Cardiac Ion Channel Genetic Testing

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Definitions

Long QT syndrome (LQTS)	A congenital disorder characterized by prolongation of the QT interval on electrocardiogram (ECG) and a propensity to ventricular tachyarrhythmias, which may lead to syncope, cardiac arrest or sudden cardiac death, typically in young individuals. Variants of LQTS include the Romano-Ward syndrome (autosomal dominant inheritance, QT prolongation and ventricular tachyarrhythmias) and the Jervell and Lang-Nielsen (JLN) syndrome (autosomal recessive
Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)	A lethal form of inherited cardiac channelopathy characterized by irregular heart rhythms (brought on by physical exertion or intense emotion) which may cause syncope, cardiac arrest or sudden cardiac death. Autosomal dominant and recessive CPVT variants arise from mutations in the cardiac ryanodine receptor (RyR2) gene and the cardiac calsequestrin (CASQ2) gene respectively.
Brugada syndrome	An inherited cardiac condition characterized by abnormal EKG findings, an increased risk of ventricular fibrillation and sudden death.
Short QT syndrome (SQTS)	An autosomal dominant channelopathy characterized by a shortened QT interval and action potential on EKG findings and an increased risk for adverse cardiac events including arrhythmias and SCD.

Guideline

1. Long QT Syndrome (LQTS)

Considered medically necessary for **any** of the following indications:

- **a.** Signs or symptoms indicating a moderate-to-high pretest probability of LQTS (e.g., Schwartz score of 2–3)[1]
- **b.** A close relative (e.g., 1st, 2nd or 3d-degree) with a known LQTS mutation

[1] A commonly used criterion to diagnose LQTS is the LQTS "diagnostic score", which is calculated by assigning different points to various criteria (e.g., ≥ 4 points indicates high probability, ≤ 1 denotes low and 2 or 3 suggests intermediate probability of LQTS.

   c. A close relative diagnosed with LQTS by clinical means whose genetic status is unavailable but has sustained an unexplained syncopal episode, ventricular fibrillation with successful resuscitation or sudden death

2. **Catecholaminergic polymorphic ventricular tachycardia (CPVT)**
   Considered medically necessary for **any** of the following indications:
   a. Children or young adults (< 40 years of age) who have a 1st degree relative with a clinical diagnosis of CPVT
   b. Children or young adults (< 40 years of age) who have a 1st, 2nd or 3d-degree relative with a known CPVT mutation
   c. Signs or symptoms indicating a moderate-to-high pretest probability of CPVT

Limitations/Exclusions

Genetic testing for Brugada Syndrome and SQT syndrome is considered investigational and not medically necessary.

Revision History

3/11/2016: Title changed from Genetic Testing for Long QT syndrome (LQTS) to Cardiac Ion Channel Genetic Testing and added indication for CPVT genetic testing.

Applicable Procedure Codes

~~81280~~	~~Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); full sequence analysis~~ (Code Deleted 01/01/2017)
~~81281~~	~~Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); known familial sequence variant~~ (Code Deleted 01/01/2017)
~~81282~~	~~Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); duplication/deletion variants~~ (Code Deleted 01/01/2017)
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)
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)
81408	Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis)

Applicable ICD-10 Diagnosis Codes

I45.81	Long QT syndrome
I47.0	Re-entry ventricular arrhythmia
I47.2	Ventricular tachycardia
I47.9	Paroxysmal tachycardia, unspecified

References

1. Brugada P, Brugada R, Antzelevitch C, et al. The Brugada syndrome. Arch Mal Coeur Vaiss. 2005; 98(2):115-122.
2. Brugada R, Brugada P, Brugada J, Hong K. Brugada syndrome. In: GeneReviews at GeneTests: Medical Genetics Information Resource [database online]. Seattle, WA: University of Washington; December 7, 2007. Available at: http://www.geneclinics.org.
3. Chiang CE. Congenital and acquired LQTS; current concepts and management. Cardiology Review. 2004 Jul-Aug;12(4):222-

34.

4. Gollob MH, Redpath CJ, Roberts JD. The short QT syndrome: proposed diagnostic criteria. J Am Coll Cardiol. 2011; 57(7):802-812
5. Maron BJ, Moller JH, Seidman CE, et al. Impact of laboratory molecular diagnosis on contemporary diagnostic criteria for genetically transmitted cardiovascular diseases: hypertrophic cardiomyopathy, long-QT syndrome, and marfan syndrome: a statement for healthcare professionals from the councils on clinical cardiology, cardiovascular disease in the young, and basic science, American Heart Association Circulation. 1998;98:1460-1471. http://circ.ahajournals.org/cgi/search?journalcode=circulationaha&fulltext=Impact+of+laboratory+molecular+diagnosis+on+contemporary+diagnostic+.
6. Schwartz PJ, Moss AJ, Vincent GM, Crampton RS. Diagnostic criteria for the long QT syndrome. An update. Circulation. 1993 Aug;88(2):782
7. Specialty matched clinical peer review.