Genetic Testing for Hereditary Cardiomyopathies and Arrhythmias

MEDICAL POLICY NUMBER: 432

Effective Date: 6/9/2025

Last Review Date: 6/2025

Next Annual Review: 3/2026

INSTRUCTIONS FOR USE: Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Company reserves the right to determine the application of medical policies and make revisions to medical policies at any time. The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

SCOPE: Providence Health Plan, Providence Health Assurance and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PLAN PRODUCT AND BENEFIT APPLICATION

☒ **Commercial** ☐ **Medicaid/OHP*** ☐ **Medicare****

*Medicaid/OHP Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

PHA members must meet the testing criteria governed by the Oregon Health Plan (OHP) - OHP Diagnostic Procedure Codes / Procedure Group 1119. Diagnostic services needed to establish a diagnosis are covered regardless of where the ultimate diagnosis appears. Once the diagnosis is determined, coverage of further treatment is reimbursed if the service appears funded by the OHA for that condition. Medicaid members must also meet the genetic testing criteria governed by the Oregon Health Plan (OHP) Prioritized List Guideline Notes D1 and D17.

**Medicare Members

This *Company* policy may be applied to Medicare Plan members only when directed by a separate *Medicare* policy. Note that investigational services are considered **"not medically necessary"** for Medicare members.

COVERAGE CRITERIA

I. Genetic testing for the diagnosis and management of hereditary cardiomyopathies and cardiac ion channelopathies/arrhythmias using next generation sequencing (NGS) (see Policy Guidelines below) may be considered **medically necessary** when all of the following criteria are met (A.-G.):

   A. Genetic Counseling general criteria have been met (see Genetic Counseling policy); **and**
   B. Suspicion of a genetic cardiac arrhythmia or cardiomyopathy based on examination of the patient's clinical history, family history, and electrocardiographic phenotype; **and**
   C. Clinical tests (e.g., EKG) are inconclusive or insufficient for a clinical diagnosis; **and**
   D. Individual has not undergone previous genetic testing for cardiomyopathies or cardiac ion channelopathies/arrhythmias; **and**
   E. Individual to be tested has a first-degree relative (i.e. parent, full sibling or child) with supporting clinical features of a cardiomyopathy syndrome or cardiac ion channelopathy/arrhythmia; **and**
   F. The individual to be tested has been clinically screened to exclude an alternate,

acquired etiology of cardiomyopathy (e.g., ischemic cardiomyopathy, cardiac amyloidosis, etc.); **and**

G. The genetic testing is focused on pathogenic variants relevant to the individual's suspected clinical diagnosis and known familial genetics.
   - **Note**: If a known familial variant has been identified, the individual must be tested with a panel that includes genes that are specifically associated with member's suspected hereditary cardiac condition.

II. Multigene panels specific to diagnosis and management of cardiomyopathies and cardiac ion channelopathies/arrhythmias using next generation sequencing (NGS) is considered **not medically necessary** when criterion I. above is not met.

Link to Evidence Summary

POLICY CROSS REFERENCES

- Genetic Counseling, MP316

The full Company portfolio of current Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

BACKGROUND

Cardiomyopathies

Cardiomyopathies represent a group of disorders of the heart muscle associated with cardiac dysfunction, aggravated by arrhythmias, heart failure, and sudden cardiac death (SCD). The most common causes of cardiomyopathy and congestive heart failure include ischemic heart disease, myocardial infarction, hypertension, and valvular heart disease. Other causes of heart failure are classified according to their structural and functional phenotypes. Rare, heritable forms of cardiomyopathy include hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), restrictive cardiomyopathy (RCM), and arrhythmogenic right ventricular (ARVC)/arrhythmogenic cardiomyopathy (ACM). These cardiomyopathies range in prevalence from 1:250 to 1:5000, with variations in frequency across different populations. In adult-onset cardiomyopathies, genetic inheritance is typically autosomal dominant, whereas in pediatric-onset cardiomyopathies, X-linked, autosomal recessive, and de novo sporadic patterns are more often observed. Identifying the specific cause of heart failure is important because there may be therapeutic and additional diagnostic implications.

