Geisinger

Geisinger Health Plan Policies and Procedure Manual

Policy: MP304

Section: Medical Benefit Policy

Subject: Genetic Testing for Inherited Cardiomyopathies and Channelopathies

Applicable Lines of Business

Commercial	**X**	**CHIP**	**X**
Medicare	**X**	**ACA**	**X**
Medicaid	**X**		

I. Policy: Genetic Testing for Inherited Cardiomyopathies and Channelopathies

II. Purpose/Objective:

To provide a policy of coverage regarding Genetic Testing for Inherited Cardiomyopathies and Channelopathies

III. Responsibility:

A. Medical Directors
B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community.
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment

Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking

into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age

DESCRIPTION:
Risk for structural heart disease and arrhythmia can run in families**.** Cardiomyopathies are diseases of the heart muscle and include hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy, restrictive cardiomyopathy (RCM), left ventricular noncompaction (LVNC), arrhythmogenic right ventricular cardiomyopathy (ARVC). HCM is a common genetic heart disease reported in pan-ethnic populations. Among patients with HCM, 30% to 60% have an genetic etiology. There are 8 genes associated with HCM with a strong degree of evidence supporting association. Around 30% of patients with DCM are thought to have a hereditary cause for disease. 10-60% of cases with restrictive cardiomyopathy will have an underlying genetic etiology, and the genes responsible for this condition share significant overlap with HCM and DCM. ARVC and CPVT, while rare, have a high likelihood of a genetic etiology. Among patients with ARVC and CPVT, current evidence suggests up to 66% and 75% of cases, respectively, will have an identifiable genetic variant

Cardiac channelopathies, also called arrythmias, are disorders involving cardiac cells membranes that allow passage of specific ions. These pathways regulate the flow of ions through the cells and are necessary to conduct electrical impulses across the heart. Cardiac channelopathies include long QT syndrome (LQTS), Brugada syndrome (BrS) (also referred to as sudden unexpected nocturnal death syndrome), short QT syndrome (SQTS) and Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT). Cardiac channelopathies are characterized by delayed repolarization of the myocardium and QT interval alteration, resulting in increased risk for syncope, seizures, and sudden cardiac death (SCD) in the setting of a structurally normal heart and otherwise healthy individual.

Among patients with long QT syndrome 75-80% have a genetic etiology. In short QT syndrome, up to 20% have a genetic etiology. Brugada syndrome can be caused by pathogenic or likely pathogenic variants in SCN5A in 30% of cases, and there are at least 40 other genes associated with the disease that account for <1% of causes. CPVT is rare, and there are two known genes involving this syndrome: RYR2, CASQ2.

Multi-gene panel testing is the most cost-effective and accurate approach to characterize familial cardiomyopathy and channelopathies (arrythmia) because there is considerable phenotypic overlap among these disorders. Therapeutic interventions may be tailored based on genetic findings. The value of genetic testing among individuals with risk for cardiomyopathy is threefold: to understand disease prognosis, to facilitate identification and subsequent screening recommendations for at-risk relatives, and to guide therapeutic options (eg: transthyretin amyloidosis, experimental treatments, need for ICD placement).

Disease-specific panels may change from year to year based on available evidence and technological advancements Test methodology should include sequencing and full deletion and duplication analysis (i.e., detection of large genomic rearrangements) with a benefit of once per lifetime, dependent upon advances in testing technology.

INDICATIONS:
When ordered by a cardiologist/electrophysiologist, medical geneticist, or board-certified and licensed (where required) genetic counselor, the following tests including multigene panels are considered to be medically necessary in ANY of the following scenarios:

Channelopathies (Arrhythmias)

The member has a personal history of ANY of the following clinical features or diagnoses:

One or more signs or symptoms of LQTS, SQTS, CPVT, or Brugada, AND a definitive diagnosis cannot be made without genetic testing:

1. Prolonged QT/QTc interval on resting electrocardiogram of >470 msec in males or >480 msec in females without additional risk factors (eg: heart failure, bradycardia, electrolyte imbalance, recent history of QT prolonging drugs); or

1. Short QT/QTc interval of <350 msec; or
2. EKG pattern suggestive of Brugada with or without additional symptoms; or
3. Schwartz score of 2-3 or greater+ (see below); or
4. History of aborted sudden cardiac arrest.
5. History of isolated cardiac conduction disease or with concomitant structural heart disease or extracardiac disease when there is an early age of dx or a suspicion of laminopathy.

The member has a family history of ANY of the following:

1. One first- or second- degree relative with a known history of sudden cardiac arrest or death
2. Two or more relatives on the same side of the family with history sudden cardiac arrest or death
3. A first, second, or third degree relative with a known mutation in an LQTS, SQTS, CPVT, Brugada, or

channelopathy gene for which medical management may impact the member's ongoing cardiac surveillance.
4. Two or more first, second, or third degree relatives with a reported clinical history of LQTS, SQTS, CPVT, Brugada, or hereditary arrhythmia but genetic testing may have not been completed or the report is unavailable to direct testing.

