;[91] **OR**
- Tests identified as investigational by available literature and/or the literature supplied by the developer and are not a part of a clinical trial[91]

These treatments and services fall within the Medicare program's statutory exclusion that prohibits payment for items and services that have not been demonstrated to be reasonable and necessary for the diagnosis and treatment of illness or injury (§1862(a)(1) of the Act). Other services/items fall within the Medicare program's statutory exclusion at 1862(a)(12), which prohibits payment.

The following **genetic tests for cardiac conditions** will not be considered medically reasonable and necessary:

- Genetic tests that have not demonstrated clinical utility, analytical and clinical validity via the MolDX Program
- Genetic testing for Brugada syndrome[66]
- Deletion/duplication information is obtained as part of the sequencing procedure but submitted as an independent analysis

- Gene testing for Marfan syndrome with any gene other than *FBN1*[50,87] (81410, 81411)

- To diagnose Marfan syndrome when a diagnosis can be established using Clinical Diagnostic Criteria for Marfan Syndrome[70]

A review of the current medical literature shows that the evidence is insufficient to determine that this service is standard medical treatment for these indications. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of this service in clinical management for these indications.

Summary of Evidence

Brugada Syndrome
The genetic and clinical heterogeneity of Brugada syndrome limit the utility of genetic testing, as the absence of a mutation in *SCN5A* or other pathogenic variant does not exclude Brugada syndrome, and the presence of such a variant does not confirm the diagnosis of Brugada syndrome.[97]

Marfan Syndrome
Marfan syndrome is diagnosed using consensus diagnostic criteria. Sequencing analysis of the *FBN1* gene can be used for an individual who does not meet clinical diagnostic criteria but the diagnosis is highly suspected. Sequencing analysis of the *FBN1* gene detects variants in approximately 90-93% of individuals with Marfan syndrome.[87]

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17)	
81226	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)	
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6)	

81229	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities	
81240	F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant	
81241	F5 (coagulation factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant	
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (eg, hereditary hypercoagulability) gene analysis, common variants (eg, 677T, 1298C)	
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G>A, c.173+1000C>T)	
81381	HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each	
81400	MOLECULAR PATHOLOGY PROCEDURE LEVEL 1	
81401	MOLECULAR PATHOLOGY PROCEDURE LEVEL 2	
81402	MOLECULAR PATHOLOGY PROCEDURE LEVEL 3	
81403	MOLECULAR PATHOLOGY PROCEDURE LEVEL 4	
81404	MOLECULAR PATHOLOGY PROCEDURE LEVEL 5	
81405	MOLECULAR PATHOLOGY PROCEDURE LEVEL 6	
81406	MOLECULAR PATHOLOGY PROCEDURE LEVEL 7	
81407	MOLECULAR PATHOLOGY PROCEDURE LEVEL 8	
81408	MOLECULAR PATHOLOGY PROCEDURE LEVEL 9	
81410	Aortic dysfunction or dilation (eg, Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); genomic sequence analysis panel, must include sequencing of at least 9 genes, including FBN1, TGFBR1, TGFBR2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, and MYLK	
81411	Aortic dysfunction or dilation (eg, Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); duplication/deletion analysis panel, must include analyses for TGFBR1, TGFBR2, MYH11, and COL3A1	
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	Hereditary cardiomyopathy (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy), genomic sequence analysis panel, must include sequencing of at least 5 cardiomyopathy-related genes (eg, DSG2, MYBPC3, MYH7, PKP2, TTN)	
81479	Unlisted molecular pathology procedure	
83006	Growth stimulation expressed gene 2 (ST2, Interleukin 1 receptor like-1)	
85415	Fibrinolytic factors and inhibitors; plasminogen activator	
0237U	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia), genomic sequence analysis panel including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions	
0401U	Cardiology (coronary heart disease [CAD]), 9 genes (12 variants), targeted variant genotyping, blood, saliva, or buccal swab, reported as a genetic risk score for a coronary event	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

References

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Appendix

Appendix A
Family Relationships

Degree of Relationship	Definition
First-degree	Child, full-sibling, parent
Second-degree	Aunt, uncle, grandchild, grandparent, nephew, niece, half-sibling
Third-degree	First cousin, great aunt, great-uncle, great-grandchild, great-grandparent, half-aunt, half-uncle

Appendix B
Clinical Diagnostic Criteria for Marfan Syndrome

No family history of Marfan syndrome and **ANY** of the following are diagnostic for Marfan syndrome:

- Ectopia lentis or Marfan syndrome systemic score at least 7 (systemic score calculator); **AND**
    - Aortic diameter Z score at least 2 (Z score calculator); **OR**
    - Aortic root dissection

Family history of Marfan syndrome and **ANY** of the following are diagnostic for Marfan syndrome:

- Individual is 20 years of age or older and aortic diameter Z score at least 7 (Z score calculator); **OR**
- Individual is 19 years of age or younger and aortic diameter Z score at least 3 (Z score calculator); **OR**
- Aortic root dissection**; OR**
- Ectopia lentis; **OR**
- Marfan syndrome systemic score at least 7 (systemic score calculator)

Change Summary

- Click or tap to enter a date. New Policy.