MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**Genetic Testing for Cardiac Ion Channelopathies**
Policy Number	**2.02.38**
Category	**Technology Assessment**
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Committee Approval Date	**04/16/09, 04/22/10, 04/21/11, 03/15/12, 03/21/13, 02/20/14, 03/19/15, 03/17/16, 03/16/17, 03/15/18, 03/21/19, 04/16/20, 05/20/21, 05/19/22, 05/18/23**
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Product Disclaimer	• *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, genetic testing for congenital long QT syndrome (LQTS) is considered **medically appropriate** for:
   A. Patients who meet the clinical criteria for congenital LQTS when:
      1. The signs and/or symptoms of LQTS are present, but a definitive diagnosis cannot be made without genetic testing; and
      2. The test results will influence decisions concerning disease treatment.
   B. Individuals at risk for congenital LQTS who do not meet the clinical criteria for LQTS, but who have:
      1. A first-, second-, or third-degree relative with a known LQTS mutation; or
      2. A first-, second-, or third-degree relative diagnosed, by clinical means, with LQTS whose genetic status is unavailable; or
      3. Signs and/or symptoms indicating a moderate-to-high pretest probability of LQTS. Determining the pretest probability of LQTS is not standardized. (An example of a patient with a moderate to high pretest probability of LQTS is a patient with a Schwartz score of 2-3); and
      4. The test results will influence decisions concerning disease treatment.

II. Based upon our criteria and assessment of the peer-reviewed literature, genetic testing for catecholaminergic polymorphic ventricular tachycardia (CPVT) is considered **medically appropriate** for:
   A. Patients who meet the clinical criteria for CPVT when:
      1. The signs and/or symptoms of CPVT are present, but a definitive diagnosis cannot be made without genetic testing; and
      2. The test results will influence decisions concerning disease treatment.

B. Individuals at risk for CPVT who do not meet the clinical criteria for CPVT, but who have:
   1. A first-, second-, or third-degree relative with a known CPVT mutation; or
   2. A first-, second-, or third-degree relative diagnosed, by clinical means, with CPVT whose genetic status is unavailable; and
   3. The test results will influence decisions concerning disease treatment.

III. Based upon our criteria and assessment of the peer-reviewed literature, genetic testing for Brugada syndrome (BrS) is considered **medically appropriate** for:
   A. Patients who meet the clinical criteria for BrS when:
      1. The signs and/or symptoms of BrS are present, but a definitive diagnosis cannot be made without genetic testing; and
      2. The test results will influence decisions concerning disease treatment.
   B. Individuals at risk for BrS who do not meet the clinical criteria for BrS, but who have:
      1. A first-, second-, or third-degree relative with a known BrS mutation; and
      2. The test results will influence decisions concerning disease treatment.

IV. Based upon our criteria and assessment of the peer-reviewed literature, genetic testing to determine future risk of short QT syndrome (SQTS) is considered **medically appropriate** for asymptomatic patients who have a first-, second-, or third-degree relative with a known SQTS variant.

POLICY GUIDELINES

I. Supporting documentation required:
   A. Family history (pedigree) which includes first-, second-, and third-degree relatives, identifying family members affected; and
   B. Genetic testing results from any other family members. If family member(s) have not been tested (and are more appropriate to be tested first), clear and distinct rationale as to why the family member(s) cannot be tested (i.e., specific reason why testing was declined); and
   C. Documentation of discussion between the physician and patient of rationale for genetic testing and treatment options for the patient, based on test results.

II. Genetic testing is appropriate only when performed by a qualified laboratory (refer to Policy Guideline V below) and offered in a setting with adequately trained health care professionals who are qualified to provide appropriate pre- and post-test counseling.

III. A first-degree relative is a blood relative with whom an individual shares approximately 50% of her/his genes (parents, full siblings, and children). A second-degree relative is a blood relative with whom an individual shares approximately 25% of her/his genes (grandparents, grandchildren, aunts, uncles, nephews, nieces and half-siblings). A third-degree relative is a blood relative with whom an individual shares approximately 12.5% of her/his genes (great-grandparents, great-grandchildren, great-aunts, great-uncles, first cousins, grand-nieces or grand-nephews.)

