Paraneoplastic Neurological Syndromes, Initial Assessment

<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 requesting coverage for the Paraneoplastic Neurological Syndromes, Initial Assessment test on behalf of my patient <patient name>. This assay tests for antibodies against the following antigens: amphiphysin, CV2 (crossveinless-2 protein), Hu (neuronal nuclear antibody type 1), Ma2 (positives tested on Ma1), Ri (neuronal nuclear antibody type 2), and Yo (Purkinje cell antibody type 1). 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 <specific paraneoplastic syndrome suspected> due to the following symptoms and clinical findings:

1. <Symptom/clinical finding #1 with ICD code>

2. <Symptom/clinical finding #2 with ICD code>

3. <Symptom/clinical finding #3 with ICD code>

<Add additional relevant clinical details.>

**Rationale for Testing**

Paraneoplastic neurological syndromes (PNS) are rare immune-mediated disorders that result from damage to the nervous system due to remote effects of a primary tumor or its metastases.1 The tumor most commonly associated with PNS is small-cell lung cancer; others include ovarian carcinoma and teratoma, testicular cancer, thymoma, and Hodgkin lymphoma.1,2 PNS often exhibit a rapid clinical course resulting in severe disability,2 although symptoms can fluctuate and be atypical or psychiatric in nature.3 The neurological symptoms of PNS usually precede identification of cancer3,4 and are often associated with antibodies directed against neural antigens ectopically expressed by tumors (onconeural antibodies). In some cases, identification of such antibodies may aid in the diagnosis of PNS and help in evaluating the likelihood of malignancy and type of tumor.1,4

PNS are classified as classical or non-classical, depending on their association with cancer.5 In the classical PNS, neurological symptoms are often associated with the underlying cancer.2,5 These syndromes include encephalomyelitis, limbic encephalitis, subacute cerebellar degeneration, opsoclonus-myoclonus, subacute sensory neuropathy, and Lambert-Eaton myasthenic syndrome (LEMS).5  Non-classical PNS, such as brainstem encephalitis and Stiff person syndrome, can result from paraneoplastic mechanisms but are less frequently associated with a detectable tumor.5

Diagnostic criteria for PNS require detection of a “well-characterized” onconeural antibody in certain situations.5 Thus, the Paraneoplastic Neurological Syndromes, Initial Assessment tests for the 6 onconeural antibodies that are generally considered to be well characterized: anti-Hu, anti-Yo, anti-CV2, anti-Ri, anti-Ma2 (MaTa), and anti-amphiphysin. Classification of an onconeural antibody as well characterized is based on several considerations: 1) recognizable patterns on routine immunohistochemistry; 2) documented association with tumors (based on the number of published cases); 3) well-described association with neurological syndromes; 4) unambiguous identification of the antibodies among different studies; and 5) the frequency of the antibodies in patients with no detectable tumor.5

In patients without confirmed cancer who present with either a classical or non-classical syndrome, detection of a well-characterized onconeural antibody is required to diagnose definite PNS.5 For patients with a classical syndrome and a known tumor, detection of an onconeural antibody is not required for diagnosis.5 Field experts recommend close tumor surveillance in patients with classical PNS, with or without paraneoplastic antibodies, and in patients with non-classical PNS who have paraneoplastic antibodies.2 A common clinical practice includes periodic cancer screening for at least 5 years.2  Confirming the autoimmune etiology of neurological symptoms may also assist in effective therapeutic planning.6 Based on the clinical presentation, cancer screening, and antibody test results, treatment of tumor and/or immunotherapy may lead to improvement or stabilization of neurological symptoms.3,4

In summary, I am requesting that <patient name> be approved for the Paraneoplastic Neurological Syndromes, Initial Assessment (test code 4500 offered by Athena Diagnostics; CPT codes 84181 [x1], 84182 [x5]). Testing for the 6 well-characterized onconeural antibodies with this assay may provide the following important benefits for my patient:

1. Confirm the diagnosis of definite PNS
2. Direct investigation of the underlying malignancy
3. Inform treatment selection, which may lead to improvement or stabilization of neurological symptoms

Please support my decision to pursue autoimmune testing for my patient. 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. Titulaer MJ, Soffietti R, Dalmau J, et al. Screening for tumours in paraneoplastic syndromes: report of an EFNS task force. *Eur J Neurol.* 2011;18:19-e3.

2. Rosenfeld MR, Dalmau JO. Paraneoplastic disorders of the CNS and autoimmune synaptic encephalitis. *Continuum (Minneap Minn ).* 2012;18:366-383.

3. de Beukelaar JW, Sillevis Smitt PA. Managing paraneoplastic neurological disorders. *Oncologist.* 2006;11:292-305.

4. Vedeler CA, Antoine JC, Giometto B, et al. Management of paraneoplastic neurological syndromes: report of an EFNS Task Force. *Eur J Neurol.* 2006;13:682-690.

5. Graus F, Delattre JY, Antoine JC, et al. Recommended diagnostic criteria for paraneoplastic neurological syndromes. *J Neurol Neurosurg Psychiatry.* 2004;75:1135-1140.

6. Gromadzka G, Karlinska AG, Lysiak Z, et al. Positivity of serum "classical" onconeural antibodies in a series of 2063 consecutive patients with suspicion of paraneoplastic neurological syndrome. *J Neuroimmunol.* 2013;259:75-80.