GENETIC TESTING FOR
LONG QT SYNDROME
HS-148

Easy Choice Health Plan, Inc.
Harmony Health Plan of Illinois, Inc.
Missouri Care, Inc.
‘Ohana Health Plan, a plan offered by
WellCare Health Insurance of Arizona, Inc.
WellCare Health Insurance of Illinois, Inc.
WellCare Health Plans of New Jersey, Inc.
WellCare Health Insurance of Arizona, Inc.
WellCare of Florida, Inc.
WellCare of Connecticut, Inc.
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WellCare of Ohio, Inc.
WellCare of South Carolina, Inc.
WellCare of Texas, Inc.
WellCare Prescription Insurance, Inc.
Windsor Health Plan
Windsor Rx Medicare Prescription Drug Plan

Genetic Long QT Syndrome
Policy Number: HS-148

Original Effective Date: 1/21/2010
Revised Date(s): 1/21/2011; 1/5/2012;
11/1/2012; 11/7/2013; 8/7/2014

APPLICATION STATEMENT
The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.
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DISCLAIMER

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member’s particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member’s benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member’s Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any. Note: The lines of business (LOB) are subject to change without notice; consult wellcare.com/Providers/CCGs for list of current LOBs.

BACKGROUND

Long QT syndrome (LQTS) is a disorder of the heart's electrical system. It is characterized by prolongation of the QT interval. The QT interval is the section on the electrocardiogram (ECG) that represents the time it takes for the electrical system to fire an impulse through the ventricles and then recharge. The electrical activity of the heart is produced by the flow of ions in and out of the cells of the heart. LQTS is a defect in the ion channels, which causes a delay in the time it takes for the electrical system to recharge after each heartbeat. LQTS disorders are considered channelopathies, or diseases that affect cardiac ion channels. This condition predisposes the individual to cardiac events and arrhythmias including: torsades de pointes ventricular tachycardia, syncopal episodes, ventricular fibrillation and cardiac arrest. LQTS may also be caused by acquired factors, most commonly by use of certain drugs that will cause prolongation of the QT interval.¹,²

LQTS is diagnosed by considering the clinical features, the family history and the ECG findings of the patient. Unexplained syncope or sudden cardiac death in a child or young adult should raise suspicion of the possibility of LQTS. Electrophysiological testing has not been demonstrated to be helpful in making this diagnosis. The clinical features are a result of the torsades, and may range from minor symptoms such as dizziness, to seizure, syncope and sudden death. Congenital LQTS will usually manifest before the age of 40 years, generally in childhood and adolescence. The age is usually dependent on the genotype. The prolongation of the QT interval is a risk factor independent of patient’s age, history of myocardial infarction, heart rate and history of drug use. Patients with QT interval corrected by heart rate (QTc) of greater than 440 milliseconds are at two to three times higher risk for sudden cardiac death than those with QTc interval of under 440 milliseconds. The mortality rate of untreated patients with LQTS is in the range of 1% to 2% per year. Sudden cardiac death may be precipitated by a triggering event, such as physical exercise, swimming, sleep deprivation, auditory stimuli, and sudden intense sympathetic stimuli. In an effort to enhance diagnostic reliability, an elaborate point score system has been proposed that incorporates QTc duration, as well as other hallmarks such as syncope and a family history of this condition.¹,²

There are several forms of LQTS, depending on the genes responsible and the features associated with the condition. Most forms of LQTS are carried in an autosomal dominant manner, with the exception being Jervell and Lange-Nielsen syndrome (JLNS), which is inherited in an autosomal recessive manner. Articles in the medical literature may use the terminology LQT1, LQT2, etc., to refer to the locus name of genes involved in LQTS, or the phenotype.²

The Familion® test (Clinical Data, Inc., Newton, MA) is a patented genetic test that is intended to provide analysis of five major cardiac ion channel genes. According to the Clinical Data website, the analysis includes sequence determination and variant detection. It is noted at the website that the genes analyzed by this test include: KCNQ1, KCNH2, SCN5A, KCNE1, and KCNE2. Testing for LQTS may be performed with one of the following configurations:¹

- Comprehensive cardiac ion channel analysis: This will provide analysis for variants in all five genes and is appropriate when there is a high index of suspicion of disease such as stress-induced syncope, prolonged QT interval, family history of sudden cardiac death and unexplained ventricular arrhythmia.
- Family specific analysis: This test provides analysis of one or more mutations found in an index case using either one of the above test configurations or confirmed results from another laboratory and is appropriate for testing blood relatives.

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POSITION STATEMENT

Applicable To:
- Medicaid – Hawaii, Kentucky*
- Medicare – Easy Choice Health Plan, Hawaii, Kentucky*

For markets noted below, please refer to Care Core National Lab Management criteria (program effective August 2014) available at www.wellcare.com/provider/CCGs.

- Medicaid – Florida, Georgia, Illinois, Missouri, New Jersey, New York, South Carolina
- Medicare – Arizona, Connecticut, Florida, Georgia, Illinois, Louisiana, Missouri, New Jersey, New York, Ohio, Texas, Windsor

* Kentucky (Medicaid and Medicare) pending state approval; CCG to be used until Care Core is effective in late 2014.

Genetic testing for long QT syndrome is considered medically necessary in the following circumstances:

- Members with a prolonged QT interval on resting electrocardiogram (a corrected QT interval (QTc) of 470 msec in adult males and 480 msec in adult females*) without an identifiable external cause for QTc prolongation (such as heart failure, bradycardia, electrolyte imbalances, certain medications and other medical conditions); OR,
- Members with first-degree relatives (siblings, parents, or offspring) with a defined LQT mutation, or long QT syndrome resulting in sudden death of a first or second degree relative.

* NOTE: A corrected QT interval (QTc) of 450 msec is used in male children, and 460 msec in female children.

Genetic testing for long QT syndrome is considered NOT medically necessary and NOT a covered benefit in the following circumstances:

- The above criteria are not met; AND,
- General population testing; AND,
- Prenatal testing

CODING

CPT<sup>®</sup> Codes and units billed specific to the Familion Long QT Syndrome Test

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>81280</td>
<td>Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); full sequence analysis</td>
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<td>Molecular diagnostics; molecular isolation or extraction, each nucleic acid type (ie, DNA or RNA)</td>
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<td>Molecular diagnostics; isolation or extraction of highly purified nucleic acid, each nucleic acid type (DNA or RNA)</td>
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<td>83892</td>
<td>Molecular diagnostics; enzymatic digestion, each enzyme treatment</td>
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<td>83897</td>
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<td>83898</td>
<td>Molecular diagnostics; amplification, target, each nucleic acid sequence</td>
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83900 Molecular diagnostics; amplification, target, multiplex, first 2 nucleic acid sequences
83901 Molecular diagnostics; amplification, target, multiplex, each additional nucleic acid sequence beyond 2 (List separately in addition to code for primary procedure)
83904 Molecular diagnostics; mutation identification by sequencing, single segment, each segment
83909 Molecular diagnostics; separation and identification by high resolution technique (e.g., capillary electrophoresis), each nucleic acid preparation
83912 Molecular diagnostics; interpretation and report

ICD-9-CM Procedure Codes - Not applicable

HCPCS Level II Codes
S3860* Genetic testing, comprehensive cardiac ion channel analysis, for variants in 5 major cardiac ion channel genes for individuals with high index of suspicion for familial Long QT Syndrome (LQTS) or related syndromes
S3861* Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada syndrome
S3862* Genetic testing, family-specific ion channel analysis, for blood-relatives of individuals (index case) who have previously tested positive for a genetic variant of a cardiac ion channel syndrome using either one of the above test configurations or confirmed results from another laboratory
*Note: S-Codes are NON COVERED FOR MEDICARE – Refer to HCPCS Level II Temporary National Codes
*For Medicare, bill the appropriate CPT code listed above

Covered ICD-9-CM Diagnoses Codes
426.82 Long QT syndrome
V17.41 Family history of sudden cardiac death (SCD)
V17.49 Family history of other cardiovascular diseases
426.89 Long QT syndrome
427.1 Paroxysmal ventricular tachycardia
427.41 Ventricular fibrillation
427.42 Ventricular flutter
427.5 Cardiac arrest
760.2 Syncope and collapse
794.31 Nonspecific abnormal electrocardiogram (ecg) (ekg)
794.31 Abnormal electrocardiogram (long QT syndrome)
996.04 Mechanical complication of cardiac device, implant, and graft due to automatic implantable cardiac defibrillator
996.61 Infection and inflammatory reaction due to cardiac device, implant, and graft
996.72 Other complications of internal prosthetic device, implant, and graft
due to other cardiac device, implant, and graft

Covered ICD-10-CM Diagnosis Codes
I45.81 Long QT Syndrome
Z82.41 Family history of sudden cardiac death
Z82.49 Family history of ischemic heart disease and other diseases of the circulatory system
I46.2- I46.9 Cardiac arrest
I47.0- I47.9 Paroxysmal tachycardia
I49.0 - I49.9 Other cardiac arrhythmias
R55 Syncope and collapse
R94.30- R94.39 Abnormal results of cardiovascular function tests
T82.110A - T82.191A Mechanical complication of cardiac electronic device
T82.817A - T82.9XXA Other specified complications of cardiac and vascular prosthetic devices, implants, grafts


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REFERENCES


MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

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<td>11/1/2012</td>
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<td>1/5/2012</td>
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<tr>
<td>12/1/2011</td>
<td>New template design approved by MPC.</td>
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