Multigene Panel Testing for Hereditary Cardiomyopathies and Arrhythmias

Laboratories offer panel testing using next generation sequencing (NGS) for multiple genes at the same time to increase the likelihood of finding a causative gene mutation in a more efficient manner. Such testing may be performed for diagnostic or predictive purposes.

- Diagnostic genetic testing is performed in individuals with clinical signs or symptoms of a genetic condition. The genetic test may confirm or rule out a clinical diagnosis.
- Predictive genetic testing is performed in individual's known to be at increased risk of developing an inherited condition based on their family history.

Tests should be chosen to:

- Maximize the likelihood of identifying mutations in the genes of interest.
- Contribute to alterations in patient management.
- Minimize the change of finding variants of uncertain significance.

Multigene Panels

Examples of potentially medically necessary multigene panels Include but are not limited to the following:

- Arrhythmia Comprehensive Panel (Invitae)
- Arrhythmia & Cardiomyopathy Comprehensive Panel (Invitae)
- Arrhythmia Panels or Channelopathies Panels (multiple labs)
- Blueprint Cardiomyopathy Panel (Blueprint Genetics)
- Cardiomyopathy Panel (Knight Diagnostic Laboratories)
- Cardiomyopathy (Panel GeneDx)
- Cardiomyopathy and Arrhythmia Panel (ARUP Labratories)
- Cardiomyopathy Comprehensive Panel (Invitae)
- Cardiomyopathy NGS Panel (Allele Diagnostics)
- Cardio Familial Arrhythmia or Cardiomyopathy Panels (GenSeq)
- Cardiomyopathies, Channelopathies, Arrhythmias, and Aortic Panels
- (HealthinCode)
- CMNext (Ambry Genetics)
- Comprehensive Cardiomyopathy Multi-Gene Panel (Mayo Clinic)
- Comprehensive Cardiomyopathy Panel (Invitae)
- DCMNext (Ambry)
- Dilated Cardiomyopathy (DCM) Left Ventricular Non-Compaction
- (LVNC) (GeneDx)
- Dilated Cardiomyopthay and Left Ventricular Noncompaction Panel (Invitae)
- Familion (Transgenomics)
- GeneSeq: Cardio Familial Cardiomyopathy Profile (Labcorp)
- HCMNext (Ambry Genetics)
- LongQT Next (Ambry Genetics)

- Pan Cardiomyopathy Panel (Prevention Genetics)

DOCUMENTATION REQUIREMENTS

In order to determine the clinical utility of a genetic test, the following documentation must be provided at the time of the request. Failure to submit complete documentation may affect the outcome of the review.

- Specific gene, trade or proprietary name of the test, or if a custom built test, include every gene(s) and/or component of the test
- Name of laboratory where the testing is being conducted or was conducted
- Clinical notes to include the following:
    - Documentation of genetic counseling as required in the policy criteria below which includes
    - how test results will impact clinical decision making
    - Reason (indication) for performing test, including the suspected condition
    - Existing signs and/or symptoms related to reason for current test request
    - Prior test/laboratory results related to reason for current test request
    - Family history, if applicable
    - How results from current test request will impact clinical decision making
- All relevant CPT/HCPCS codes billed

REGULATORY STATUS

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Approval or clearance by the Food and Drug Administration (FDA) does not in itself establish medical necessity or serve as a basis for coverage. Therefore, this section is provided for informational purposes only.

CLINICAL EVIDENCE AND LITERATURE REVIEW

EVIDENCE REVIEW

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of genetic testing for the diagnosis and management of hereditary cardiomyopathies and cardiac ion channelopathies/arrhythmias. Given the extensive body of available evidence, this medical policy is based largely on clinical practice guidelines identified as of February 2025.

CLINICAL PRACTICE GUIDELINES

American Heart Association/American College of Cardiology/American Medical Society for Sports Medicine, the Heart Rhythm Society, Pediatric & Congenital Electrophysiology Society, and the Society for Cardiovascular Magnetic Resonance

- In 2024, the AHA/ACC/AMSSM/HRS/PACES/SCMR published a guideline for the management of hypertrophic cardiomyopathy (HCM).[1] Authors made the following recommendations surrounding genetic testing of patients with HCM:
    - In patients with HCM, genetic testing is beneficial to elucidate the genetic basis to facilitate the identification of family members at risk for developing HCM (cascade testing).
    - In patients with an atypical clinical presentation of HCM or when another genetic condition is suspected to be the cause, a workup including genetic testing for HCM and other genetic causes of unexplained cardiac hypertrophy ("HCM phenocopies") is recommended.
    - In first-degree relatives of patients with HCM, both clinical screening (ECG and 2D echocardiogram) and cascade genetic testing (when a pathogenic/ likely pathogenic variant has been identified in the proband) should be offered.

