

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

CLINICAL BENEFIT	☒ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☐ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	RETIRED 7/1/2026

[POLICY
RATIONALE
CODING INFORMATION](#)

[PRODUCT VARIATIONS
DEFINITIONS
REFERENCES](#)

[DESCRIPTION/BACKGROUND
DISCLAIMER
POLICY HISTORY](#)

I. POLICY

Genetic testing for predisposition to hypertrophic cardiomyopathy (HCM) may be considered **medically necessary** for individuals who are at risk for development of HCM, defined as having a first-degree relative with established HCM, when there is a known pathogenic gene variant present in that affected relative (See Policy Guidelines Section).

Genetic testing for predisposition to HCM is considered **investigational** for individuals with a family history of HCM in which a first-degree relative with established hypertrophic cardiomyopathy has tested negative for pathologic variants. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Genetic testing for predisposition to HCM is considered **investigational** for all other patient populations, including but not limited to individuals who have a first-degree relative with clinical HCM, but in whom genetic testing is unavailable. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Policy Guidelines

Due to the complexity of genetic testing for hypertrophic cardiomyopathy (HCM) and the potential for misinterpretation of results, the decision to test and the interpretation of test results should be performed by, or in consultation with, an expert in the area of medical genetics and/or HCM.

To inform and direct genetic testing for at-risk individuals, genetic testing should initially be performed in at least one (1) close relative with definite HCM (index case), if possible.

Because there are varying degrees of penetrance for different HCM variants, consideration for testing of second- or third-degree relatives may be appropriate in certain circumstances. Some judgment should be allowed for these decisions, for example, in the case of a small family

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

pedigree. Consultation with an expert in medical genetics and/or the genetics of HCM, in conjunction with a detailed pedigree analysis, is appropriate when testing of second- or third-degree relatives is considered.

Genetics Nomenclature Update

Human Genome Variation Society (HGVS) nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the Human Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics (ACMG) and Association for Molecular Pathology (AMP) standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, and the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology—“pathogenic,” “likely pathogenic,” “uncertain significance,” “likely benign,” and “benign”—to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Diseased- Assoc.Variant	Disease-associated change in the DNA sequence.
	Variant	Change in DNA sequence
	Familial Variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives.

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely Pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

ACMG: American College of Medical Genetics and Genomics; AMP: Association of Molecular Pathology.

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

Genetic Counseling

Experts recommend formal genetic counseling for patients who are at risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

II. PRODUCT VARIATIONS

[TOP](#)

This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>

III. DESCRIPTION/BACKGROUND

[TOP](#)

Familial Hypertrophic Cardiomyopathy

Familial hypertrophic cardiomyopathy (HCM) is the most common genetic cardiovascular condition, with a phenotypic prevalence of approximately 1 (0.2%) in 500 adults. It is the most common cause of sudden cardiac death (SCD) in adults younger than 35 years of age and is probably the most common cause of death in young athletes. The overall mortality rate for patients with HCM is estimated to be 1% per year in the adult population.

The genetic basis for HCM is a defect in the cardiac sarcomere, which is the basic contractile unit of cardiac myocytes and is composed of different protein structures. Around 1400 disease-associated variants in at least 18 different genes have been identified. About 90% of pathogenic variants are missense (i.e., 1 amino acid is replaced for another), and the strongest evidence for pathogenicity is available for 11 genes coding for thick filament proteins (*MYH7*, *MYL2*, *MYL3*), thin filament proteins (*TNNT2*, *TNNI3*, *TNNC1*, *TPM1*, *ACTC*), intermediate filament proteins (*MYBPC3*), and the Z-disc adjoining the sarcomere (*ACTN2*, *MYOZ2*). Variants in myosin heavy chain (*MYH7*) and myosin-binding protein C (*MYBPC3*) are the most common and account for roughly 80% of sarcomeric HCM. These genetic defects are inherited in an autosomal dominant pattern with rare exceptions. In patients with clinically documented HCM, genetic abnormalities can be identified in approximately 60%. Most patients with the clinically documented disease are demonstrated to have a familial pattern, although some exceptions are found presumably due to de novo variants.

