TITLE: GENETIC TESTING FOR CARDIOMYOPATHIES

EFFECTIVE DATE: November 20, 2017

This policy was developed with input from specialists in cardiology and genetics 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 cardiomyopathies. The Coverage Issues box below outlines the process for addressing the needs of individuals who do not meet these criteria.

BACKGROUND
Definitions:
A. Cardiomyopathies are a group of diseases that cause the heart muscle to become abnormally enlarged, thickened, and/or stiffened, diminishing the heart’s ability to function and creating the potential for arrhythmias, heart failure and sudden cardiac death. The wall thickness, chamber size, contraction, relaxation, conduction and rhythm of the heart may all be affected. Some people with these conditions remain asymptomatic. However, the disorders can produce an irregular heart rhythm that may result in dizziness, palpitations, fainting, seizures, heart failure and sudden death. The World Health Organization (WHO) recognizes four classes of cardiomyopathy: hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, dilated cardiomyopathy, and restrictive cardiomyopathy. However, other rarer forms of cardiomyopathy have been identified as well. These cardiomyopathies may have overlapping features with any of the previous types described and include, but are not limited to, left ventricular non-compaction (LVNC) and mitochondrial cardiomyopathies. Cardiomyopathies may be acquired or inherited.

1. Hypertrophic cardiomyopathy (HCM) is an autosomal dominant disorder caused by mutation in one of the genes currently known to encode different components of the sarcomere, the basic contractile unit of the cardiac myocyte. HCM is characterized by left ventricular hypertrophy (LVH) in the absence of predisposing cardiac conditions or cardiovascular conditions and occurs in approximately one in 500 individuals world-wide. Genes for which clinical genetic testing is available, include but are not limited to: beta myosin heavy chain (MYH7); myosin binding protein C (MYBPC3); troponin T (TNNT2), troponin I (TNNI3); alpha tropomyosin (TPM1); actin (ACTC); regulator light chain (MYL2); and essential light chain (MYL3).

2. Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an autosomal dominant disorder of the cardiac desmosome, the protein complexes that maintain cell-to-cell connections and provide mechanical attachments among adjacent cells. ARVC is characterized by progressive fibrofatty replacement of the myocardium that predisposes to ventricular tachycardia and sudden death in young individuals and athletes. It primarily affects the right ventricle. However, with time, it may also involve the left ventricle. The disease prevalence is estimated at 1:1000 to 1:2500, but may be higher.
in certain populations and because of non-diagnosed or misdiagnosed cases. Genes for which clinical testing is available, include but are not limited to: transforming growth factor beta-3 (TGFB3); ryanodine receptor 2 (RYR2); transmembrane protein 43 (TMEM43); desmoplakin (DSP); plakophilin-2 (PKP2); desmoglein-2 (DSG2); desmocollin-2 (DSC2) and junction plakoglobin (JUP). Six of these genes (TGFB3, DSP, PKP2, DSG2, DSC2, and JUP) encode desmosomal proteins, while the other two (RYR2 and TMEM43) encode proteins that maintain calcium homeostasis.

3. **Dilated cardiomyopathy (DCM)**, the most common of the cardiomyopathies, is a disorder characterized by left ventricular enlargement and systolic dysfunction. Genetic forms of DCM must be distinguished from the many acquired (non-genetic) causes of DCM. Genetic DCM can be inherited in an autosomal dominant, autosomal recessive or X-linked manner. A number of gene mutations have been associated with DCM. However, the most commonly associated variants include, but are not limited to, mutations in the LMNA, SCN5A, TTN, MYH6, and MYH7 genes.

4. **Left ventricular noncompaction (LVNC) cardiomyopathy**, which has only recently been described, is a disorder characterized by deep trabeculations in the muscle wall of the left ventricle. These trabeculations can also occur in the right ventricle. The heart muscle abnormalities occur during the development of the heart in the embryo and may occur on its own or along with other congenital heart conditions. LVNC may be inherited in an autosomal dominant or X-linked inheritance pattern. To date, mutations in at least nine genes have been associated with LVNC.

5. **Restrictive cardiomyopathy (RCM)** is a disorder of the heart muscle in which the walls of the ventricles become stiff, but not necessarily thickened, so they resist normal filling with blood. The least common of the cardiomyopathies, RCM can be idiopathic or secondary to a number of rare cardiac and systemic disorders such as endomyocardial fibrosis (tropical, hypereosinophilic syndrome), infiltrative disorders (amyloidosis, sarcoidosis), and rare metabolic disorders (Gaucher's disease, Mucopolysaccharidoses, Fabry's disease, carcinoid syndrome). Patients with the idiopathic form may have a family history of cardiomyopathy. Recent evidence suggests that inherited RCM may be caused by the same genetic abnormalities that result in the more common hypertrophic cardiomyopathy (HCM), including variants in TNNI3, TNN2, MYH7, and ACTC1.

B. **Close relative** includes first or second degree blood relatives. **First degree relative** is a relative with whom one half of an individual's genes are shared (i.e., parent, sibling, and 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, and 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. NGS is used to test multiple genes simultaneously. 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.

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**MEDICAL NECESSITY CRITERIA**

**Indications**

Genetic testing for HCM, ARVC and DCM, using single gene or multigene panels, is considered medically necessary.
necessary when documentation in the medical records indicates that all of the following criteria are met:

A. The member has one of the following:
   1. A close relative (1st or 2nd degree) with a known HCM, ARVC or DCM pathogenic mutation
   2. Clinically diagnosed HCM, ARVC or DCM for the purposes of identifying a pathogenic mutation that can be used for family-specific screening in at-risk blood relatives.

B. Medical records document all of the following:
   1. A detailed family history or creation of a pedigree
   2. Genetic counseling by a cardiologist/electrophysiologist, medical geneticist, or certified and licensed (where required) genetic counselor not associated with the laboratory performing the testing
   3. 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.

C. 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.

COVERAGE ISSUES
1. Prior authorization is required for genetic testing for HCM, ARVC and DCM.
2. Genetic testing for all other inherited cardiomyopathies, including, but not limited to LVNC and RCM 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).
4. Coverage may vary according to the terms of the member’s plan document.
5. For Medicare members, refer to the following, as applicable, available at: https://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx.
6. If the Medical Necessity and Coverage Criteria are met, Medica will authorize benefits within the limits in the member’s plan document.
7. 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 reminded of the appeals process in their Medica Provider Administrative Manual.

DOCUMENT HISTORY

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<tr>
<th>Original Effective Date</th>
<th>February 2012</th>
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<tr>
<td>MPC Endorsement Date(s)</td>
<td>11/2011, 11/2012, 04/2013, 04/2014, 02/2015, 04/2016, 09/2016, 09/2017</td>
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<td>Administrative Update(s)</td>
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References:
Pre-04/2016 MPC


01/2016 MTAC:


04/2016 MPC:

09/2016 MPC:
No new references added.

09/2017 MPC:
76. Abrams DJ. How to develop a clinic for sudden cardiac arrest survivors and families of non-survivors. Cardiol Young. 2017;27(S1):S3-S9. doi: 10.1017/S104795111600216X.