**Letter of Medical Necessity for *FMR1* CGG Repeat Analysis**

**Patient Information**

**Date:**

**Patient Name:**

**Patient DOB:**

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

**Policy Number:**

**Group Number:**

**ICD10 Codes:**

**Test Information**

**Test Name:** *FMR1* CGG Repeat Analysis

**CPT Codes:** 81243x1

**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 *FMR1* CGG Repeat 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**

*FMR1* genetic testing can detect several *FMR1*-related disorders, including fragile X syndrome, fragile X-associated tremor/ataxia syndrome (FXTAS), and premature ovarian insufficiency (POI).

Fragile X syndrome type A (FXS or FRAXA) is the most common inherited cause of intellectual disability.1,2 Nearly all cases of FXS are caused by the expansion of an unstable CGG repeat in the 5’ untranslated region of the *FMR1* gene. Males with FXS exhibit mild to severe intellectual disability, often associated with autism spectrum disorders, ADHD, speech and language delay, anxiety, macrocephaly, and a distinctive facial appearance. Females with full mutations exhibit a broad spectrum of clinical presentations ranging from significant cognitive, behavioral, and physical features of FXS similar to those observed in males, while others have normal intelligence with only subtle learning disabilities.1

An estimated 1 in 259 females and 1 in 755 males in the general population have an *FMR1* premutation.1 Premutation carriers have an increased risk for neurological, psychiatric, and physical disorders. Approximately 40% of male and 8-17% of female premutation carriers over the age of 50 report experiencing symptoms of FXTAS.3 FXTAS is a neurodegenerative disorder characterized by cerebellar ataxia, intention tremor, parkinsonism, progressive cognitive decline, and psychiatric disorders.3 Additionally, approximately 21% of female premutation carriers develop POI leading to early menopause and infertility.3

This patient’s healthcare provider recommended, and ordered, this testing because the results will guide appropriate medical management for this patient. The American College of Medical Genetics (ACMG), American Academy of Pediatrics (AAP), and the American Academy of Neurology (AAN) support fragile X syndrome genetic testing as a first-tier diagnostic test for individuals with developmental delay, intellectual disability, and/or autism spectrum disorders.4,5,6

**Patient Clinical Utility and Medical Management Implications**

The test results will guide and tailor appropriate medical management and treatment for this patient, which would not be possible without this testing. The American Academy of Pediatrics has established Health Supervision Guidelines for individuals with fragile X syndrome.7 Identification of a definitive genetic diagnosis enables healthcare providers to identify associated medical risks that may require intervention or ongoing management and to select appropriate therapeutic interventions.7 For example, individuals with fragile X syndrome are at increased to develop mitral valve prolapse, so they should have regular monitoring and be referred for an echocardiogram if a murmur is noted.7,8 Confirmation of the diagnosis also prevents additional, unnecessary diagnostic testing and provides information about future prognosis and recurrence risk.1,7

Specifically for this patient, the results of *FMR1* CGG Repeat Analysis will {ADD ADDITIONAL INFORMATION}

**Summary**

The *FMR1* CGG Repeat Analysis test 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

1. McConkie-Rosell et al. (2005) Genetic counseling for fragile x syndrome: updated recommendations of the national society of genetic counselors. Journal Of Genetic Counseling 14 (4):249-70 (PMID: 16047089)
2. Pirozzi et al. (2011) The FRAXopathies: definition, overview, and update. American Journal of Medical Genetics. Part A 155A (8):1803-16 (PMID: 21739597)
3. Monaghan et al. (2013) ACMG Standards and Guidelines for fragile X testing: a revision to the disease-specific supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the American College of Medical Genetics and Genomics. Genetics In Medicine : Official Journal Of The American College Of Medical Genetics 15 (7):575-86 (PMID: 23765048)
4. Schaefer et al. (2013) Professional Practice and Guidelines Committee. Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions. Genetics In Medicine: Official Journal Of The American College Of Medical Genetics 15 (5):399-407 (PMID: 23519317)
5. Moeschler et al. (2014) Comprehensive evaluation of the child with intellectual disability or global developmental delays. Pediatrics 134 (3):e903-18 (PMID: 25157020)
6. Michelson et al. (2011) Evidence report: Genetic and metabolic testing on children with global developmental delay: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology* 77 (17):1629-35 (PMID: 21956720)
7. Hersh et al. (2011) Health supervision for children with fragile X syndrome. Pediatrics 127 (5):994-1006 (PMID: 21518720)
8. Saul RA, Tarleton JC. FMR1-Related Disorders. 1998 Jun 16 [Updated 2012 Apr 26]. 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/NBK1384/