IV. The Health Plan and its employees adhere to all state and federal laws concerning the confidentiality of genetic testing and the results of genetic testing. All records, findings and results of any genetic test performed on any person shall be deemed confidential and shall not be disclosed without the written informed consent of the person to whom such genetic test relates. This information shall not be released to any person or organization not specifically authorized by the individual subject of the test.

V. Laboratories performing clinical tests must be certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).

VI. Genetic testing is contract dependent. Coverage only applies to members with a valid contract; coverage is not provided for family members without a valid contract.

DESCRIPTION

Congenital Long QT Syndrome (LQTS)

LQTS is an inherited disorder characterized by the lengthening of the repolarization phase of the ventricular action potential. This lengthening increases the risk for arrhythmic events, such as torsades de pointes, which may in turn result in syncope and sudden cardiac death. Management has focused on the use of beta blockers as first-line treatment, with pacemakers or implantable cardioverter defibrillators (ICD) as second-line therapy.

LQTS usually manifests itself before the age of 40 years, and may be suspected when there is a history of seizure, syncope, or sudden death in a child or young adult; this history may prompt additional testing in family members. It is estimated that more than one half of the 8,000 sudden unexpected deaths in children may be related to LQTS. The mortality of untreated patients with LQTS is estimated at one percent to two percent per year, although this figure will vary with the genotype. Frequently, syncope or sudden death occurs during physical exertion or emotional excitement, and thus LQTS has received some publicity regarding evaluation of adolescents for participation in sports. In addition, LQTS may be considered when a long QT interval is incidentally observed on an electrocardiogram **(**EKG). Diagnostic criteria for LQTS have been established, which focus on EKG findings and clinical and family history (e.g., Schwartz criteria). However, measurement of the QT interval is not well standardized, and in some cases, patients may be considered borderline.

In recent years, LQTS has been characterized as an "ion channel disease," with abnormalities in the sodium and potassium channels that control the excitability of the cardiac myocytes. A genetic basis for LQTS has also emerged, with seven different variants (LQT1- LQT7) recognized, each corresponding to mutations in different genes as indicated here. In addition, typical ST-T-wave patterns are also suggestive of specific subtypes. Some genetic subtypes are associated with abnormalities outside the cardiac conduction system.

In addition to identifying the locus name of the genes involved in LQTS, there are several syndrome names that identify forms of LQTS, depending on the genes responsible and the features associated with the condition. Most forms of LQTS are carried in an autosomal dominant manner, with the exception of Jervell and Lange-Nielsen syndrome (JLNS), which is inherited in an autosomal recessive manner.

The Romano-Ward syndrome (RWS) is the most common form of inherited LQTS, with an estimated prevalence of 1:7000. A syncopal event is the most common symptom and typically occurs without warning. About 50 to 70 percent of individuals with a disease-causing mutation in one of the genes associated with RWS have symptoms. Cardiac events may occur from infancy through middle age, but are most common from the preteen years through the 20s. Most individuals diagnosed with RWS have an affected parent. The proportion of cases caused by de novo mutations is small. Each child of an individual with RWS has a 50 percent risk of inheriting the disease-causing mutation. However, about 30 percent of families known to be clinically affected with RWS do not have detectable mutations in any one of the known genes. Clinical methods of genetic testing for this condition include mutation scanning and sequence analysis. The known genes, along with the locus name, that are responsible for this form include: KCNQ1 (LQT1), KCNH2 (LQT2), HERG, SCN5A (LQT3), KCNE1 (LQT5), MiRP1, CAV3, SCN4B, SNTAI, KCNJ5 and KCNE2 (LQT6).

Other less common and more severe forms of LQTS include Jervell and Lange-Nielsen Syndrome (JLNS), Andersen-Tawil syndrome (ATS), Ankyrin B syndrome, and Timothy syndrome or Syndactyly-Related LQTS.