Cardiomyopathies:

The member has a personal history of ANY of the following clinical features or diagnoses:

1. Hypertrophic Cardiomyopathy (HCM)
2. Dilated Cardiomyopathy (DCM)
3. Restrictive Cardiomyopathy (RCM)
4. Arrhythmogenic cardiomyopathy (ACM) not secondary to ischemic, hypertensive, or valvular heart disease, such arrhythmogenic right/left ventricular cardiomyopathy (ARVC/ALVC), cardiac amyloidosis, sarcoidosis, and left ventricular noncompaction (LVNC).
5. Member has sub-clinical signs suggestive of HCM, DCM, RCM, or ACM AND a first degree or second-degree relative with a cardiomyopathy.

The member has a family history of ANY of the following diagnoses:

1. One first- or second- degree relative with a known history of sudden cardiac arrest or death <40y; or
2. Two or more relatives on the same side of the family with history sudden cardiac arrest or death at any age; OR
3. A first, second, or third degree relative with a known mutation in a cardiomyopathy gene for which medical management may impact the member's cardiac surveillance strategy.
4. Two or more first, second, or third degree relatives with a reported cardiomyopathy but genetic testing may have not been completed or the report is unavailable to direct testing.

*Swartz Score Calculator for Clinical Diagnosis of Long QT Syndrome

Findings			Points
ECG [1]	QTc [2]	≥480 ms	3
		=460-479 ms	2
		=450-459 ms (in males)	1
		≥480 ms during 4th minute of recovery from exercise stress test	1
	Torsade de pointes		2
	T wave alternans		1
	Notched T wave in 3 leads		1
	Low heart rate for age		0.5
Clinical history	Syncope [3]	With stress	2
		Without stress	1
Family history	Family member(s) with definite LQTS		1
	Unexplained sudden cardiac death at age <30 years in immediate family		0.5
Total score			___

Adapted from: Schwartz PJ, Crotti L. QTc behavior during exercise and genetic testing for the long-QT syndrome. Circulation. 2011;124:2181–4

Scoring:

- ≤1.0 point = low probability of LQTS
- 1.5-3.0 points = intermediate probability of LQTS
- ≥3.5 points = high probability of LQTS

EXCLUSIONS:

Genetic testing for inherited cardiomyopathies and channelopathies not meeting the criteria described above is considered to be experimental, investigational or unproven and therefore **NOT COVERED**. There is insufficient evidence in the published, peer-reviewed medical literature to support the use of this protesting outside of the indications listed above.

Medicaid Business Segment:

Any requests for services that do not meet criteria set in the PARP may be evaluated on a case by case basis.

CODING ASSOCIATED WITH:
The coding listed in this document may not represent the comprehensive range of codes that may be associated with this service.

81161 – DMD (dysptophin) (eg, Duschenne/Becker muscular dystrophy) deletion analysis and duplication analysis, if performed
81170 – ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase)(eg, acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain
81280 Long QT Syndrome gene analysis (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); full sequence analysis
81281 Long QT Syndrome gene analysis (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); known familial sequence variant
81282 Long QT Syndrome gene analysis (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); duplication / deletion variants
81400 – Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg, SNP] by techniques such as restriction enzyme digestion or melt curve analysis)
81401 - Molecular pathology procedure, Level 2 (eg, 2-10 SNP's, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
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)
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)
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)
81407 - Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons in a single gene by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)
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 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
0231U CACNA1A (calcium voltage-gated channel subunit alpha 1A) (eg, spinocerebellar ataxia), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) gene expansions, mobile element insertions, and variants in non-uniquely mappable regions
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

LINE OF BUSINESS:
Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supercede this policy.

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This policy will be revised as necessary and reviewed no less than annually.

Devised: 7/21

Revised: 7/22 (add indication for CPVT), 7/23 (grammatical revisions)

Reviewed:

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Coverage for experimental or investigational treatments, services and procedures is specifically excluded under the member's certificate with Geisinger Health Plan. Unproven services outside of an approved clinical trial are also specifically excluded under the member's certificate with Geisinger Health Plan. This policy does not expand coverage to services or items specifically excluded from coverage in the member's certificate with Geisinger Health Plan. Additional information can be found in MP015 Experimental, Investigational or Unproven Services.

Prior authorization and/or pre-certification requirements for services or items may apply. Pre-certification lists may be found in the member's contract specific benefit document. Prior authorization requirements can be found at https://www.geisinger.org/health-plan/providers/ghp-clinical-policies