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

Diagnosis and Management

The clinical diagnosis of HCM depends on the presence of left ventricular hypertrophy, measured by echocardiography or magnetic resonance imaging, in the absence of other known causative factors such as valvular disease, long-standing hypertension, or another myocardial disease. In addition to primary cardiac disorders, there are systemic diseases that can lead to left ventricular hypertrophy and thus mimic HCM. They include infiltrative diseases such as amyloidosis, glycogen storage diseases (e.g., Fabry disease, Pompe disease), and neuromuscular disorders (e.g., Noonan syndrome, Friedreich ataxia). These disorders need to be excluded before a diagnosis of familial HCM is made.

HCM is a very heterogeneous disorder. Manifestations range from subclinical, asymptomatic disease to severe, life-threatening disease. Wide phenotypic variability exists among individuals, even when an identical variant is present, including among affected family members. This variability in clinical expression may be related to environmental factors and modifier genes. A large percentage of patients with HCM, perhaps the majority, are asymptomatic or have minimal symptoms. These patients do not require treatment and are not generally at high risk for SCD. A subset of patients has severe disease that causes a major impact on quality of life and life expectancy. Severe disease can lead to disabling symptoms, as well as complications of HCM, including heart failure and malignant ventricular arrhythmias. Symptoms and presentation may include SCD due to unpredictable ventricular tachyarrhythmias, heart failure, or atrial fibrillation, or some combination.

Management of patients with HCM involves treating cardiac comorbidities, avoiding therapies that may worsen obstructive symptoms, treating obstructive symptoms with β -blockers, calcium channel blockers, and (if symptoms persist) invasive therapy with surgical myectomy or alcohol ablation, optimizing treatment for heart failure, if present, and SCD risk stratification. Implantable cardioverter defibrillator implantation may be indicated if there is a family history of SCD.

Diagnostic screening of first-degree relatives and other family members is an important component of HCM management. Guidelines have been established for screening clinically unaffected relatives of affected individuals. Screening with physical examination, electrocardiography, and echocardiography is recommended every 12 to 18 months for individuals ages 12 to 18 years and every 3 to 5 years for adults. Additional screening is recommended for any change in symptoms that might indicate the development of HCM.

Genetic Testing

Genetic testing has been proposed as a component of screening at-risk individuals to determine predisposition to HCM among those patients at risk. Patients at risk for HCM are defined as individuals who have a close relative with established HCM. Results of genetic testing may influence the management of at-risk individuals, which may, in turn, lead to improved outcomes. Furthermore, results of genetic testing may have implications for decision making in the areas of reproduction, employment, and leisure activities. However, the likelihood of obtaining a positive genetic test in the proband is only about 50% because all genes causing HCM have not yet been identified or are absent from testing panels. Failure to identify the causative variant in the

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

proband is an indeterminate result that provides no useful information and precludes predictive testing in 33% to 67% of cases.

Commercial testing has been available since 2003, and numerous companies offer genetic testing for HCM. Testing is performed either as a comprehensive or targeted gene test. Comprehensive testing, which is done for an individual without a known genetic variant in the family, analyzes the genes most commonly associated with genetic variants for HCM and evaluates whether any potentially pathogenic variants are present. Some available panels include testing for multisystem storage diseases that may include cardiac hypertrophy, such as Fabry disease (*GLA*), familial transthyretin amyloidosis (*TTR*), and X-linked Danon disease (*LAMP2*).

Other panels include testing for genes related to hypertrophic cardiomyopathy and those associated with other cardiac disorders. For example, the Pan Cardiomyopathy panel (Laboratory for Molecular Medicine) is a next-generation sequencing panel of 62 genes associated with hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, catecholaminergic polymorphic ventricular tachycardia, left ventricular noncompaction syndrome, Danon syndrome, Fabry disease, Brugada syndrome, and transthyretin amyloidosis.

For a patient with a known variant in the family, targeted testing is performed. Targeted variant testing evaluates for the presence or absence of a single variant known to exist in a close relative.

