Epilepsy Advanced Sequencing and CNV Evaluation—Neuronal Ceroid Lipofuscinosis

<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 following test: Epilepsy Advanced Sequencing and CNV Evaluation—Neuronal Ceroid Lipofuscinosis. This letter documents the medical necessity for the test in light of my patient’s medical <and family> history. Results from the test will be used to help confirm the diagnosis and identify the specific type of neuronal ceroid lipofuscinosis (NCL).

**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 a suspected diagnosis of <type of NCL suspected> due to 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 biochemical or genetic tests>

<Add relevant family history>

Taken together, the patient’s clinical <and family> history is nonspecific but consistent with <type of NCL suspected>.

**Rationale for Testing**

The NCLs are a group of clinically and genetically heterogeneous progressive neurodegenerative disorders that often present in children as epilepsy. As lysosomal storage diseases, NCLs are characterized by abnormal accumulation of autofluorescent lipopigments in neurons and other cell types. Most NCLs are inherited in an autosomal recessive pattern. Specific manifestations vary among NCL types, but common clinical features include vision loss, seizures, dementia, motor decline, and premature death.

Historically, NCL classification has been based on clinical features and age of onset: i.e., congenital, infantile, late-infantile, variant late infantile, juvenile, and adult (Kufs disease). However, the precise age of onset and clinical features show substantial overlap among the NCLs, and current nomenclature emphasizes the genetic basis of disease.2 Genetic testing has thus assumed a key role in determining NCL type.2-5

Genetic testing is complicated by the large number of mutations linked to NCLs. To date, more than 400 mutations in more than 10 genes have been associated with NCLs.6 Traditional Sanger sequencing-based detection of individual mutations can be time-consuming and costly. Next-generation sequencing (NGS) 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.1

The Epilepsy Advanced Sequencing and CNV Evaluation—Neuronal Ceroid Lipofuscinosis test uses NGS to identify the genetic cause of NCL associated with seizures and is appropriate for patients exhibiting clinical features consistent with NCL. Specifically, it identifies mutations in 13 genes1 that have been associated with one of the various types of NCL: *CLN3, CLN5, CLN6, CLN8, CTSD, DNAJC5, KCTD7, MFSD8, PPT1, TPP1, ATP13A2, CTSF, and GRN.*

This test may provide several important benefits:

1. Results may help confirm diagnosis and identify the specific NCL.
2. Because the NGS assay covers multiple relevant genes using a single blood draw, it can potentially help avoid additional diagnostic procedures.
3. Results may allow genetic counseling for relatives of affected individuals.

In summary, I am requesting that <Patient Name> be approved for the Epilepsy Advanced Sequencing and CNV Evaluation—Neuronal Ceroid Lipofuscinosis (test code 6022 offered by Athena Diagnostics; CPT codes 81406 (x1), 81479 (x1)). Results from this test could minimize additional testing and inform treatment selection. Please support my decision to pursue NGS testing for 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. Williams RE, Mole SE. New nomenclature and classification scheme for the neuronal ceroid lipofuscinoses. *Neurology.* 2012;79:183-191.

3. Schulz A, Kohlschutter A, Mink J, et al. NCL diseases - clinical perspectives. *Biochim Biophys Acta.* 2013;1832:1801-1806.

4. Adams HR, Rose K, Augustine EF, et al. Experience, knowledge, and opinions about childhood genetic testing in Batten disease. *Mol Genet Metab.* 2014;111:197-202.

5. Kousi M, Lehesjoki AE, Mole SE. Update of the mutation spectrum and clinical correlations of over 360 mutations in eight genes that underlie the neuronal ceroid lipofuscinoses. *Hum Mutat.* 2012;33:42-63.

6. NCL Mutation and Patient Database. October 14, 2013. <http://www.ucl.ac.uk/ncl/mutation.shtml>. Accessed March 14, 2014.