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The Department of Vermont Health Access Clinical Criteria

Subject: Fragile X Mental Retardation 1 (FMR1) Genetic Testing
Last Review: May 5, 2023
Past Revisions: September 3, 2021, & June 1, 2018

***Please note: Most current content changes will be highlighted in yellow.**

Description of Service or Procedure

The Fragile X Mental Retardation gene (FMR1) is found on the X chromosome and is responsible for making a protein called FMRP, which is present in many tissues of the body, including the brain, ovaries, and testes. In the brain, the FMR1 gene is responsible for producing a protein essential for development of connections of the nerve cells. Alterations, or mutations, in the genetic material of the FMR1 gene can result in disorders such as Fragile X syndrome, premature ovarian insufficiency, and the neurologic disease Fragile X-associated tremor/ataxia syndrome (FXTAS). FXTAS primarily affects men over the age of 50 and is associated with signs and symptoms including tremor, ataxia, and dementia.

Fragile X syndrome is the most common inherited cause of intellectual disability and the most common cause of autism linked to a single gene. Associated with physical, cognitive, and behavioral abnormalities, Fragile X syndrome has an X-linked dominant inheritance pattern. Female offspring inherit an X chromosome from each parent, whereas male offspring always inherit the X chromosome from their mother and the Y chromosome from their father. This means that the FMR1 gene is inherited by females from their mother or father and by males from their mother only. Prevalence and symptoms of Fragile X syndrome in females are often milder than in males because with two X chromosomes, one X chromosome may compensate for the other with the mutation.

In these conditions, the pattern of the building blocks of the FMR1 gene, or trinucleotides, are altered by an increased repeat of patterns of nucleotides cytosine-guanine-guanine (CGG) on the FMR1 gene. Dependent upon the degree of increased CGG repeats, the mutation is referred to as either a premutation or a full mutation, and can change over generations by inheritance. Clinical signs and symptoms of Fragile X syndrome present with full mutation of the CGG repeats on the FMR1 gene while clinical presentation of FXTAS or premature ovarian insufficiency may develop in individuals with the FMR1 CGG premutation.

- Normal 5-44 CGG repeats.
  Premutation 55-200 CGG repeats means they carry the unstable mutation and can expand in future generations.
  Full mutation > 200 CGG repeats

Disclaimer

Coverage is limited to that outlined in Medicaid Rule or Health Care Administrative Rules that pertains to the member's aid category. Prior Authorization (PA) is only valid if the member is eligible for the applicable item or service on the date of service.

Medicaid Rule

Medicaid and Health Care Administrative Rules can be found at https://humanservices.vermont.gov/rules-policies/health-care-rules/health-care-administrative-rules-hcar/adopted-rules

7102.2	Prior Authorization Determination
7405	Laboratory and Radiology Services
4.101	Medical Necessity for Covered Services
4.104	Medicaid Non-Covered Services
4.106	Early and Periodic Screening, Diagnostic and Treatment (EPSDT) Services

Coverage Position

FMRI may be covered for members:

- When the device is prescribed by a licensed medical provider, enrolled in the Vermont Medicaid program, operating within their scope of practice as described on the Vermont Office of Professional Regulation's website*, Statute, or rule who is knowledgeable regarding genetic testing, and who provides medical care to the member AND
- When the clinical criteria below are met.

* Vermont's Office of Professional Regulation's website: https://sos.vermont.gov/opr/

Coverage Criteria

FMRI genetic testing may be covered for members when:

1. The individual is age 20 years or younger and has clinical documentation of a developmental delay, intellectual disability, or autism spectrum disorder **OR**
2. The individual is seeking reproductive counseling and has a family history of Fragile X syndrome or autism spectrum disorder **OR**
3. Prenatal testing of fetus(es) of known carrier mothers **OR**
4. Individuals who have ovarian failure before the age of 40 in whom Fragile X-associated ovarian failure is suspected **OR**
5. Individuals with neurologic symptoms and findings consistent with FXTAS **OR**
6. Affected individuals or relatives of affected individuals who have had a positive cytogenetic Fragile X test result who are seeking further counseling related to the risk of carrier status.

Considerations: Providers requesting this test should provide pre- and post-test genetic counseling for the member and family, if applicable.

Early and Periodic Screening, Diagnostic and Treatment (EPSDT) exception: Vermont Medicaid will provide comprehensive services and furnish all Medicaid coverable, appropriate, and medically necessary services needed to correct and ameliorate health conditions for Medicaid members under age 21.

Clinical criteria for repeat service or procedure

Once per lifetime.

Type of service or procedure covered

FMRI DNA test.

Type of service or procedure not covered (this list may not be all inclusive)

Genetic testing for FMR1 mutations is **investigational** for all other uses.

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