**Letter of Medical Necessity for Childhood Epilepsy Panel**

**Patient Information**

**Date:**

**Patient Name:**

**Patient DOB:**

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

**Policy Number:**

**Group Number:**

**ICD10 Codes:**

**Test Information**

**Test Name:** Childhood Epilepsy Panel

**CPT Codes:** 81185x1, 81404x2, 81405x2, 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 Childhood Epilepsy 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**

Epilepsy can be caused by genetic disorders, metabolic diseases, trauma, infection, and structural brain abnormalities. A genetic cause is identified more commonly in individuals with early-onset seizures, seizures that are intractable to treatment, and/or epileptic encephalopathy. Specifically, genes have been identified that are known to cause infantile spasms/West syndrome, Ohtahara syndrome, benign familial neonatal, infantile, and neonatal-infantile seizures (BFNS, BFIS, and BFNIS), generalized epilepsy with febrile seizures plus (GEFS+), progressive myoclonic epilepsies such as neuronal ceroid lipofuscinosis and Lafora disease, and others.1-4

Genetic testing is supported by evidence based medical literature to assist in confirming a diagnosis of a specific electroclinical syndrome and can elucidate the specific genetic cause for the disorder, which has important implications for medical management. Additionally, genetic testing can help individuals avoid other expensive, invasive, and potentially risky diagnostic testing, such as lumbar puncture, muscle biopsy, video EEG, and multiple imaging studies.1,5 Due to the heterogeneous nature of epilepsy and the significant overlap in clinical symptoms among individuals with different types of epilepsy, multi-gene panels result in a higher diagnostic yield than traditional diagnostic methods and single gene testing.1,6

**Patient Clinical Utility and Medical Management Implications**

Knowing the specific genetic cause of epilepsy can provide essential information about prognosis and can assist with decisions about treatment and management. For example, individuals with variants in the *SCN1A* gene respond optimally to antiepileptic drugs (AEDs) that bind to the GABA receptor such as clobazam or stiripentol, whereas other common AEDs such as carbamazepine, lamotrigine, vigabatrin, and phenytoin may actually induce or increase the frequency of seizures and movement disorders.7 Genetic testing was reported to enable an earlier definitive diagnosis and optimized treatment for Dravet syndrome or another *SCN1A*-related disorder in nearly half of individuals with infantile-onset seizures, compared to diagnosis using EEG findings and clinical phenotype alone.8 Moreover, identification of a pathogenic *SCN1A* variant altered the treatment approach in 69% of cases.8 Molecular genetic testing is also critical for determining appropriate treatment for individuals with Alpers syndrome and other *POLG*-related disorders, who should avoid valproate and sodium divalproate due to the risk that these medications may induce or accelerate liver disease.9 Other gene-specific therapies include use of the ketogenic diet for individuals with glucose transporter type 1 deficiency syndrome (GLUT1-DS) due to *SLC2A1* pathogenic variants, quinidine for individuals with *KCNT1* gain-of-function pathogenic variants, and sodium channel blockers for individuals with *SCN8A* gain-of-function pathogenic variants.10-12

Genetic testing may also lead to an unexpected diagnosis of a metabolic disease or other genetic disorder, which require very specific and potentially urgent life-saving treatment. For example, individuals with pathogenic variants in the *ALDH7A1* gene typically do not respond to treatment with AEDs, but seizures respond to supplemental pyridoxine.13 Similarly, treatment with pyridoxyl-5’-phosphate is effective for individuals with pathogenic variants in the *PNPO* gene, treatment with supplemental folinic acid is effective for individuals with cerebral folate deficiency due to pathogenic variants in the *FOLR1* gene, treatment with biotin and thiamine supplementation is effective for individuals with thiamine metabolism dysfunction disorders due to variants in *SLC19A3*, and treatment with oral creatine can improve seizures in individuals with creatine deficiency syndromes due to pathogenic variants in the *GAMT* and *GATM* genes.13-16

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

**Summary**

The Childhood Epilepsy 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. Pong et al., (2011) Developments in molecular genetic diagnostics: an update for the pediatric epilepsy specialist. *Pediatr Neurol* 44:317-327.
2. Nicita et al., (2011) The genetics of monogenic idiopathic epilepsies and epileptic encephalopathies. *Seizure: Eur J Epilepsy* doi:10.1016/j.seizure.2011.08.007
3. Ottman et al., (2010) Genetic testing in the epilepsies—report of the ILAE Genetics Commission. *Epilepsia* 51:655-670.
4. Pal et al., (2010) Genetic evaluation and counseling for epilepsy. *Nat Rev Neurol* 6:445-453.
5. Ream et al. (2014) Clinical utility of genetic testing in pediatric drug-resistant epilepsy: a pilot study. *Epilepsy & Behavior: E&B* 37:241-8
6. Miller IO, Sotero de Menezes MA. SCN1A-Related Seizure Disorders. 2007 Nov 29 [Updated 2014 May 15]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1318/>
7. Brunklaus et al. (2013) The clinical utility of an SCN1A genetic diagnosis in infantile-onset epilepsy. *Dev Med Child Neurol* 55 (2):154-61
8. Cohen BH, Chinnery PF, Copeland WC. POLG-Related Disorders. 2010 Mar 16 [Updated 2014 Dec 18]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK26471/>
9. Gospe SM Jr. Pyridoxine-Dependent Epilepsy. 2001 Dec 7 [Updated 2017 Apr 13]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1486/>
10. Wang D, Pascual JM, De Vivo D. Glucose Transporter Type 1 Deficiency Syndrome. 2002 Jul 30 [Updated 2015 Jan 22]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1430/>
11. Hammer MF, Wagnon JL, Mefford HC, et al. SCN8A-Related Epilepsy with Encephalopathy. 2016 Aug 25. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK379665/>
12. Milligan et al. (2014) KCNT1 gain of function in 2 epilepsy phenotypes is reversed by quinidine. *Annals Of Neurology* 75 (4):581-90 (PMID: 24591078)
13. Gospe et al., (2010) Neonatal vitamin-responsive epileptic encephalopathies. *Chang Gung Med* 33:1-12.
14. Grapp et al., (2012) Molecular characterization of folate receptor 1 mutations delineates cerebral folate transport deficiency. *Brain* 135:2022-2031.
15. Braissant et al., (2011) Creatine deficiency syndromes and the importance of creatine synthesis in the brain. *Amino Acids* 40:1315-1324.
16. Ortigoza-Escobar et al. (2017) Thiamine deficiency in childhood with attention to genetic causes: Survival and outcome predictors. Ann. Neurol. 82 (3):317-330