Clinical Diagnosis

The Schwartz criteria are commonly used as a diagnostic scoring system for LQTS. The most recent version of this scoring system is shown below. A score of 3.5 or greater indicates a high probability that LQTS is present; a score of 1.5 to 3 indicates an intermediate probability; and a score of 1 or lower indicates a low probability of the disorder. Prior to the availability of genetic testing, it was not possible to test the sensitivity and specificity of this scoring system; therefore, the accuracy of this scoring system is ill-defined.

Diagnostic Scoring System for LQTS (Schwartz criteria)

Criteria	**Points**
Electrocardiographic findings:	
*QT_c >480 msec	3
*QT_c 460-470 msec	2
*QT_c <450 msec	1
History of torsades de pointes	2
T-wave alternans	1
Notched T-waves in three leads	1
Low heart rate for age	0.5
Clinical history:	
*Syncope brought on by stress	2
*Syncope without stress	1
*Congenital deafness	0.5
Family history:	
*Family members with definite LQTS	1
*Unexplained sudden death in immediate family members younger than 30 years of age	0.5

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

Variants in four genes are known to cause CPVT, and investigators believe that other unidentified loci are involved as well. Currently, only 55 percent to 65 percent of patients with CPVT have an identified causative variant. Variants of the RYR2, the gene encoding the cardiac ryanodine receptor or KCNJ2 result in an autosomal dominant form of CPVT. CASQ2 (cardiac calsequestrin) and TRDN-related CPVT exhibit autosomal recessive inheritance. Some investigators have reported heterozygotes for CASQ2, as well as, TRDN variants for rare, benign arrhythmias. RYR2 variants represent most CPVT cases (50%-55%), with CASQ2 accounting for one percent to two percent and TRDN accounting for an unknown proportion of cases. The penetrance of RYR2 variants is approximated at 83 percent. An estimated 50 percent to 70 percent of patients will have the dominant form of CPVT with a disease-causing variant. Most variants (90%) to RYR2 are missense variants, but in a small proportion of unrelated CPVT patients, large gene rearrangements or exon deletions have been reported. Additionally, nearly a third of patients diagnosed as LQTS with normal QT intervals have CPVT due to identified RYR2 variants. Another misclassification, CPVT diagnosed as Anderson-Tawil syndrome may result in more aggressive prophylaxis for CPVT whereas a correct diagnosis can spare a patient this treatment because Anderson-Tawil syndrome is rarely fatal.

Brugada Syndrome (BrS)

BrS is typically inherited in an autosomal dominant manner with incomplete penetrance. The proportion of cases that are inherited, versus de novo variants, is uncertain. Although some investigators have reported that up to 50 percent of cases are sporadic, others have reported that the instance of de novo variants is very low and is estimated to be only one percent of cases. Variants in 16 genes have been identified as causative of BrS, all of which lead to a decrease in the inward sodium or calcium current or an increase in one of the outward potassium currents. Of these, SCN5A is the most important, accounting for more than an estimated 20 percent of cases; SCN10A has also been implicated. The other genes

are of minor significance and account together for approximately five percent of cases. The absence of a positive test does not indicate the absence of BrS, with more than 65 percent of cases not having an identified genetic cause. Penetrance of BrS among persons with an SCN5A variant is 80 percent when undergoing electrocardiogram with sodium-channel blocker challenge and 25 percent when not using the electrocardiogram challenge.

Short QT Syndrome (SQTS)

SQTS has been linked predominantly to variants in three genes (KCNH2, KCNJ2, KCNQ1). Variants in genes encoding alpha- and beta-subunits of the L-type cardiac calcium channel (CACNA1C, CACNB2) have also been associated with SQTS. Some individuals with SQTS do not have a variant in these genes, suggesting changes in other genes may also cause this disorder. SQTS is believed to be inherited in an autosomal dominant pattern. Although sporadic cases have been reported, patients frequently have a family history of the syndrome or sudden cardiac death (SCD).

Genetic Testing

Genetic testing for LQT syndrome is performed at multiple academic and commercial laboratories, generally by next-generation sequencing or Sanger sequencing. In addition, panel testing for one or more cardiac ion channelopathies is available from a number of genetic diagnostics laboratories. The John Welsh Cardiovascular Diagnostic Laboratory, GeneDX, and Transgenomic all offer panels that genotype LQTS, CPVT, BrS, and SQTS, but there is some variation among manufacturers on the included genes.

