**Letter of Medical Necessity for the Ehlers-Danlos Syndrome Panel**

**Patient Information**

**Date:**

**Patient Name:**

**Patient DOB:**

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

**Policy Number:**

**Group Number:**

**ICD10 Codes:**

**Test Information**

**Test Name:** Ehlers-Danlos Syndrome Panel

**CPT Codes:** 81479x2

**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 Ehlers-Danlos Syndrome 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 Ehlers-Danlos Syndrome (EDS) Panel includes germline analysis of genes causing classical and vascular EDS. Panel testing includes both sequencing and deletion/duplication analysis of multiple genes simultaneously.

The Ehlers-Danlos syndromes (EDS) are a heterogeneous group of heritable disorders of connective tissue characterized by overlapping symptoms that can involve the skeletal, cardiovascular, skin, and ocular systems. There are at least 13 distinct subtypes.1 This panel includes the *COL3A1, COL5A1*, and *COL5A2* genes, which are the most common genetic causes of classical EDS and vascular EDS. Classical EDS (cEDS) is typically characterized by joint hypermobility, skin hyperextensibility, and widened atrophic scarring.2 Vascular EDS (vEDS) is typically characterized by arterial aneurysm, dissection, and/or rupture; spontaneous bowel perforation; and/or uterine rupture in pregnancy.3 Phenotypic variability occurs in both conditions and additional connective tissue symptoms may also be present, such as easy bruising and thin/fragile skin. A family history of cEDS or vEDS is informative when present but does not exclude the diagnosis, as approximately 50% of cases are due to de novo occurrence of a pathogenic variant.4,5

In addition to the clinical overlap between the different types and subtypes of EDS, many of the common presenting symptoms of can also be seen in other genetic syndromes. For example, joint hypermobility can be seen not only with EDS, but also with skeletal dysplasias, hereditary myopathies, and other syndromes associated with multiple congenital anomalies or intellectual disability.6,7

Although clinical diagnostic criteria exist for EDS, a definitive diagnosis often relies on molecular testing given the significant clinical overlap between these disorders, including among the subtypes of EDS.1,6,7 The International EDS Consortium recommends testing for a panel of genes as the most cost effective approach, given the clinical overlap between different subtypes of EDS.1

**Patient Clinical Utility and Medical Management Implications**

Genetic testing can provide important information that is essential for appropriate treatment and management. Undiagnosed or untreated vascular EDS can lead to life-threatening acute cardiovascular and gastrointestinal complications, including thoracic aortic aneurysm and dissection (TAAD) and bowel rupture.3 Diagnosis of EDS allows for potential life-saving surveillance and surgical/pharmacological interventions.

Medical management for vascular complications of EDS is based on clinical guidelines and peer reviewed literature, such as the 2010 American Heart Association Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease, which states that individuals with a pathogenic variant in a gene associated with aortic aneurysm and/or dissection should undergo aortic imaging.25 In addition, accumulating data indicates that the genetic cause of TAAD, and in some cases the specific variant identified, can indicate the risk of a patient developing a thoracic aortic aneurysm and dissection and provide important information for decisions about the appropriate timing of surgical repair, and the risk for additional vascular disease and guidance for management.20 Furthermore, surgical decisions and approach, surveillance, and lifestyle modifications can be guided with results from this test for this patient.22-24

In addition to the vascular complications of EDS, patients often have medical issues affecting other organ systems such as the eyes and skeleton. Confirmation of the diagnosis is important to enable management decisions and avoidance of medications that can lead to complications.25 For example, individuals with classic EDS may benefit from the use of DDAVP to reduce bleeding time.5 Additionally, individuals with vascular EDS should avoid collision sports, heavy lifting, and elective surgery due to the increased risk for vascular rupture or other complications.4

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

**Summary**

The Ehlers-Danlos Syndrome 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. Malfait F, Francomano C, Byers P, et al. 2017. The 2017 International Classification of the Ehlers-Danlos syndromes. Am J Med Genet Part C Semin Med Genet 175 (1):8-26. (PMID 28306229)
2. Bowen JM, Sobey GJ, Burrows NP, et al., Ehlers-Danlos Syndrome, Classical Type. Am J Med Genet Part C Semin Med Genet 175C (1):27-39. (PMID 28192633)
3. Byers PH, Belmont J, Black J, et al. 2017. Diagnosis, natural history, and management in vascular Ehlers–Danlos syndrome. Am J Med Genet Part C Semin Med Genet 175C:40–47. (PMID 28306228)
4. Pepin MG, Murray ML, Byers PH. Vascular Ehlers-Danlos Syndrome. 1999 Sep 2 [Updated 2015 Nov 19]. 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/NBK1494/>
5. Malfait F, Wenstrup R, De Paepe A. Classic Ehlers-Danlos Syndrome. 2007 May 29 [Updated 2018 Jul 26]. 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/NBK1244/>
6. Castori M et al. A framework for the classification of joint hypermobility and related conditions. *Am J Med Genet* *C Semin Med Genet.* 2017 Mar 175(1):148-157. (PMID: 28145606)
7. Alazami AM et al. Expanding the clinical and genetic heterogeneity of hereditary disorders of connective tissue. *Hum Genet.* 2016 May 135(5):525-40. (PMID: 27023906)