Epilepsy Advanced Sequencing and CNV Evaluation—Syndromic Disorders

<Date>

ATTN: <Medical Director/ Physician Name>, M.D.

<Institution/Insurance Company>

<Street Address>

<City>**,** <State>, <Zip>

RE: <Patient Name>

DOB: <MM/DD/YYYY>

Member ID: <Insurance ID Number>

Group #: <Enter Group #>

Dear Medical Director:

I am writing this letter on behalf of my patient <Patient Name> to request coverage for the Epilepsy Advanced Sequencing and CNV Evaluation - Syndromic Disorders. In general, the definition of a “syndromic disorder” is the presence of at least 1 major and 2 minor anomalies. This letter documents the medical necessity for this test in light of the patient’s medical history. The results from the test will be used to determine the genetic basis for epilepsy in this patient.

**Patient Medical History and/or Diagnosis**

I have determined that this test is medically necessary because of the following aspects of my patient’s presentation:

<Patient Name> is a <age> -year-old <gender > with the following symptoms and clinical findings:

1. <Symptom #1 with ICD code>

2. <Symptom #2 with ICD code>

3. <Symptom #3 with ICD code>

<Add additional details, such as results of EEG or neuroimaging tests>

<Add relevant family history>

In summary, my patient exhibits a constellation of nonspecific syndromic phenotypic anomalies associated with recurrent seizures of unknown etiology.

**Rationale for Testing**

Epilepsy is a phenotypically and etiologically heterogeneous condition. Once physical causes such as trauma, tumors, and infection have been ruled out in cases of sporadic epilepsy, a genetic cause or predisposition can reasonably be suspected.2

Testing for underlying genetic aberrations is complicated by the large number of genes with putative links to epilepsy, many of which have a relatively low prevalence and limited impact individually.1 Traditional Sanger sequencing-based detection of individual mutations can be time-consuming and costly. Next-generation sequencing (NGS), on the other hand, allows sequencing of numerous genes simultaneously and can be leveraged to detect copy number variants (CNV). CNVs, when detected, can then be confirmed through customer Microarrays. Thus, NGS with CNV targeted at disease-associated genes is appropriate for detecting mutations in disorders with a highly heterogeneous genetic background, such as epilepsy.1 Although syndromes associated with epilepsy account for a small proportion of the epilepsies individually, together they account for a significant proportion of epilepsy.3

The Epilepsy Advanced Sequencing and CNV Evaluation - Syndromic Disorders test uses NGS to simultaneously identify mutations in 31 genes that have been associated with syndromic disorders as described by Lemke *et al*.1: *ATP2A2, ATP6V0A2, VPS13B, KCNA1, KCNJ10, KIAA1279, LBR, LGI1, KMT2D, NIPBL, PANK2, SERPINI1, PIGV, PLA2G6, RAI1, SETBP1, SMC3, SYNGAP1, TBX1, TSC1, TSC2, VPS13A, ADGRV1, ANKRD11, GFAP, HPRT1, KANSL1, MAGI2, PIGA, PIGN,* and *ROGDI*. The syndromes represented by this panel include intractable seizures, focal cortical dysplasia, Taylor balloon cell type, tuberous sclerosis, SESAME (seizures, sensorineural deafness, ataxia, mental retardation, and electrolyte imbalance) syndrome, episodic ataxia/myokymia syndrome, Darier disease, congenital hydrocephalus, Bartter syndrome, Cohen syndrome, Goldberg-Shprintzen megacolon syndrome, Pelger-Huer anomaly, Kabuki syndrome, Cornelia de Lange syndrome, infantile neuroaxonal dystrophy, Schinzel-Giedion midface retraction syndrome, DiGeorge syndrome, choreoacanthocytosis, EAST syndrome, SESAME syndrome, and Koolen-DeVries syndrome.

This NGS test may provide several important benefits for my patient:

1. It may identify the underlying genetics and potentially reveal the true phenotypic spectrum of the of the epilepsy phenotype.
2. Results may help in counseling my patient or family members concerning recurrence risk.
3. Because the NGS assay covers multiple relevant genes using a single blood draw, it can potentially help avoid additional diagnostic procedures.
4. Results may allow genetic counseling for relatives.

In summary, I am requesting that <Patient Name> be approved for the Epilepsy Advanced Sequencing and CNV Evaluation - Syndromic Disorders (test code 6033) offered by Athena Diagnostics; CPT codes 81404 (x1), 81405 (x3), 81406 (x2), 81407 (x2), 81408 (x1), 81479 (x1). Results from this test could minimize additional testing. I hope that you will support this request to pursue NGS testing to determine the cause of epilepsy in my patient. Please feel free to contact me at <physician phone> if you have additional questions.

Sincerely,

<Physician Name>, MD

NPI #: <Physician NPI#>

Contact information:

< Address>

<City>**,** <State>, <Zip>

Contact Phone No.: <phone number>

**References**

1. Lemke JR, Riesch E, Scheurenbrand T, et al. Targeted next generation sequencing as a diagnostic tool in epileptic disorders. *Epilepsia.* 2012;53:1387-1398.

2. Garofalo S, Cornacchione M, Di CA. From genetics to genomics of epilepsy. *Neurol Res Int.* 2012;2012:876234.

3. Merwick A, O'Brien M, Delanty N. Complex single gene disorders and epilepsy. *Epilepsia.* 2012;53 Suppl 4:81-91.