The Arrhythmia Panel at GeneDx includes sequence analysis of 30 genes that cause various arrhythmia syndromes. Many of these genes code for ion channel proteins of the heart muscle that help regulate the movement of sodium, potassium and calcium ions in and out of cardiac cells, as well as their associated regulatory factors and interaction partners. Disease-causing variants in genes that cause arrhythmia syndromes, including ARVC, BrS, CPVT, and LQTS, have been reported to exhibit reduced penetrance and variable expressivity, even among individuals in the same family. Four other tests are offered by GeneDx as part of the Long QT syndrome testing.

The absence of a mutation does not imply the absence of LQTS; it is estimated that mutations are only identified in 60 percent to 70 percent of patients with a clinical diagnosis of LQTS. For these reasons, the most informative result of testing would come from symptomatic relatives known to have LQTS. Interpretation of the results will likely be improved as the databases grow. Another factor complicating interpretation of the genetic analysis is the penetrance of a given mutation or the presence of multiple phenotypic expressions. For example, approximately 50 percent of carriers of mutation never have any symptoms. There is variable penetrance for the LQTS, and penetrance may differ for the various subtypes. While linkage studies in the past indicated that penetrance was 90 percent or greater, more recent analysis by molecular genetics has challenged this number, and suggested that penetrance may be as low as 25 percent for some families.

RATIONALE

Long QT Syndrome

Indications for LQTS genetic testing will depend on a variety of factors, including family history, presence or absence of a known mutation in the family, symptoms, length of the QTc interval on EKG, etc. For diagnostic testing, patients who have a moderate-to-high pretest probability of LQTS, but in whom the diagnosis cannot be made by clinical methods, will derive the most benefit from testing. For individuals who have a known LQTS mutation in the family, but who do not themselves meet the clinical criteria for LQTS, genetic testing will improve outcomes. These individuals have a high pretest probability of disease and LQTS can be diagnosed with certainty if the test is positive. Treatment of these individuals with beta blocker medication will reduce the incidence of subsequent cardiovascular events. Furthermore, because the specific mutation is known prior to testing, the disease can be ruled out with certainty if results are negative.

For diagnosis of LQTS in other patient populations, there may be a benefit as well. For patients who have some signs and symptoms of LQTS, but no known mutation in the family, testing may be beneficial. In this situation, LQTS can be diagnosed with reasonable certainty if a class I mutation is identified; however, the likelihood of false-positive results is higher than if a known mutation were present in the family. In patients with lower pretest probabilities of disease, the utility of testing declines, although precise risk/benefit thresholds cannot be established.

Genetic testing to determine LQTS subtype and/or the specific mutation present has been recognized to be of clinical value. The literature reviewed suggests that different subtypes of LQTS may have variable prognoses, thus indicating that genetic testing may assist in risk stratification. This evidence is from case series and prospectively collected registry data. Among the syndromes, there appears to be relatively large differences in risk of clinical events. Because of the low prevalence of LQTS (1:7000) it is not possible to assess the benefit of suggested therapies through prospective randomized trials. The data regarding therapeutic efficacy in affected patients are based on observational long-term studies.

In 2006, evidenced-based practice guidelines were published by the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (ACC/AHA/ESC) regarding management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. The guidelines note "In patients affected by LQTS, genetic analysis is useful for risk stratification and for making therapeutic decisions. Although genetic analysis is not yet widely available, it is advisable to try to make it accessible to LQTS patients."

