TITLE: GENETIC TESTING FOR CARDIAC CHANNELOPATHIES

EFFECTIVE DATE: September 20, 2017

This policy was developed with input from specialists in cardiology, pediatrics, genetics and pathology and endorsed by the Medical Policy Committee.

IMPORTANT INFORMATION – PLEASE READ BEFORE USING THIS POLICY
These services may or may not be covered by all Medica plans. Please refer to the member’s plan document for specific coverage information. If there is a difference between this general information and the member’s plan document, the member’s plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica utilization management policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica utilization management policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

PURPOSE
To promote consistency between reviewers in utilization management decision-making by providing the criteria that generally determine the medical necessity of genetic testing for cardiac channelopathies. The Coverage Issues box below outlines the process for addressing the needs of individuals who do not meet these criteria.

BACKGROUND
Definitions:
A. Cardiac channelopathies are disorders involving the ion-transferring channels (openings in cell membranes that allow the passage of specific ions) of cardiac cells. These pores regulate the flow of critical ions through the cells and are vital in conducting electrical impulses across the heart. Cardiac channelopathies include the following syndromes:
1. Brugada syndrome (BrS) is an inherited cardiac arrhythmia syndrome characterized by specific electrocardiographic findings and an increased risk of sudden cardiac death. BrS is believed to account for approximately 4% of all sudden cardiac deaths and 20% of unexplained deaths among individuals with structurally normal hearts. Genes associated with BrS for which clinical testing is available, include but are not limited to: SCN5A, SCN1B, SCN2B, SCN3B, GPD1L, CACNA1C, CACNB2, CACNA2D1, KCND3, KCNE3, KCNE1L (KCNE5), KCNJ8, HCN4, RANGRF, SLMAP, or TRPM4. However, only approximately 25%-30% of Brugada syndrome is accounted for by pathogenic variants in the 16 genes mentioned above.
2. Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited cardiac disease characterized by irregular heart rhythms brought on by physical exertion or intense emotion. CPVT may cause syncope (fainting), cardiac arrest, or sudden cardiac death in affected individuals. Mutations in four genes are known to cause CPVT, RYR2, CASQ2, TRDN, and CALM1.
3. Long QT syndrome (LQTS) is a congenital disorder characterized by a prolongation of the QT interval on electrocardiogram (ECG) and a propensity to ventricular tachyarhythmias, which may lead to syncope, cardiac arrest, or sudden death. At least 15 forms of congenital LQTS have been identified, depending on the genes responsible and the features associated with the condition. Examples include Romano-Ward Syndrome, Timothy Syndrome, Jervell and Lange-Nielsen Syndrome, and Andersen-Tawil Syndrome. The most common genes for which clinical testing is available include KCNQ1 (LQT1), KCNH2 (LQT2) and SCN5A (LQT3). Other, less frequently involved genes include, but are not limited to, ANK2 (LQT4), KCNE1 (LQT5), KCNE2 (LQT6), KCNJ2 (LQT7), CACNA1C (LQT8), CAV3 (LQT9), SCN4B (LQT10), AKAP9 (LQT11), SNTA1 (LQT12), KCNJ5 (LQT13), CALM1 (LQT14), and CALM2 (LQT15).
4. **Short QT syndrome (SQTS)** is a condition that causes a disruption of the heart's normal rhythm (arrhythmia). In individuals with this condition, the heart muscle takes less time than usual to recharge between beats. If untreated, the irregular heartbeats can lead to a spectrum of signs and symptoms, from dizziness and fainting to cardiac arrest and sudden death. The most common genes for testing include **KCNH2 (SCTS1)**, **KCNQ1 (SQTS2)**, and **KCNU2 (SQTS3)**. Other less frequently involved genes include, but are not limited to, **CACNA1C** and **CACNB2**.

**B. Close relative** includes first or second degree relatives. First degree relative is a relative with whom one half of an individual's genes are shared (i.e., parent, sibling, offspring). Second degree relative is a relative with whom one quarter of an individual's genes is shared (i.e., grandparent, grandchild, uncle, aunt, nephew, niece, half-sibling).