American Heart Association

- In 2021, the American Heart Association published a scientific statement on genetic testing for heritable cardiovascular diseases (including channelopathies) in children.[2] The statement recommends that genetic testing be performed when a cardiac channelopathy is likely to be present, including after a variant has been found in a family member. Testing to identify at-risk relatives can be considered. Brugada syndrome is difficult to identify since not all adults' express genetic variants; therefore, identifying at-risk children may require clinical evaluation, electrocardiogram (ECG) testing, and/or pharmacologic challenge of all of the child's first-degree relatives. Genetic testing should also be performed in children who are resuscitated from cardiac arrest with no clear cause. Several factors can be considered when deciding the appropriate age for genetic testing of an individual child, including whether the disease is expected to present during childhood, whether the channelopathy can be fatal, whether therapies exist to mitigate mortality risk, and family preferences. Ongoing follow-up genetic testing can confirm pathogenicity of the variant over time.

- In 2020, the American Heart Association published guidelines addressing genetic testing for inherited cardiovascular diseases.[3] Authors stated that DCM testing can aid targeted treatments and aid in identifying family members at risk for the condition. Authors also listed the genes to be considered for testing for various conditions including DCM. Genes included: TTN, LMNA, MYH7, TNNT2, BAG3, RBM20, TNNC1, TNNI3, TPM1, SCN5A, PLN; for testing, all HCM and ARVC genes are recommended to be included.

American College of Medical Genetics and Genomics (ACMG)

In 2018, the American College of Medical Genetics and Genomics (ACMG) published clinical practice recommendations for the genetic evaluation of cardiomyopathy.[4] The following recommendations were made for all types of cardiomyopathies:

- Genetic testing is recommended for the most clearly affected family member.
- Cascade genetic testing of at-risk family members is recommended for pathogenic and likely pathogenic variants.
- In addition to routine newborn screening tests, specialized evaluation of infants with cardiomyopathy is recommended, and genetic testing should be considered.

The ACMG also provided information on specific variants, noting that TTNtv represents the most common genetic variant found in DCM (10% to 20% of cases), with LMNA being the second most common variant identified (diagnostic yield of 5.5%). When a cardiovascular phenotype has been identified, the ACMG recommends family based genetic evaluations and surveillance screening.

Heart Failure Society

In 2018, the Heart Failure Society of America published practice guidelines on the genetic evaluation of cardiomyopathy.[5] The following recommendations for genetic testing for cardiomyopathy were made: Guideline 4:

- Genetic testing is recommended for patients with cardiomyopathy (level of evidence A)
- Genetic testing is recommended for the most clearly affected family member.
- Cascade genetic testing of at-risk family members is recommended for pathogenic and like pathogenic variants

Genetic testing is recommended to determine if pathogenic variant can be identified to facilitate patient management and family screening. The guideline also states that molecular genetic testing for multiple genes with the use of a multigene panel is now the standard of practice for cardio-vascular genetic medicine.

American Heart Association, American College of Cardiology, and the Heart Rhythm Society

In 2017, the American Heart Association, American College of Cardiology, and the Heart Rhythm Society published guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death.[6] The recommendations relating to cardiac ion channelopathies are summarized as follows:

- In first-degree relatives of patients who have a causative mutation for long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, short QT syndrome, or Brugada syndrome, genetic counseling and mutation-specific genetic testing are recommended. Class of Recommendation: I (strong) Level of Evidence B-NR- moderate level of evidence