In 2011, the HRS and EHRA issued a joint expert consensus statement on genetic testing for channelopathies and cardiomyopathies with the following recommendations for LQTS testing: individuals with a strong clinical index of suspicion for LQTS based on their clinical history, family history, and expressed ECG phenotype (Class I); asymptomatic individuals with idiopathic QT prolongation on serial 12-lead ECGs defined as QTc longer than 480 ms (prepuberty) or longer than 500 ms (adults) (Class I). Genetic testing may be considered for QTc values above 460 ms (prepuberty) or over 480 ms (adults) (Class IIb). The guidelines defined several terms related to specific types of sudden cardiac death, including sudden unexplained death syndrome, which refers to an unexplained sudden death in an individual older than one year of age; sudden arrhythmic death syndrome, which refers to an unexplained sudden death in an individual with negative pathologic and toxicologic assessment, and sudden unexplained death in infancy, which refers to an unexplained sudden death in an individual younger than one year of age with negative pathologic and toxicologic assessment.

Catecholaminergic Polymorphic Ventricular Tachycardia

For individuals with suspected CPVT who receive genetic testing for variants associated with congenital CPVT, the evidence includes observational studies reporting on testing yields. Relevant outcomes are OS, changes in reproductive decision making, and morbid events. A genetic variant can be identified in approximately 60 percent of CPVT patients. There is a chain of evidence to suggest that testing is appropriate for variants associated with CPVT in individuals who are suspected to have these disorders. Confirming the diagnosis of CPVT is likely to lead to a health outcome benefit by initiating changes in management that reduce the risk of ventricular arrhythmias and SCD. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic and have one or more close relatives with a known CPVT variant who receive genetic testing for variants associated with congenital CPVT, the evidence includes observational studies reporting testing yields. Relevant outcomes are OS, changes in reproductive decision making, and morbid events. For close relatives of patients with known CPVT variants, who are found to have a pathogenic variant, preventive treatment can be initiated. Also, a negative test in the setting of a known familial variant should have a high negative predictive value. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Brugada Syndrome

For individuals with suspected BrS who receive genetic testing for variants associated with BrS, the evidence includes observational studies reporting on testing yields. Relevant outcomes are OS, changes in reproductive decision making, and morbid events. The clinical validity of testing for BrS is low: a genetic variant can only be identified in approximately 15 percent to 35 percent of BrS. BrS management changes, primarily use of ICDs, are directed by clinical symptoms. It is not clear that a genetic diagnosis, in the absence of other clinical signs and symptoms leads to a change in management that improves outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are asymptomatic and who have one or more close relatives with a known BrS variant who receive genetic testing for variants associated with congenital BrS, the evidence includes observational studies reporting on testing yields. Relevant outcomes are OS, changes in reproductive decision making, and morbid events. BrS management changes, primarily use of ICDs, are directed by clinical symptoms. There is limited evidence on the effect of changes in

management based on genetic testing in an individual with family members who have a known variant. However, a negative test would allow family members to defer further testing. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Given the limited available evidence on genetic testing for BrS, clinical input was obtained. There was a consensus among the specialty societies and academic medical centers providing clinical input that genetic testing for BrS is medically necessary to establish a definitive diagnosis in patients with BrS symptoms and to evaluate family members of an individual with a known genetic variant of BrS. A review of guidelines from American and international cardiac specialty societies (American Heart Association, Heart Rhythm Society, European Heart Rhythm Association, Asia Pacific Heart Rhythm Society) was also conducted. The guidelines acknowledged that although the evidence is weak, genetic testing is recommended for both individuals with a suspected but not a definitive diagnosis of BrS and asymptomatic family members of individuals with known BrS variants.