C. **A genetic counselor** is a health professional with specialized training and clinical experience in the areas of medical genetics and counseling that has completed an accredited Masters or Doctorate Degree program and has been certified by the American Board of Genetic Counseling or the American Board of Medical Genetics. Genetic counselors work as members of a health care team providing information and support to individuals and/or families who have birth defects or genetic disorders or who may be at risk for a variety of inherited conditions. **Genetic counseling services** may be provided both before and after genetic testing and include, but are not limited to the following services:
   1. The collection, documentation and interpretation of family and medical histories to assess the risk of disease occurrence or recurrence
   2. Education regarding inheritance and the nature, risks, and potential outcomes of genetic testing
   3. Assessment and review of the psychological and societal risks and benefits of genetic testing
   4. Supportive counseling to promote informed consent
   5. Identification of and referral to appropriate support services.

D. **A medical geneticist** is a licensed physician with specialty training in medical genetics and counseling who has been certified by the American Board of Medical Genetics. In addition to genetic counseling, the medical geneticist can conduct physical examinations, make diagnoses of genetic disorders, and manage the clinical care of these disorders.

E. **Next-generation sequencing (NGS)**, also known as massively parallel or high throughput sequencing, is an automated method of sequencing DNA, that can process many genes at one time. This is known as **multigene panel testing**, also known as multiple-gene panel testing or multiple-gene testing. Using NGS, DNA sequencing is less costly and less time-consuming than traditional manual DNA sequencing of one gene at a time.

F. The **QT interval** on the ECG, measured from the beginning of the QRS complex to the end of the T wave, represents the duration of activation and recovery of the ventricular myocardium.

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**MEDICAL NECESSITY CRITERIA**

**I. Indications**

A. Genetic testing for **LQTS**, using single gene or multigene panels, is considered medically necessary when documentation in the medical record indicates that all of the following criteria are met:

   1. The member has one of the following:
      a. A prolonged QT interval (a corrected QT interval [QTc] of 470 msec in males and 480 msec in females) on resting electrocardiogram without an identifiable external cause and in whom familial LQTS is suspected
      b. A close relative (1st or 2nd degree) with a known LQTS mutation
      c. A close relative (1st or 2nd degree) with sudden death due to LQTS
      d. Clinically diagnosed LQTS for the purposes of identifying a LQTS mutation that can be used for family-specific screening in at-risk blood relatives.

2. Medical records document all of the following:

   a. A detailed family history or pedigree
   b. Genetic counseling by a cardiologist/electrophysiologist, medical geneticist, or certified and licensed (where required) genetic counselor, not associated with the laboratory performing the testing
   c. How the test results will lead to changes in treatment decisions (i.e., medical or surgical management, lifestyle modifications, surveillance and/or other protective measures) of the member.

3. The test is ordered by a cardiologist/electrophysiologist, medical geneticist, or board-certified and licensed (where required) genetic counselor not associated with the laboratory performing the testing.
B. Genetic testing for SQTS, using single gene or multigene panels, is considered medically necessary when documentation in the medical record indicates that all of the following criteria are met:

1. The member has one of the following:
   a. A QT or QTc interval less than or equal to 360 msec on electrocardiogram (ECG) that does not significantly change with heart rate, displaying tall and peaked T waves and a structurally normal heart.
   b. A close relative (1<sup>st</sup> or 2<sup>nd</sup> degree) with a known SQTS mutation
   c. A close relative (1<sup>st</sup> or 2<sup>nd</sup> degree) with sudden death due to SQTS
   d. Clinically diagnosed SQTS for the purposes of identifying a SQTS mutation that can be used for family-specific screening in at-risk blood relatives.

2. Medical records document all of the following:
   a. A detailed family history or pedigree
   b. Genetic counseling by a cardiologist/electrophysiologist, medical geneticist, or certified and licensed (where required) genetic counselor, not associated with the laboratory performing the testing
   c. How the test results will lead to changes in treatment decisions (i.e., medical or surgical management, lifestyle modifications, surveillance and/or other protective measures) of the member.

