**Letter of Medical Necessity for Tuberous Sclerosis (TSC) Panel**

**Patient Information**

**Date:**

**Patient Name:**

**Patient DOB:**

**Insurance Company Name, Address, City, State:**

**Policy Number:**

**Group Number:**

**ICD10 Codes:**

**Test Information**

**Test Name:** Tuberous Sclerosis (TSC) Panel

**CPT Codes:** 81405x1, 81406x2, 81407x1

**Laboratory:**

GeneDx, Inc.

(NPI#1487632998 / TAXID#205446298 / CLIA#21D0969951)

207 Perry Parkway

Gaithersburg, MD 20877

Telephone: (301) 519-2100

Fax: (201) 421-2010

This letter is in regards to my patient, [FIRST NAME LAST NAME], to request full coverage for the Tuberous Sclerosis (TSC) Panel to be performed by GeneDx. It is my professional determination that testing is medically necessary and will have a direct impact on this patient’s treatment and management.

**Patient Clinical and Family History**

This testing is requested due to this patient’s personal medical history, which includes the following clinical findings:

* Add Phenotype
* Add Phenotype
* Add Phenotype

The patient’s family history is negative for related conditions / unknown / remarkable for the following related clinical features:

The patient has previously had the following uninformative genetic and other testing:

* Add test
* Add test
* Add test

**Clinical Evidence and Guidelines for Testing**

Tuberous sclerosis complex (TSC) is characterized by abnormalities of the skin, brain, kidney, heart, and lungs. Confirmation of the diagnosis is essential to allow optimal direct and supportive care, which includes surveillance for early treatment of tumors as well as potentially severe dysfunction of the renal, cardiac, pulmonary, and other systems.1

The International Tuberous Sclerosis Consensus Group has established major and minor clinical criteria, including skin findings and effects on other body systems including multiple retinal nodular hamartomas, cortical tubers, subependymal nodules, subependymal giant cell astrocytoma, cardiac rhabdomyoma, lymphangiomyomatosis, and renal angiomyolipoma.2 Minor features involving the central nervous system, teeth, gums, eyes, kidneys, or other organ systems are often also present. Individuals with TSC have a significantly increased risk for other neurodevelopmental disorders. Approximately 50% have intellectual disability or developmental delay, 40% have autism spectrum disorders, and greater than 80% have seizures, including infantile spasms with hypsarrhythmia.1

A definitive diagnosis of TSC can also be established in individuals with a pathogenic variant in the *TSC1* or *TSC2* genes.2 Overall, approximately 80-85% of individuals who meet clinical criteria for definite TSC have a detectable variant in the *TSC1* or *TSC2* genes.1,3 Genetic testing can be particularly helpful for individuals who meet clinical criteria for possible or probable TSC, as the finding of a pathogenic variant in the *TSC1* or *TSC2* gene establishes a definite diagnosis of TSC in an individual whose prognosis and management are otherwise uncertain.

**Patient Clinical Utility and Medical Management Implications**

Genetic testing for TSC can provide information about prognosis and assist with decisions about treatment and management.1 Pathogenic variants in *TSC1* and *TSC2* cause overlapping clinical phenotypes, but *TSC2* variants are typically associated with a more severe clinical presentation.1 Individuals with *TSC2* variants have a higher likelihood of developing renal malignancy, intellectual disability, infantile spasms, and autism spectrum disorders than individuals with *TSC1* variants. Additionally, individuals with a contiguous gene deletion syndrome including the *TSC2* gene and all or part of the neighboring *PKD1* gene may also exhibit features of polycystic kidney disease (PKD), which results in multiple renal cysts often leading to end-stage renal disease and also increases the risk for Berry aneurysms and for cysts in other organs.1

Identification of a pathogenic variant in the *TSC1* or *TSC2* gene may also have a direct impact on preventive measures and treatment for individuals with tuberous sclerosis. Surveillance for TSC-related neoplasms and renal, cardiac, pulmonary and other medical complications is indicated at regular intervals.1 Identification of a pathogenic variant causing TSC can also impact treatment for patients with epilepsy. Nearly 75% of individuals with TSC who have infantile spasms respond to treatment with vigabatrin.4 Early control of infantile spasms can help prevent epileptic encephalopathy and improve long-term neurocognitive development; therefore, genetic testing for TSC is important for infants with infantile spasms who have a clinical suspicion of TSC.1 Additionally, the mTOR inhibitor Everolimus is FDA approved for the treatment of TSC-associated subependymal giant cell astrocytoma (SEGA) and renal angiomyolipomas, and studies suggest it may be beneficial for the treatment of other TSC-associated features.5

Specifically for this patient, the results of this test will also {ADD ADDITIONAL INFORMATION}

**Summary**

The Tuberous Sclerosis (TSC) Panel at GeneDx is a highly sensitive and cost-effective genetic test. I am requesting coverage for this medically necessary test in order to establish appropriate medical management for this patient. Without testing, treatment would be suboptimal, subjecting this patient to increased morbidity and potentially early mortality.

Thank you for your review and consideration. If you have questions, or if I can be of further assistance, please do not hesitate to call me at (XXX) XXX-XXXX.

Sincerely,

Signature

Ordering Provider’s Name

References:

1. Northrup H, Koenig MK, Au KS. Tuberous Sclerosis Complex. 1999 Jul 13 [Updated 2015 Sept 3]. In: Pagon RA, Adam MP, Bird TD, et al., editors. GeneReviews™ [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2013. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK1220/>.
2. Northrup H and Krueger DA,. Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference. Pediatric Neurology. 2013 Oct 49(4):243-54
3. Au KS et al. Genotype/phenotype correlation in 325 individuals referred for a diagnosis of tuberous sclerosis complex in the United States. Genetics in Medicine: Official Journal of the American College of Medical Genetics. 2007 Feb 9(2):88-100.
4. Camposano SE et al. Vigabatrin in the treatment of childhood epilepsy: a retrospective chart review of efficacy and safety profile. Epilepsia. 2008 49(7):1186-91.
5. Capal JK and Franz DN. Profile of everolimus in the treatment of tuberous sclerosis complex: an evidence-based review of its place in therapy. Neuropsychiatric Disease and Treatment. 2016 12:2165-72.