It can be difficult to determine the pathogenicity of genetic variants associated with HCM. Some studies have reported that assignment of pathogenicity has a relatively high error rate and that classification changes over time. With next-generation sequencing and whole-exome sequencing techniques, the sensitivity of identifying variants on the specified genes has increased substantially. At the same time, the number of variants of uncertain significance is also increased with next-generation sequencing. Also, the percentage of individuals who have more than 1 variant that is thought to be pathogenic is increasing. A 2013 study reported that 9.5% (19/200) patients from China with HCM had multiple pathogenic variants and that the number of variants correlated with severity of disease.

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Sequencing tests for HCM are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

No assay kits have been approved by the Food and Drug Administration for genetic testing for HCM.

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

IV. RATIONALE

[TOP](#)

SUMMARY OF EVIDENCE

For individuals who are asymptomatic with risk for HCM because of a positive family history who receive testing for a specific HCM-related variant identified in affected family member(s), the evidence includes studies reporting on the clinical validity of testing. Relevant outcomes are overall survival, test accuracy and validity, changes in reproductive decision making, symptoms, and morbid events. For individuals at risk for HCM (first-degree relatives), genetic testing is most useful when there is a known disease-associated variant in the family. In this situation, genetic testing will establish the presence or absence of the same variant in a close relative with a high degree of certainty. Presence of the variant indicates that the relative should undergo a cardiac evaluation upon receiving the variant-positive results. If a hypertrophic cardiomyopathy diagnosis is not made at that time, the patient should be monitored for development of symptoms. Absence of this variant will establish that the individual has not inherited the familial predisposition to HCM and thus has a similar risk of developing HCM as the general population. Such patients will no longer need ongoing surveillance for the presence of clinical signs of HCM. Although no direct evidence comparing outcomes for at-risk individuals managed with and without genetic testing was identified, there is a strong chain of evidence that management changes can improve outcomes with genetic testing when there is a known familial variant. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic with risk for HCM because of a positive family history who receive nonspecific testing for an HCM-related variant, the evidence includes studies reporting on the clinical validity of testing. Relevant outcomes are overall survival, test accuracy and validity, changes in reproductive decision making, symptoms, and morbid events. Given the wide genetic variation in HCM and the likelihood that not all causative variants have been identified, there is imperfect clinical sensitivity. Therefore, a negative test is not sufficient to rule out a disease-associated variant in patients without a known family variant. For at-risk individuals without a known variant in the family, there is no clear relation between testing and improved outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

V. DEFINITIONS

[TOP](#)

FIRST DEGREE RELATIVE refers to parent, sibling, or child.

SECOND DEGREE RELATIVE refers to an aunt, uncle, niece, nephew, or grandparent.

THIRD DEGREE RELATIVE refers to a great aunt/uncle, first cousin, or great grandmother/grandfather.

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

VI. DISCLAIMER

[TOP](#)

Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as required by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These policies are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.

VII. CODING INFORMATION

[TOP](#)

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

INV; therefore, not covered:

Procedure Codes							
S3865	81439						

Covered when medically necessary:

Procedure Codes							
S3866	81403	81405	81406	81407	81479		

ICD-10-CM Diagnosis Codes:	Description
I42.1	Obstructive hypertrophic cardiomyopathy
I42.2	Other hypertrophic cardiomyopathy
Z13.71	Encounter for nonprocreative screening for genetic disease carrier status
Z31.430	Encounter of female for testing for genetic disease carrier status for procreative management
Z31.440	Encounter of male for testing for genetic disease carrier status for procreative management
Z82.41	Family history of sudden cardiac death

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

ICD-10-CM Diagnosis Codes:	Description
Z82.49	Family history of ischemic heart disease and other diseases of the circulatory system

VIII. REFERENCES

[TOP](#)