Short QT Syndrome

For individuals with suspected SQTS who receive genetic testing for variants associated with SQTS, the evidence includes limited data on testing yields. Relevant outcomes are OS, changes in reproductive decision making, and morbid events. The yield of genetic testing in SQTS is not well-characterized. SQTS management changes, primarily use of ICDs, are directed by clinical symptoms. There is limited evidence on changes in management based on genetic testing in a symptomatic proband without a definitive diagnosis. It is not clear that a genetic diagnosis in the absence of other clinical signs and symptoms leads to a change in management that improves outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are asymptomatic with a close relative(s) with a known SQTS variant who receive genetic testing for variants associated with congenital SQTS, the evidence includes observational studies reporting on testing yields. Relevant outcomes are OS, changes in reproductive decision making, and morbid events. For patients with SQTS, management changes, primarily use of ICDs, are directed by clinical symptoms. There is limited evidence on changes in management based on genetic testing in an individual with family members who have a known variant. It is not clear that a genetic diagnosis in the absence of other clinical signs and symptoms leads to a change in management that improves outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Given the limited available evidence on genetic testing for SQTS, clinical input was obtained. Among the specialty societies and academic medical centers providing input, there was no consensus on the use of genetic testing for variants associated with SQTS; however, there was consensus that genetic testing to predict future risk of disease in individuals with close relatives who have a known variant associated with SQTS is useful in management that may lead to improved outcomes. A review of guidelines was also conducted. The use of genetic testing for patients with suspected SQTS was not addressed in many guidelines; however, one did state that testing may be considered if a cardiologist has established a strong clinical index of suspicion. Additionally, the guidelines acknowledged that although the evidence is weak, genetic testing may be considered for asymptomatic family members of individuals with known SQTS variants.

For individuals who are asymptomatic, who have one or more close family members who experienced sudden cardiac death resulting from a specific known diagnosis who receive genetic testing for variants associated with cardiac ion channelopathies, the evidence includes cohort studies that describe the genetic testing yield. In all studies identified, genetic testing was obtained only after a specific diagnosis was suspected based on history or ancillary testing. The evidence is insufficient to determine the effects of the technology on health outcomes.

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/appropriate = (NMN)*

CPT Codes

Code	Description
81403	Molecular pathology procedure, Level 4; Includes: KCNJ2 (potassium inwardly-rectifyingchannel, subfamily J, member 2) (eg, Andersen-Tawil syndrome), full gene sequence.
81405	Molecular pathology procedure, Level 6; Includes: CASQ2 (calsequestrin 2 [cardiac muscle]) (eg,catecholaminergic polymorphic ventricular tachycardia), full gene sequence.
81406	Molecular pathology procedure, Level 7; Includes: KCNH2 (potassium voltage-gated channel, subfamily H[ead-related], member 2) (eg, short QT syndrome, long QT syndrome), full genesequence and KCNQ1 (potassium voltage-gated channel, KQT-like subfamily, member 1) (eg, short QT syndrome, long QT syndrome), full gene sequence
81407	Molecular pathology procedure, Level 8; Includes: SCN5A (sodium channel, voltage-gated, typeV, alpha subunit) (eg, familial dilated cardiomyopathy), full gene sequence.
81408	Molecular pathology procedure, Level 9; Includes: RYR2 (ryanodine receptor 2 [cardiac]) (eg,catecholaminergic polymorphic ventricular tachycardia, arrhythmogenic right ventriculardysplasia), full gene sequence or targeted sequence analysis of > 50 exons.
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
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 (Genomic Unity® Cardiac Ion Channelopathies Analysis, Variantyx Inc.)

HCPCS Codes

Code	Description
S3861	Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada syndrome

ICD10 Codes

Code	Description
I45.81	Long QT syndrome

Code	Description
Q23.8 - Q23.9	Other or unspecified congenital malformations of aortic and mitral valves (code range)
Q24.8 - Q24.9	Other or unspecified congenital malformations of heart
Z13.6	Encounter for screening for cardiovascular disorders
Z13.79	Encounter for other screening for genetic and chromosomal anomalies

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*Key Article

KEY WORDS

Andersen-Tawil syndrome, Brugada syndrome, Jervell and Lange-Nielsen syndrome, Long QT syndrome, Romano-Ward syndrome, Syndactyly-related LWTS, Timothy syndrome.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a Local Coverage Determination (LCD) for Molecular Pathology Procedures. Please refer to the following LCD website for Medicare Members: [https://www.cms.gov/medicare-coverage-database/details/lcd-

details.aspx?LCDId=35000&ver=133&CntrctrSelected=298*1&Cntrctr=298&s=41&DocType=Active&bc=AAgAAAQAoAAA&]

There is currently a Local Coverage Article (LCA) for Molecular Pathology Procedures. Please refer to the following LCD website for Medicare Members: [https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=56199&ver=82&keywordtype=starts&keyword=Molecular%20Pathology%20Procedures&bc=0]