

Corporate Medical Policy

Genetic Testing for Long QT Syndrome

File Name:	genetic_testing_for_long_qt_syndrome
Origination:	10/2008
Last CAP Review:	4/2012
Next CAP Review:	4/2013
Last Review:	4/2012

Description of Procedure or Service

Congenital long QT syndrome (LQTS) is an inherited disorder characterized by the lengthening of the repolarization phase of the ventricular action potential, increasing the risk for arrhythmic events, such as torsades de pointes, which may in turn result in syncope and sudden cardiac death. Management has focused on the use of beta blockers as first-line treatment, with pacemakers or implantable cardiac defibrillators (ICD) as second-line therapy.

Congenital LQTS usually manifests itself before the age of 40 years, and may be suspected when there is a history of seizure, syncope, or sudden death in a child or young adult; this history may prompt additional testing in family members. It is estimated that more than one half of the 8,000 sudden unexpected deaths in children may be related to LQTS. The mortality of untreated patients with LQTS is estimated at 1%–2% per year, although this figure will vary with the genotype. Frequently, syncope or sudden death occurs during physical exertion or emotional excitement, and thus LQTS has received some publicity regarding evaluation of adolescents for participation in sports. In addition, LQTS may be considered when a long QT interval is incidentally observed on an EKG. Diagnostic criteria for LQTS have been established, which focus on EKG findings and clinical and family history (i.e., Schwartz criteria, see following section, “Clinical Diagnosis”). However, measurement of the QT interval is not well standardized, and in some cases, patients may be considered borderline cases.

In recent years, LQTS has been characterized as an “ion channel disease,” with abnormalities in the sodium and potassium channels that control the excitability of the cardiac myocytes. A genetic basis for LQTS has also emerged, with 7 different variants recognized, each corresponding to mutations in different genes as indicated here. In addition, typical ST-T-wave patterns are also suggestive of specific subtypes.

LQT1 is associated with mutations in the gene *KNQ1* located on chromosome 11. LQT1 is responsible for about 50% of all LQTS, and arrhythmic events prompted by exercise may occur most commonly in this subtype. Therefore, patients with LQT1 may be advised to minimize exercise.

LQT2 is associated with mutations in the gene *KCNH2* located on chromosome 7 and is seen in 45% of patients with LQTS. Arrhythmic events appear to be precipitated by auditory stimuli, and these patients may be advised to avoid clock alarms, etc.

LQT3 is associated with mutations in the gene *SCN5A* located on chromosome 3. This subtype is seen in 3%–4% of patients with LQTS. In this subtype, the majority of cardiac events occur during sleep. LQT3 variant is also known as the Brugada syndrome.

LQT 4-7 involve *KCN* genes located on chromosomes 21 and 17. These variants each account for

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less than 1% of LQTS.

Clinical Diagnosis

The Schwartz criteria are commonly used as a diagnostic scoring system for LQTS. The most recent version of this scoring system is shown below. A score of 4 or greater indicates a high probability that LQTS is present, a score of 2–3 indicates an intermediate probability and a score of 1 or less indicates a low probability of the disorder. Prior to the availability of genetic testing, it was not possible to test the sensitivity and specificity of this scoring system; therefore, the accuracy of this scoring system is ill-defined.

Diagnostic Scoring System for LQTS

<u>Criteria</u>	<u>Points</u>
Electrocardiographic findings	
QTc >480 msec	3
QTc 460-470 msec	2
QTc <450 msec	1
History of torsades de pointes	2
T-wave alternans	1
Notched T-waves in three leads	1
Low heart rate for age	0.5
Clinical history	
Syncope brought on by stress	2
Syncope without stress	1
Congenital deafness	0.5
Family history	
Family members with definite LQTS	1
Unexplained sudden death in immediate family members younger than 30 years of age	0.5

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for genetic testing for Long QT Syndrome when the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Genetic Testing for Long QT Syndrome is covered

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Genetic testing in patients with suspected congenital long QT syndrome may be considered medically necessary for the following indications:

Individuals who do not meet the clinical criteria for LQTS (those with a Schwartz score less than 4), but who have:

- a close relative (i.e., first-, second-, or third-degree relative) with a known LQTS mutation;
or
- a close relative diagnosed with LQTS by clinical means whose genetic status is unavailable; **or**
- signs and/or symptoms indicating a moderate-to-high pretest probability of LQTS.

When Genetic Testing for Long QT Syndrome is not covered

Genetic testing for LQTS to determine prognosis and/or direct therapy in patients with known LQTS is considered investigational.

Genetic screening for LQTS in the general population is of unproven benefit and is considered not medically necessary.