1. Semsarian C, Ingles J, Maron MS, et al. New perspectives on the prevalence of hypertrophic cardiomyopathy. *J Am Coll Cardiol*. Mar 31 2015; 65(12): 1249-1254. PMID 25814232
2. Alcalai R, Seidman JG, Seidman CE. Genetic basis of hypertrophic cardiomyopathy: from bench to the clinics. *J Cardiovasc Electrophysiol*. Jan 2008; 19(1): 104-10. PMID 17916152
3. Spirito P, Autore C, Formisano F, et al. Risk of sudden death and outcome in patients with hypertrophic cardiomyopathy with benign presentation and without risk factors. *Am J Cardiol*. May 01 2014; 113(9): 1550-5. PMID 24630786
4. Keren A, Syrris P, McKenna WJ. Hypertrophic cardiomyopathy: the genetic determinants of clinical disease expression. *Nat Clin Pract Cardiovasc Med*. Mar 2008; 5(3): 158-68. PMID 18227814
5. Maron BJ, Maron MS, Semsarian C. Genetics of hypertrophic cardiomyopathy after 20 years: clinical perspectives. *J Am Coll Cardiol*. Aug 21 2012; 60(8): 705-15. PMID 22796258
6. Cirino AL, Ho C. Hypertrophic Cardiomyopathy Overview. In: Adam MP, Ardinger HH, Pagon RA, et al., eds. *GeneReviews*. Seattle, WA: University of Washington; 2014.
7. Ghosh N, Haddad H. Recent progress in the genetics of cardiomyopathy and its role in the clinical evaluation of patients with cardiomyopathy. *Curr Opin Cardiol*. Mar 2011; 26(2): 155-64. PMID 21297463
8. Teo LY, Moran RT, Tang WH. Evolving Approaches to Genetic Evaluation of Specific Cardiomyopathies. *Curr Heart Fail Rep*. Dec 2015; 12(6): 339-49. PMID 26472190
9. Cirino AL, Ho C. Hypertrophic Cardiomyopathy Overview. 2008 Aug 5 [Updated 2021 Jul 8]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. *GeneReviews* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020
10. Elliott P, McKenna WJ. Hypertrophic cardiomyopathy. *Lancet*. Jun 05 2004; 363(9424): 1881-91. PMID 15183628
11. Maron BJ, McKenna WJ, Danielson GK, et al. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy. A report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the European Society of Cardiology Committee for Practice Guidelines. *J Am Coll Cardiol*. Nov 05 2003; 42(9): 1687-713. PMID 14607462
12. Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

- Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. Dec 13 2011; 124(24): e783-831. PMID 22068434
13. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. Dec 22 2020; 76(25): e159-e240. PMID 33229116
 14. Arya A, Bode K, Piorkowski C, et al. Catheter ablation of electrical storm due to monomorphic ventricular tachycardia in patients with nonischemic cardiomyopathy: acute results and its effect on long-term survival. *Pacing Clin Electrophysiol*. Dec 2010; 33(12): 1504-9. PMID 20636312
 15. Das K J, Ingles J, Bagnall RD, et al. Determining pathogenicity of genetic variants in hypertrophic cardiomyopathy: importance of periodic reassessment. *Genet Med*. Apr 2014; 16(4): 286-93. PMID 24113344
 16. Andreassen C, Nielsen JB, Refsgaard L, et al. New population-based exome data are questioning the pathogenicity of previously cardiomyopathy-associated genetic variants. *Eur J Hum Genet*. Sep 2013; 21(9): 918-28. PMID 23299917
 17. Zou Y, Wang J, Liu X, et al. Multiple gene mutations, not the type of mutation, are the modifier of left ventricle hypertrophy in patients with hypertrophic cardiomyopathy. *Mol Biol Rep*. Jun 2013; 40(6): 3969-76. PMID 23283745
 18. Niimura H, Bachinski LL, Sangwatanaroj S, et al. Mutations in the gene for cardiac myosin-binding protein C and late-onset familial hypertrophic cardiomyopathy. *N Engl J Med*. Apr 30 1998; 338(18): 1248-57. PMID 9562578
 19. Richard P, Charron P, Carrier L, et al. Hypertrophic cardiomyopathy: distribution of disease genes, spectrum of mutations, and implications for a molecular diagnosis strategy. *Circulation*. May 06 2003; 107(17): 2227-32. PMID 12707239
 20. Van Driest SL, Ommen SR, Tajik AJ, et al. Sarcomeric genotyping in hypertrophic cardiomyopathy. *Mayo Clin Proc*. Apr 2005; 80(4): 463-9. PMID 15819282
 21. Van Driest SL, Jaeger MA, Ommen SR, et al. Comprehensive analysis of the beta-myosin heavy chain gene in 389 unrelated patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol*. Aug 04 2004; 44(3): 602-10. PMID 15358028
 22. Van Driest SL, Ellsworth EG, Ommen SR, et al. Prevalence and spectrum of thin filament mutations in an outpatient referral population with hypertrophic cardiomyopathy. *Circulation*. Jul 29 2003; 108(4): 445-51. PMID 12860912
 23. Mogensen J, Murphy RT, Kubo T, et al. Frequency and clinical expression of cardiac troponin I mutations in 748 consecutive families with hypertrophic cardiomyopathy. *J Am Coll Cardiol*. Dec 21 2004; 44(12): 2315-25. PMID 15607392
 24. Sedaghat-Hamedani F, Kayvanpour E, Tugrul OF, et al. Clinical outcomes associated with sarcomere mutations in hypertrophic cardiomyopathy: a meta-analysis on 7675 individuals. *Clin Res Cardiol*. Jan 2018; 107(1): 30-41. PMID 28840316
 25. Michels M, Soliman OI, Pfeifferkorn J, et al. Disease penetrance and risk stratification for sudden cardiac death in asymptomatic hypertrophic cardiomyopathy mutation carriers. *Eur Heart J*. Nov 2009; 30(21): 2593-8. PMID 19666645