- In patients with clinically diagnosed long QT syndrome, genetic counseling and genetic testing are recommended. Genetic testing offers diagnostic, prognostic, and therapeutic information. Class of Recommendation: I (strong) Level of Evidence B-NR- moderate level of evidence
- In patients with catecholaminergic polymorphic ventricular tachycardia and with clinical VT or exertional syncope, genetic counseling and genetic testing are reasonable. Genetic testing may confirm a diagnosis; however, therapy for these patients is not guided by genotype status. Class of Recommendation: Iia (moderate) Level of Evidence B-NR- moderate level of evidence
- In patients with suspected or established Brugada syndrome, genetic counseling and genetic testing may be useful to facilitate cascade screening of relatives, allowing for lifestyle modification and potential treatment. Class of Recommendation: IIb (weak) Level of Evidence C-EO- consensus of expert opinion based on clinical experience
- In patients with short QT syndrome, genetic testing may be considered to facilitate screening of first-degree relatives. IIb (weak) Level of Evidence CEO- consensus of expert opinion based on clinical experience

EVIDENCE SUMMARY

Genetic testing for certain inherited cardiomyopathy syndromes and inherited arrhythmia syndromes are recommended by cardiovascular societies. Finding a genetic cause for these inherited cardiac diseases makes an important impact by establishing a precise diagnosis, allowing predictive testing for family members, guiding choice of therapies, assisting in reproductive decisions (including preimplantation genetic diagnosis), and providing additional prognostic information. Family history may be informative in determining the likelihood of finding a pathogenic variant that fits the clinical picture of a pre-symptomatic individual. Based on review of the peer reviewed medical literature over 30 gene variants have been identified related to cardiomyopathy Based on review of the peer reviewed medical literature at this time multigene panels for cardiac ion channelopathies/arrhythmias are available and when at least 5 genes related to the condition being evaluated is part of the panel and no prior genetic testing has been completed the panel may be clinically useful in changing patient management in which subset of individuals may have increased risk of sudden cardiac death (SCD) which may be the first symptom. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome. Guidelines also state that molecular genetic testing for multiple genes with the use of a multigene panel is now the standard of practice for cardiovascular genetic medicine.

HEALTH EQUITY CONSIDERATIONS

The Centers for Disease Control and Prevention (CDC) defines health equity as the state in which everyone has a fair and just opportunity to attain their highest level of health. Achieving health equity requires addressing health disparities and social determinants of health. A health disparity is the occurrence of diseases at greater levels among certain population groups more than among others. Health disparities are linked to social determinants of health which are non-medical factors that influence health outcomes such as the conditions in which people are born, grow, work, live, age, and the wider set of forces and systems shaping the conditions of daily life. Social determinants of health include unequal access to health care, lack of education, poverty, stigma, and racism.

The U.S. Department of Health and Human Services Office of Minority Health calls out unique areas where health disparities are noted based on race and ethnicity. Providence Health Plan (PHP) regularly reviews these areas of opportunity to see if any changes can be made to our medical or pharmacy policies to support our members obtaining their highest level of health. Upon review, PHP creates a Coverage Recommendation (CORE) form detailing which groups are impacted by the disparity, the research surrounding the disparity, and recommendations from professional organizations. PHP Health Equity COREs are updated regularly and can be found online here.

BILLING GUIDELINES AND CODING

CODES*		
CPT	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 (eg, DSG2, MYBPC3, MYH7, PKP2, TTN)

***Coding Notes:**

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

1. Ommen SR, Ho CY, Asif IM, et al. 2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation.* 2024;149(23):e1239-e1311
2. Landstrom AP, Kim JJ, Gelb BD, et al. Genetic testing for heritable cardiovascular diseases in pediatric patients: a scientific statement from the American Heart Association. *Circulation: Genomic and Precision Medicine.* 2021;14(5):e000086
3. Musunuru K, Hershberger RE, Day SM, et al. Genetic testing for inherited cardiovascular diseases: a scientific statement from the American Heart Association. *Circulation: Genomic and Precision Medicine.* 2020;13(4):e000067

4. Hershberger RE, Givertz MM, Ho CY, et al. Genetic evaluation of cardiomyopathy: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2018;20(9):899-909
5. Hershberger RE, Givertz MM, Ho CY, et al. Genetic evaluation of cardiomyopathy—a Heart Failure Society of America practice guideline. *Journal of cardiac failure.* 2018;24(5):281-302
6. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Heart Rhythm.* 2018;15(10):e190-e252

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
6/2025	New policy.
6/9/2025	Interim update. Changed criterion I. from referencing the Genetic and Molecular Testing policy to Genetic Counseling specific requirement.