Policy Guidelines

The clinical utility of genetic testing for LQTS is high when there is a moderate to high pre-test probability of LQTS and when the diagnosis cannot be made with certainty by other methods. A definitive diagnosis of LQTS leads to treatment of LQTS with beta blockers in most cases, and sometimes to treatment with an ICD. As a result, confirming the diagnosis of LQTS will lead to a health outcome benefit by reducing the risk for ventricular arrhythmias and sudden cardiac death. The clinical utility of testing is also high for close relatives of patients with known LQTS, since these individuals should also be treated if they are found to have a pathologic LQTS mutation.

Genetic testing has not been demonstrated to improve the outcomes of those individuals who already meet clinical criteria for LQTS. Once diagnosed with LQTS, all patients should be treated with beta blockers and lifestyle modifications. There is no evidence to suggest that genetic testing influences clinical decisions on whether or not to treat with an implantable cardioverter-defibrillator (ICD).

Currently, two laboratories in the United States perform genetic testing for congenital LQTS: PGxHealth and John Welsh Cardiovascular Diagnostic Laboratory.

The Familion® test, performed by PGxHealth, is a patented genetic test intended to provide analysis of five major cardiac ion channel genes. The John Welsh Cardiovascular Diagnostic Laboratory offers more limited LQTS testing, focusing only on mutations in KCNJ2 and CAVEOLIN (CAV3) sequencing. Individuals are tested by automatic fluorescent DNA sequencing.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it

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will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: S3861, 81280, 81281, 81282

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.43, 12/13/07

BCBSA TEC Assessment [Electronic Version]. February 2008

Adelaide Health Technology Assessment (AHTA). Genetic testing for long QT syndrome; Horizon scanning prioritizing summary-volume 13. Adelaide, Australia: Adelaide Health Technology Assessment (AHTA) on behalf of National Horizon Scanning Unit (Health-PACT and MSAC0; June 2006. Retrieved 10/3/08 from <http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/prioritizing-summaries-2006-2>

Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, Gregoratos, G, Klein G, Moss AJ, Myerburg RJ, Pirori SG, Quinones MA, Roden DM, Silka MJ, Tracy C. ACC/AHA/ESC 2006 Guidelines 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 and European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). *Circulation*. 2006;114:1088-1032. Retrieved 10/3/08 from <http://circ.ahajournals.org/cgi/reprint/114/10/1088>

Familion® Genetic Tests for Inherited Cardiac Syndromes. Technical Specifications. August 2008. Available at: http://www.pgxhealth.com/genetictests/familion/pdf/FAMILION_TechSheet_08TS0801_RAC.PDF

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.43, 12/11/08

Schwartz PJ, Moss AJ, Vincent GM et al. Diagnostic criteria for the long QT syndrome. An update. *Circulation* 1993; 88(2):782-4.

Baylor College of Medicine (BCM). John Welsh cardiovascular diagnostic laboratory. [BCM Web site]. 08/07/08. Available at: http://www.bcm.edu/pediatrics/index.cfm?Realm=99992426&This_Template=Genetic_Testing. Accessed June 16, 2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.43, 7/8/10

Specialty Matched Consultant Advisory Panel review 4/2011

Albert CM, MacRae CA, Chasman DI et al. Common variants in cardiac ion channel genes are associated with sudden cardiac death. *Circ Arrhythm Electrophysiol* 2010; 3(3):222-9. Retrieved on August 15, 2011 from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2891421/?tool=pubmed>

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.43, 7/14/11

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Policy Implementation/Update Information

- 11/17/08 New policy issued. Coverage is provided for genetic testing for long QT syndrome when the medical criteria and guidelines outlined in the policy are met. (adn)
- 12/7/09 Specialty Matched Consultant Advisory Panel review meeting 10/30/09. No change to policy statement. Policy approved as written. (adn)
- 6/22/10 Policy Number(s) removed (amw)
- 7/20/10 Description section extensively revised to include the Schwartz Diagnostic Scoring System for LQTS. Policy Guidelines updated. References updated. No change to Policy Statement. (mco)
- 5/10/11 Specialty Matched Consultant Advisory Panel review 4/2011. References updated. (mco)
- 8/30/11 References updated. No changes to Policy Statements. (mco)
- 12/30/11 Added new codes 81280, 81281, 81282 to “Billing/Coding” section. Effective date 1/1/2012. (mco)
- 3/30/12 Deleted the following codes from the “Billing/Coding” section: S3860, S3862. (mco)
- 5/15/12 Specialty Matched Consultant Advisory Panel review 4/2012. Medical Director review 3/2012. Policy Guidelines updated. (mco)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.