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

26. Cardoso B, Gomes I, Loureiro P, et al. Clinical and genetic diagnosis of familial hypertrophic cardiomyopathy: Results in pediatric cardiology. *Rev Port Cardiol.* Mar 2017; 36(3): 155-165. PMID 28214152
27. van Velzen HG, Schinkel AFL, Baart SJ, et al. Outcomes of Contemporary Family Screening in Hypertrophic Cardiomyopathy. *Circ Genom Precis Med.* Apr 2018; 11(4): e001896. PMID 29661763
28. Lorenzini M, Norrish G, Field E, et al. Penetrance of Hypertrophic Cardiomyopathy in Sarcomere Protein Mutation Carriers. *J Am Coll Cardiol.* Aug 04 2020; 76(5): 550-559. PMID 32731933
29. Ko C, Arscott P, Concannon M, et al. Genetic testing impacts the utility of prospective familial screening in hypertrophic cardiomyopathy through identification of a nonfamilial subgroup. *Genet Med.* Jan 2018; 20(1): 69-75. PMID 28640247
30. Lopes LR, Brito D, Belo A, et al. Genetic characterization and genotype-phenotype associations in a large cohort of patients with hypertrophic cardiomyopathy - An ancillary study of the Portuguese registry of hypertrophic cardiomyopathy. *Int J Cardiol.* Mar 01 2019; 278: 173-179. PMID 30554928
31. Nightingale BM, Hovick SR, Brock P, et al. Hypertrophic cardiomyopathy genetic test reports: A qualitative study of patient understanding of uninformative genetic test results. *J Genet Couns.* Dec 2019; 28(6): 1087-1097. PMID 31408576
32. Ho CY, Day SM, Ashley EA, et al. Genotype and Lifetime Burden of Disease in Hypertrophic Cardiomyopathy: Insights from the Sarcomeric Human Cardiomyopathy Registry (SHaRe). *Circulation.* Oct 02 2018; 138(14): 1387-1398. PMID 30297972
33. Maurizi N, Passantino S, Spaziani G, et al. Long-term Outcomes of Pediatric-Onset Hypertrophic Cardiomyopathy and Age-Specific Risk Factors for Lethal Arrhythmic Events. *JAMA Cardiol.* Jun 01 2018; 3(6): 520-525. PMID 29710196
34. Robyns T, Breckpot J, Nuyens D, et al. Clinical and ECG variables to predict the outcome of genetic testing in hypertrophic cardiomyopathy. *Eur J Med Genet.* Mar 2020; 63(3): 103754. PMID 31513939
35. Erdmann J, Daehmlow S, Wischke S, et al. Mutation spectrum in a large cohort of unrelated consecutive patients with hypertrophic cardiomyopathy. *Clin Genet.* Oct 2003; 64(4): 339-49. PMID 12974739
36. Olivetto I, Girolami F, Ackerman MJ, et al. Myofilament protein gene mutation screening and outcome of patients with hypertrophic cardiomyopathy. *Mayo Clin Proc.* Jun 2008; 83(6): 630-8. PMID 18533079
37. Chiou KR, Chu CT, Charng MJ. Detection of mutations in symptomatic patients with hypertrophic cardiomyopathy in Taiwan. *J Cardiol.* Mar 2015; 65(3): 250-6. PMID 25086479
38. Adalsteinsdottir B, Teekakirikul P, Maron BJ, et al. Nationwide study on hypertrophic cardiomyopathy in Iceland: evidence of a MYBPC3 founder mutation. *Circulation.* Sep 30 2014; 130(14): 1158-67. PMID 25078086
39. Ingles J, Goldstein J, Thaxton C, et al. Evaluating the Clinical Validity of Hypertrophic Cardiomyopathy Genes. *Circ Genom Precis Med.* Feb 2019; 12(2): e002460. PMID 30681346