3. The test is ordered by a cardiologist/electrophysiologist, medical geneticist, or board-certified and licensed (where required) genetic counselor not associated with the laboratory performing the test.

C. Genetic testing for CPVT, using single gene or multigene panels, is considered medically necessary when documentation in the medical record indicates that all of the following criteria are met:

1. The member has one of the following:
   a. A close relative (1<sup>st</sup> or 2<sup>nd</sup> degree) with a known CPVT mutation
   b. A close relative (1<sup>st</sup> or 2<sup>nd</sup> degree) with sudden death due to CPVT
   c. Clinically diagnosed CPVT for the purposes of identifying a CPVT mutation that can be used for family-specific screening in at-risk blood relatives.

2. Medical records document all of the following:
   a. A detailed family history or pedigree
   b. Genetic counseling by a cardiologist/electrophysiologist, medical geneticist, or certified and licensed (where required) genetic counselor not associated with the laboratory performing the testing
   c. How the test results will lead to changes in treatment decisions (i.e., medical or surgical management, lifestyle modifications, surveillance and/or other protective measures) of the member.

3. The test is ordered by a cardiologist/electrophysiologist, medical geneticist, or board-certified and licensed (where required) genetic counselor not associated with the laboratory performing the test.

D. Genetic testing for BrS, using single gene or multigene panels, is considered medically necessary when documentation in the medical record indicates that all of the following criteria are met:

1. The member has a type 1 Brugada ECG pattern that appears spontaneously or after the administration of an antiarrhythmic drug

2. The member has one of the following:
   a. A close relative (1<sup>st</sup> or 2<sup>nd</sup> degree) with a known BrS mutation
   b. A close relative (1<sup>st</sup> or 2<sup>nd</sup> degree) with sudden death due to BrS
   c. Clinically diagnosed BrS for the purposes of identifying a BrS mutation that can be used for family-specific screening in at-risk blood relatives.

3. Medical records document all of the following:
   a. A detailed family history or pedigree
   b. Genetic counseling by a cardiologist/electrophysiologist, medical geneticist, or certified and licensed (where required) genetic counselor, not associated with the laboratory performing the testing
   c. How the test results will lead to changes in treatment decisions (i.e., medical or surgical management, lifestyle modifications, surveillance and/or other protective measures) of the member.

4. The test is ordered by a cardiologist/electrophysiologist, medical geneticist, or board-certified and licensed (where required) genetic counselor not associated with the laboratory performing the testing.
1. Prior authorization is required for genetic testing for LQTS, CPVT, SQTS, and BrS.
2. Genetic testing for all other cardiac channelopathies is investigative and therefore not covered.
3. Genetic testing is excluded and therefore not covered when performed in the absence of symptoms or high risk factors for a genetic disease or when knowledge of genetic status will not affect treatment decisions or screening for the disease. (See Medica’s coverage policy entitled: Genetic and Pharmacogenetic Testing). Coverage may vary according to the terms of the member’s plan document.
4. For Medicare members, refer to the following as applicable, available at: http://www.cms.hhs.gov/mcd/search.asp?
5. If the Medical Necessity and Coverage Criteria are met, Medica will authorize benefits within the limits in the member’s plan document.
6. If it appears that the Medical Necessity and Coverage Criteria are not met, the individual’s case will be reviewed by the medical director or an external reviewer. Practitioners are advised of the appeal process in their Medica Provider Administrative Manual.

**DOCUMENT HISTORY**

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<tr>
<th>Original Effective Date</th>
<th>December 2009</th>
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<tr>
<td>Administrative Update(s)</td>
<td>05/01/2017</td>
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**References:**

**Pre-04/2016 MPC:**


04/2016 MPC:

09/2016 MTAC:
No new references added.

06/2017 MTAC:

09/2017 MPC:


