



GENETIC TESTING FOR TUBEROUS SCLEROSIS COMPLEX HS-143



Harmony Behavioral Health, Inc.

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Genetic Testing for Tuberous Sclerosis Complex

Policy Number: HS-143

Original Effective Date: 11/19/2009

Revised Date(s): 11/12/2010; 10/6/2011

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.

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.

BACKGROUND

TSC is a variable multisystem disorder characterized by hamartomas that result in abnormalities of the skin (including hypomelanotic macules, facial angiofibromas, shagreen patches, fibrous facial plaques, and ungual fibromas), brain (including cortical tubers and subependymal nodules), kidneys (including angiomyolipomas and renal cysts), and heart (including rhabdomyomas and arrhythmias). Affected individuals may also exhibit seizures and developmental delay or intellectual disability. Although TSC is inherited in an autosomal dominant fashion, approximately two thirds of cases are de novo. Two genes have been identified that are associated with TSC: *TSC1*, which is located on chromosome 9 at band q34; and *TSC2*, which is located on chromosome 16 at band p13.3. Approximately 80% of TSC patients will have a variant in 1 of these 2 genes, with approximately 20% in *TSC1* and 60% in *TSC2*. Although the penetrance of sequence variants in the *TSC1* and *TSC2* genes is high, expressivity is variable. Sequence variants in *TSC1* are primarily small deletions/insertions and nonsense variants, while up to 10% of the variants in *TSC2* are larger deletions or rearrangements involving multiple exons or the entire gene. While the small deletions/insertions and sequence variants can be detected by direct sequence analysis, larger rearrangements require specialized methods such as multiplex ligation-dependent amplification (MLPA) (from Hayes GTE, 2009).

Revised Diagnostic Criteria for TSC

A definitive diagnosis of TSC requires two major features. Cerebral MRI or non-enhanced CT, renal ultrasound or cardiac echo *may be necessary* to arrive at the diagnosis.

- Facial angiofibromas or forehead plaque
- Non-traumatic ungula or periungual fibromas
- Shagreen patch (connective tissue nevus)
- Multiple retinal nodular hamartomas
- Cortical tubera
- Subependymal nodule
- Subependymal giant cell astrocytoma
- Cardiac rhabdomyoma, single or multiple
- Lymphangiomyomatosis and/or renal angiomyolipomas^b
- Hypomelanotic macules (more than three)

Suggestive Features Requiring Further Investigation

- Multiple randomly distributed pits in dental enamel
- Hamartomatous rectal polyps
- Bone cysts^a
- Cerebral white matter radial migration lines^{a,d,e}
- Gingival fibromas
- Non-renal hamartoma^c
- Retinal achromic patch
- “Confetti” skin lesions
- Multiple renal cysts^c
- Skin tags
- Positive family history in first degree relative

^a When cerebral cortical dysplasia and cerebral white matter migration tracts occur together, they should be counted as one rather than two features of TSC.

^b When both lymphangiomyomatosis and renal angiomyolipomas are present, other features of TSC should be present before

- a definitive diagnosis is assigned.
- c histological confirmation is suggested.
- d Radiological confirmation is sufficient.
- e On echo in child or at post portem.

POSITION STATEMENT

Genetic testing for tuberous sclerosis complex (TSC) is considered medically necessary if the following criteria are met:

- Diagnostic criteria (see below) are inconclusive;

AND,

- A specific mutation has been identified in an affected family member; **OR,**
- Reproductive partners of members affected with TSC; **OR,**
- Adult members with a family history of TSC that puts them at higher than the general population risk to be a carrier

Prenatal testing for TSC is considered medically necessary if either of the following criteria are met:

- A specific mutation in the TSC1 and TSC2 gene has been identified in an affected family member; **OR,**
- There is a family history of TSC

Genetic testing for tuberous sclerosis complex (TSC) is considered NOT medically necessary in the following circumstances:

- A conclusive clinical diagnosis of TSC has been made; **OR,**
- A member has no family history of TSC

CLINICAL EVIDENCE

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CODING

PT®* Codes

83891	Molecular diagnostics; isolation or extraction of highly purified nucleic acid
83896	Molecular diagnostics; nucleic acid probe, each
83898	Molecular diagnostics; amplification, target, each nucleic acid sequence
83900	Molecular diagnostics; amplification, target, multiplex, first two 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 (eg, capillary electrophoresis)
83912	Molecular diagnostics; interpretation and report
83914	Mutation identification by enzymatic ligation or primer extension, single segment, each segment, (OLA, SBCE, ASPE)

ICD-9-CM Procedure Codes No applicable codes

HCPCS Code No applicable codes

ICD-9-CM Diagnosis Codes

V18.9 Family History - Genetic disease carrier

*Current Procedural Terminology (CPT®) ©2011 American Medical Association: Chicago, IL.

REFERENCES

Peer Reviewed

1. Hayes Directory. (2009, October 16). Tuberous Sclerosis Complex (TSC; Bourneville Disease). Retrieved from <http://www.hayesinc.com>

Government Agencies, Professional and Medical Organizations

1. Tuberous Sclerosis Association. (2002). Clinical guidelines for the care of patients with Tuberous Sclerosis Complex: summary. Retrieved from <http://www.tuberous-sclerosis.org/publications/clinicalguidelinessummary.pdf>

HISTORY AND REVISIONS

Date	Action
12/1/2011	<ul style="list-style-type: none">• New template design approved by MPC.
10/6/2011	<ul style="list-style-type: none">• Approved by MPC. Reformatted references. No major changes.