**Letter of Medical Necessity for *FBN1* Sequencing and Deletion/Duplication Analysis**

**Patient Information**

**Date:**

**Patient Name:**

**Patient DOB:**

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

**Policy Number:**

**Group Number:**

**ICD10 Codes:**

**Test Information**

**Test Name:** *FBN1* Sequencing and Deletion/Duplication Analysis

**CPT Codes:** 81408x1, 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 *FBN1* Sequencing and Deletion/Duplication Analysis 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**

*FBN1* sequencing and deletion/duplication analysis includes germline analysis of a gene that causes conditions that can result in life-threatening aortic rupture and other complications such as loss of vision or severe and potentially lethal pulmonary or gastrointestinal effects.

Pathogenic variants in the *FBN1* gene most commonly cause Marfan syndrome, a connective tissue disorder that affects the skeletal, ocular, and cardiovascular systems. Skeletal features can include chest malformations (pectus carinatum/excavatum), tall stature, increased joint mobility, and scoliosis. Eye findings most commonly include lens dislocation (ectopia lentis) and myopia. The cardiovascular features are typically mitral valve prolapse and/or aortic root dilatation, which can progress to aortic dissection, and which can result in significant morbidity and mortality. 1,2

Pathogenic variants in the *FBN1* gene have also been observed in families with some clinical features suggestive of Marfan syndrome but who do not meet full clinical (Ghent) criteria. For example, pathogenic *FBN1* variants have been identified in families with MASS syndrome, which results in myopia, mitral valve prolapse, borderline/non-progressive aortic root dilation, skeletal and skin findings.3,4,5 MASS is typically associated with milder cardiovascular findings, as thoracic aortic aneurysms are usually asymptomatic and enlarge over time.3 Pathogenic *FBN1* variants have also been identified in families with isolated ectopia lentis, predominant aortic aneurysm with subclinical features in other organ systems, and mitral valve prolapse syndrome.3

Because Marfan syndrome is a progressive disorder and many of the clinical features may not develop until adulthood, it is difficult to distinguish MASS and other *FBN1*-related disorders from "emerging" Marfan syndrome when assessing an isolated individual, especially during childhood.2,3  Genetic testing is important for individuals who are suspected of having Marfan syndrome or another FBN1-related disorder but do not meet Ghent criteria since these individuals would benefit from imaging to monitor for aortic root dilatation and other severe, potentially life-threatening complications.4,5 Additionally, genetic testing allows for targeted testing of at-risk family members to identify presymptomatic family members who carry a *FBN1* pathogenic variant and are at risk for developing features of Marfan syndrome.

**Patient Clinical Utility and Medical Management Implications**

Medical management options for early detection or risk reduction are available based on clinical guidelines and peer reviewed literature. The American Academy of Pediatrics (AAP) and American College of Medical Genetics and Genomics (ACMG) have published guidelines for the evaluation and management of individuals with features of Marfan syndrome.4,5

Patient management and treatment is focused on slowing the progression of aortic root dilation, the most common cause of morbidity and early mortality. Imaging with appropriate surgical and pharmacological interventions can be utilized in patients with a clinical diagnosis of Marfan syndrome or the presence of a pathogenic *FBN1* variant to reduce the risk of disease progression and death. The 2010 American Heart Association Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Diseasestate that individuals with a pathogenic variant in a gene associated with aortic aneurysm and/or dissection should undergo aortic imaging.6 In addition to aortic root dilatation, individuals with Marfan syndrome often have medical issues affecting other organ systems such as the eyes and skeleton, and diagnosis is important to enable management decisions.

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

**Summary**

*FBN1* Sequencing and Deletion/Duplication Analysis 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. De Paepe et al. (1996) Revised diagnostic criteria for the Marfan syndrome. American Journal Of Medical Genetics 62 (4): 417-26 (PMID: 8723076).
2. Loeys et al. (2010) The revised Ghent nosology for the Marfan syndrome. Journal Of Medical Genetics 47 (7): 476-85 (PMID: 20591885).
3. Dietz HC. Marfan Syndrome. 2001 Apr 18 [Updated 2017 Feb 2]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1335/>
4. Tinkle et al. (2013) Health supervision for children with Marfan syndrome. Pediatrics 132 (4):e1059-72 (PMID: 24081994).
5. Pyeritz et al. (2012) Evaluation of the adolescent or adult with some features of Marfan syndrome. Genet. Med. 14 (1):171-7 (PMID: 22237449).
6. Hiratzka et al. (2010) 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease: Executive summary: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. Anesth. Analg. 111 (2):279-315 (PMID: 20664093).