**Charcot-Marie-Tooth Disease (CMT) Advanced Evaluation—Initial Genetic Assessment**

<Date>

ATTN: <Medical Director/ Physician Name>, MD

<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 on behalf of my patient <Patient Name> to request coverage for the Charcot-Marie-Tooth Disease (CMT) Advanced Evaluation – Initial Genetic Assessment. I have determined that this test is medically necessary because of the following aspects of my patient’s history:

<Patient Name> is a <age> -year-old <gender > with a suspected diagnosis of CMT 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 if relevant >

The patient’s family history of polyneuropathy is <negative or unknown; add additional details if relevant>.

Additionally, all other metabolic, infectious, autoimmune, and toxic etiologies have been ruled out. The lack of a specific etiology suggests that genetic testing may help diagnose the cause of the polyneuropathy.

**Rationale for Testing**

CMT is the most common inherited peripheral neuropathy, with a prevalence of 1:2,500 individuals. CMT comprises a group of chronic motor and sensory polyneuropathies that may manifest with distal muscle weakness and atrophy, mild to moderate sensory loss, depressed tendon reflexes, and high arched feet (pes cavus). The clinical diagnosis is generally based on the findings of physical examination, electromyography (EMG), nerve conduction velocity (NCV) testing, and family history. Genetic testing is useful for accurate diagnosis and classification of hereditary forms of polyneuropathy such as CMT.1 The CMT Advanced Evaluation—Initial Genetic Assessment uses next-generation sequencing (NGS) to test for the four most common genetic causes of CMT (*PMP22* duplication or deletion, and point mutations in *GJB1*, *MFN2,*and *MPZ*), which account for 90% to 95% of CMT cases.6, 7 Initial testing of these four genes should help avoid the need for painful, expensive, and sometimes contraindicated or uninformative electrodiagnostic tests such as EMG and NCV.

Traditional Sanger sequencing-based detection of individual mutations can be time-consuming and costly when testing for mutations in large numbers of genes. Next-generation sequencing, on the other hand, allows sequencing of numerous genes simultaneously. Thus, NGS targeted at disease-associated genes seems appropriate for detecting mutations in disorders that have highly heterogeneous genetic backgrounds, such as CMT.

Results from the test will be used to confirm the diagnosis of CMT in this patient and to guide medical management and treatment. Specifically, the results may:

* Inform treatment decisions; for example:
  + - Selection of appropriate treatment options.4,5
    - Avoidance of medications that are 1) contraindicated because they could exacerbate symptoms3; or 2) likely to be ineffective (eg, immunotherapy for autoimmune peripheral neuropathy, which may present with features suggestive of CMT).
* Help avoid a long series of laborious and potentially costly diagnostic procedures.
* Provide information useful for family planning.

In summary, I am requesting that <Patient Name> be approved for the CMT Advanced Evaluation—Initial Genetic Assessment test (test code 4010) offered by Athena Diagnostics. The CPT codes for this test are 81324(1), 81403(1), 81405(1), and 81406(1). I hope you will support my decision to perform CMT genetic testing for this 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. England JD, Gronseth GS, Franklin G, et al. Practice parameter: evaluation of distal symmetric polyneuropathy: role of laboratory and genetic testing (an evidence-based review). Report of the American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation. *Neurology*. 2009;72:185-192.

2. ACMG Board of Directors. Points to consider in the clinical application of genomic sequencing. *Genet Med*. 2012;14:759-761.

3. Weimer LH, Podwall D. Medication-induced exacerbation of neuropathy in Charcot Marie Tooth disease. *J Neurol Sci*. 2006;242:47-54.

4. Casasnovas C, Cano LM, Alberti A, et al. Charcot-Marie-tooth disease. *Foot Ankle Spec*. 2008;1:350-354.

5. Chan G, Bowen JR, Kumar SJ. Evaluation and treatment of hip dysplasia in Charcot-Marie-Tooth disease. *Orthop Clin North Am*. 2006;37:203-209, vii.

6. DiVincenzo C, Elzinga CD, Medeiros AC, et al. The allelic spectrum of Charcot-Marie-Tooth disease in over 17,000 individuals with neuropathy. *Mol Genet Genomic Med* 2014;(in press).

7. Murphy SM, Laura M, Fawcett K, et al. Charcot-Marie-Tooth disease: frequency of genetic subtypes and guidelines for genetic testing. *J Neurol Neurosurg Psychiatr* 2012;83:706-710.