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

40. Alejandra Restrepo-Cordoba M, Campuzano O, Ripoll-Vera T, et al. Usefulness of Genetic Testing in Hypertrophic Cardiomyopathy: an Analysis Using Real-World Data. *J Cardiovasc Transl Res*. Feb 2017; 10(1): 35-46. PMID 28138913
41. Hershberger RE, Givertz MM, Ho CY, et al. Genetic Evaluation of Cardiomyopathy-A Heart Failure Society of America Practice Guideline. *J Card Fail*. May 2018; 24(5): 281-302. PMID 29567486
42. Maron BJ, Zipes DP, Kovacs RJ. Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Preamble, Principles, and General Considerations: A Scientific Statement From the American Heart Association and American College of Cardiology. *Circulation*. Dec 01 2015; 132(22): e256-61. PMID 26621642
43. Maron BJ, Udelson JE, Bonow RO, et al. Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 3: Hypertrophic Cardiomyopathy, Arrhythmogenic Right Ventricular Cardiomyopathy and Other Cardiomyopathies, and Myocarditis: A Scientific Statement From the American Heart Association and American College of Cardiology. *J Am Coll Cardiol*. Dec 01 2015; 66(21): 2362-2371. PMID 26542657
44. Ackerman MJ, Priori SG, Willems S, et al. HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). *Heart Rhythm*. Aug 2011; 8(8): 1308-39. PMID 21787999

IX. POLICY HISTORY

[TOP](#)

MP 2.248	03/02/2020 Consensus Review. No change to policy statement. Coding reviewed.
	04/26/2021 Consensus Review. No change to policy statement. References added.
	04/27/2022 Consensus Review. No change to policy statement. Updated FEP, background, rationale, references. Coding reviewed.
	06/30/2023 Consensus Review. Updated coding table; moved S3865 and 81439 to correct coding table (non-covered). Updated references.
	05/23/2024 Consensus Review. Updated references. No changes to coding.
	07/11/2025 Consensus Review. Updated not medically necessary statement to investigational. No coding changes.
	09/24/2025 Administrative Update. Removed Benefit Variations Section and updated Disclaimer.
	03/06/2026 Retirement Review. EviCore Delegation.

[Top](#)

MEDICAL POLICY

POLICY TITLE	GENETIC TESTING FOR PREDISPOSITION TO INHERITED HYPERTROPHIC CARDIOMYOPATHY
POLICY NUMBER	MP 2.248

Health care benefit programs issued or administered by Capital Blue Cross and/or its subsidiaries, Capital Advantage Insurance Company®, Capital Advantage Assurance Company®, and Keystone Health Plan® Central. Independent licensees of the Blue Cross BlueShield Association. Communications issued by Capital Blue Cross in its capacity as administrator of programs and provider relations for all companies.

RETIRED