**Letter of Medical Necessity for the Hemiplegic Migraine Panel**

**Patient Information**

**Date:**

**Patient Name:**

**Patient DOB:**

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

**Policy Number:**

**Group Number:**

**ICD10 Codes:**

**Test Information**

**Test Name:** Hemiplegic Migraine Panel

**CPT Codes:** 81406x1, 81407x1, 81479x1

**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 Hemiplegic Migraine 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**

The Hemiplegic Migraine Panel includes germline analysis of genes causing migraine with aura. Panel testing includes both sequencing and deletion/duplication analysis of multiple genes simultaneously.

Hemiplegic migraine (HM) is a rare subtype of migraine that is characterized by the presence of an aura and temporary numbness and/or muscle weakness that is typically unilateral.1 Symptoms of HM may include visual disturbances such as blind spots, flashing lights, or double vision; sensory loss, including numbness and parasthesias of the face or extremities; and speech difficulties including dysphasia and dysarthria.1,2,3,4 Approximately 40% of individuals experience prolonged aura attacks that can lead to impaired consciousness, confusion, agitation, fever, psychosis, or in severe cases even coma.1,4 The hemiplegic attacks may alternate with non-hemiplegic aura in some people. Individuals with HM may also experience cerebellar nystagmus and ataxia that is often episodic but in some cases may be progressive and chronic, and intellectual disability may occur in some individuals.1,3 Additionally, there is an association between migraine and epilepsy.5 Individuals with HM have an increased risk for seizures, and overall 8%–24% of individuals with epilepsy also experience migraines.2  HM attacks may be triggered by stress, sleep deprivation, light, food, sound, or head trauma.1,3 The prevalence of HM is estimated to be approximately 0.01% in European populations.1

An estimated 50% of individuals with HM have at least one other close relative with the disorder and are diagnosed with familial hemiplegic migraine (FHM).3 Individuals with no known family history are labeled with sporadic hemiplegic migraine (SHM), although absence of a family history does not exclude the possibility of a genetic form of HM.3 FHM is inherited in an autosomal dominant manner. The penetrance has been estimated to be 70–90%.1 The type, severity, and age-of-onset of symptoms can vary among individuals in the same family.1

Pathogenic variants causing HM have been identified in three ion channel genes: *CACNA1A*, *SCN1A*, and *ATP1A2*. Pathogenic variants in these genes can also cause other neurological disorders, including ataxia and epilepsy. Individuals with a pathogenic variant in one of these genes may have isolated HM, HM in conjunction with other neurological features as part of a more complex disorder, or they may exhibit only the other neurological features and not experience HM.3 Pathogenic variants in these three ion channel genes result in abnormal neuronal excitability that is hypothesized to cause HM due to cortical spreading depression CSD), which is the strong depolarization of a large group of nerve cells or neuroglia that spreads to adjacent areas and inhibits neural activity.2 Less commonly, pathogenic variants in the *PRRT2* gene have been identified in individuals with FHM.3, The *PRRT2* gene plays a role in presynaptic function and causes benign familial infantile seizures (BFIS) and/or paroxysmal kinesigenic dyskinesia (PKD). The risk for HM is increased in individuals with *PRRT2-*related BFIS and PKD, although isolated HM is uncommon.3,6,7 Individuals with a pathogenic variant in one of the genes included on this panel typically have onset of attacks at an earlier age, have more frequent attacks, and are more likely to have associated neurological features such as progressive ataxia or intellectual disability.3,4,8

**Patient Clinical Utility and Medical Management Implications**

Knowing the specific genetic cause of hemiplegic migraine can provide essential information about prognosis and can assist with decisions about treatment and management. For example, individuals with variants in the *SCN1A* gene who also have seizures 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.10 Identification of a pathogenic *SCN1A* variant has been found to alter the treatment approach in 69% of individuals.11

Confirmation of a diagnosis of HM by genetic testing can also help individuals make lifestyle choices to reduce the likelihood of future attacks, such as avoiding triggers like stress, sleep deprivation, light, food, sound, or head trauma.1,3 Individuals with HM should also avoid cerebral angiography as it may precipitate an attack.4  Vasoconstricing agents should not be used as they can increase the risk of stroke.4

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

**Summary**

The Hemiplegic Migraine 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. Albury et al. (2017) Ion channelopathies and migraine pathogenesis. Molecular Genetics And Genomics. Mol. Genet. Genomics 292 (4):729-739 (PMID: 28389699)
2. Huang et al. (2017) The genetic relationship between epilepsy and hemiplegic migraine.Neuropsychiatr Dis Treat 13 :1175-1179 (PMID: 28479855)
3. Pelzer et al. (2018) Clinical spectrum of hemiplegic migraine and chances of finding a pathogenic mutation. Neurology (PMID: 29343472)
4. Jen JC. Familial Hemiplegic Migraine. 2001 Jul 17 [Updated 2015 May 14]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1388/
5. Noebels et al. (2012) Migraine and Epilepsy—Shared Mechanisms within the Family of Episodic Disorders. (PMID: 22787613)
6. Ebrahimi-Fakhari et al. (2015) The evolving spectrum of PRRT2-associated paroxysmal diseases. Brain 138 (Pt 12):3476-95 (PMID: 26598493)
7. Pelzer et al. (2014) PRRT2 and hemiplegic migraine: a complex association. Neurology 83 (3):288-90 (PMID: 24928127)
8. Riant et al. (2010) De novo mutations in ATP1A2 and CACNA1A are frequent in early-onset sporadic hemiplegic migraine. Neurology 75 (11):967-72 (PMID: 20837964)