**[LMN Template for Whole Exome Sequencing]**

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 Whole Exome Sequencing (WES) 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.

**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 genetic etiology. However, at the present time we cannot recognize a specific clinical diagnosis. Due to the heterogeneous nature of rare genetic diseases, the most efficient and cost effective way to confirm a genetic diagnosis in this patient is to perform whole exome sequencing genetic testing. **Results from this genetic test will have a direct impact on this patient’s treatment and management and will provide prognostic information that will assist in clinical management.**

**Specific Phenotype** **with ICD-10.0 Codes:**

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**Family History: [delete if no family history]**

**\*\*\***

As mentioned above, knowledge of this patient's genetic information is important for me to more accurately assess prognosis and will guide my recommendations for care. I am requesting WES because this patient has exhausted currently available diagnostic tests including:

[LIST OF PREVIOUS TESTING DONE]

The next step is to sequence candidate genes in the patient’s DNA to look for a causative mutation. Rather than sequencing the many potential individual genes, WES is the fastest and most cost effective way to look for a mutation amongst the large number of potential genes that could be causing this condition. Recent studies have supported this strategy through the identification of genes/diseases that were not recognized that would not have been investigated though traditional single gene or multi-gene panels (Worthey, 2011). WES has been used in a clinical setting to find the molecular causes of a variety of diseases including intractable bowel disease (Worthey, 2011), intellectual disability (Vissers, 2010), and brain malformations (Pagnamenta, 2012) among many others.

WES has been well established as an effective testing modality for determining underlying genetic etiology in patients with epilepsy. A systematic review of diagnostic yield of genetic testing among patients with epilepsy performed in 2022 determined that WGS had a 48% yield in this population (compared to 24% yield with WES, 19% for multi-gene panels, and 9% with CMA) (*Sheidley*). 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).*

Comparing this individual’s exome sequence to additional family member’s exomic data will significantly increase the utility of the test results and increase the likelihood of identifying a disease-causing gene while decreasing the chance of obtaining variants of unknown clinical significance. This method of evaluation is especially important for individuals with apparently sporadic disease (Pagnamenta, 2012), when no one else in the family is similarly affected. By analyzing parents and unaffected siblings in cases of sporadic disease, it is frequently possible to identify de novo or new mutations in the child not present in either parent or to identify recessive diseases with one mutation inherited from each parent. [Remove if inapplicable]

Additionally, if a mutation or mutations are identified in this individual, family studies can be used to identify carriers of the disease-causing mutation(s) and allow for accurate genetic counseling regarding recurrence risk, and prenatal diagnosis for future children. I am specifying [Lab Name] because this laboratory has a highly sensitive and cost-effective test, and extensive experience in identifying mutations in rare genetic syndromes. Pre-test counseling will be provided by a certified genetic counselor, and a genetic counselor (along with a physician) will also be involved in post-test results discussion if testing is abnormal. [Remove if inapplicable]

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 Information].

Sincerely,

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**References:**

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