**[LMN Template for Epilepsy Panel]**

Patient: \*\*\*

Insurance Company: \*\*\*

Subscriber Name: \*\*\*

Policy #:\*\*\*

Reference Number: \*\*\*

Dear Claims Specialist,

I am writing this letter of medical necessity on behalf of my patient [Patient Name] to request coverage for genetic testing for epilepsy offered through [Lab Name], a high complexity CLIA certified laboratory located in [Lab Location]. The purpose of this test is to identify a pathogenic mutation(s) in the nuclear genome, and the methodology used by this laboratory is able to find these mutations with a very high degree of sensitivity. Results of this test will allow me to better care for my patient as well as allow me to offer correct genetic counseling information to my patient and their family. ***Full sequence analysis and deletion/duplication testing of [# genes] nuclear genes associated with various types and causes or epilepsy*** through [Lab Name] is performed by next generation sequencing (aka massive parallel sequencing) , with a detection rate of 99%.

**Information on Patient’s Condition:**

[Patient Name] is a [age][sex] with [symptoms, family history information]. [Patient Name]’s clinical symptoms and results of the routine diagnostic tests suggest a diagnosis of a genetic epilepsy disorder. However, the only way to confirm a specific diagnosis is to perform genetic testing on this patient. Results from this genetic test may have a direct impact on this patient’s treatment and management.

**This [patient/family] has had pre-test counseling regarding the potential outcomes of this test, and a certified genetic counselor will be involved in discussion of any abnormal results.** [Remove if inapplicable]

**Information on Epilepsy Disorders and Genetic Testing:**

Epilepsy is defined by the occurrence of at least two unprovoked seizures occurring more than 24 hours apart. It is a common neurological disorder that affects at least 0.8% of the population. Epilepsy may be an isolated neurological symptom, or it may occur in association with other neurological symptoms or medical problems. Epilepsy can be caused by genetic disorders, metabolic diseases, trauma, infection, and structural brain abnormalities, although the cause is not known in many cases. A genetic etiology underlies epilepsy in approximately 40% of individuals. Genes have been identified that cause both generalized seizures and focal seizures, as well as unclassified epilepsy types such as infantile spasms. The inheritance pattern can be autosomal dominant, autosomal recessive, or X-linked. Mutations in a single gene may be associated with different types of seizures (clinical heterogeneity), and conversely, mutations in different genes can cause the same epilepsy phenotype (genetic heterogeneity). Knowledge of the genetic etiology of epilepsy may guide selection of the most appropriate treatment options in some cases. A number of antiepileptic medications are used in the treatment of epilepsy.

**Clinical Utility of Epilepsy Genetic Testing:**

* **The specific type and etiology of seizures may influence the selection of antiepileptic medication for each patient.** For example, certain medications may be more effective for infantile spasms and are therefore first choices for patients with spasms. Further examples:
  + Vigabatrin is the treatment therapy for infantile spasms in patients with mutations in *TSC1, TSC2, CDKL5, ARX, STXBP1,* or *MEF2C*
  + Oral creatine is prescribed for epilepsy patients with mutations in *SLC6A8, GAMT, GATM*
  + Valproate, clobazam, stiripentol and levetiracetam are the treatment therapies for epilepsy patients with SCN1A mutations
* **Some medications may be contraindicated for patients with a specific electroclinical or genetic diagnosis.** Further examples:
  + Valproic acid should be avoided for epilepsy patients with *POLG* mutations
  + Phenytoin, carbamazepine, and lamotrigine should be avoided for epilepsy patients with *SCN1A* mutations
  + Channel blockers and GABAergic drugs should be avoided for epilepsy patients with *CSTB* mutations
  + Results will directly impact medical management of the individual being tested- **As noted above understanding the underlying genetic etiology of seizures can provide guidance for medication choices, surgical intervention and prognostic factors.**
  + Clinical presentation is consistent with a genetic etiology – **[Patient Name]'s history of ongoing seizures despite medication interventions along with a history of developmental delay increases the likelihood that there is an underlying genetic cause. Genetic factors are thought to have a role in ~70% of all epilepsies, and a variety of inheritance patterns have been described for seizure-associated gene defects**
  + Phenotype warrants testing of multiple genes and a relevant differential diagnosis list is documented. **The phenotypes of epilepsy syndromes are known to overlap significantly, making single gene testing obsolete in a majority of cases. Additionally, NGS has greatly expanded the phenotypes of many genetic epilepsy syndromes introducing additional burdens in the selection of individual genes for testing.**
  + A 2023 National Society of Genetic Counselors (NSGC) workgroup established robust practice guidelines for genetic testing in epilepsy, recommending multi-gene panel testing or exome/genome sequencing as first tier testing for all individuals with unexplained epilepsy, based on yield of testing, ‘as well as the clinical utility of genetic testing to guide treatment/medical management, revise, or establish prognosis and/or provide reproductive risk counseling’ (*Smith).*
  + A systematic review of diagnostic yield of genetic testing among patients with epilepsy performed in 2022 determined that multi-gene panels have a 19% yield in this population. More comprehensive testing such as WGS/WES had even higher yield but may not be accessible to some patients/families.
  + Test results may preclude the need for multiple and/or invasive procedures or tests, follow-up, or screening that would be recommended in the absence of panel testing. **NGS for epilepsy has proven to be cost and time efficient for providers and families compared to testing of multiple single genes in a tiered fashion. A genetic diagnosis allows for the elimination of the diagnostic odyssey and additional costly genetic tests. With a definitive genetic diagnosis we are better able to tailor screening requirements for patients.**
  + **A specific genetic diagnosis of epilepsy will allow for family members to be tested for the specific mutation for a drastically lower cost**

**We request your review of the following testing for preauthorization:**

Test Requested:  \*\*\*

Test Code: \*\*\*

Lab Name: \*\*\*

Lab Phone: \*\*\*

CPT codes: \*\*\*

**ICD10 Codes:** \*\*\*

The blood draw would be completed at [Lab/Hospital] for the family’s convenience. Billing would be coordinated by [Billing Institution/Provider]. Ordering provider would be [Ordering Provider].

Thank you for your review and consideration. I hope you will support this request for genetic testing coverage for [Patient Name]. If you have questions, or if I can be of further assistance, please do not hesitate to contact me at [Clinician Contact Info].

Sincerely,

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