



Status

Active

## Medical and Behavioral Health Policy

Section: Laboratory

Policy Number: VI-44

Effective Date: 03/26/2014

Blue Cross and Blue Shield of Minnesota medical policies do not imply that members should not receive specific services based on the recommendation of their provider. These policies govern coverage and not clinical practice. Providers are responsible for medical advice and treatment of patients. Members with specific health care needs should consult an appropriate health care professional.

## GENETIC TESTING FOR *FMR1* MUTATIONS (INCLUDING FRAGILE X SYNDROME)

**Description:** Fragile X syndrome is the most common cause of heritable mental retardation and is due to a mutation of the X-linked *FMR1* gene. Fragile X syndrome affects approximately one in 4,000 males and one in 8,000 females. Because the *FMR1* gene is X-linked, males are more severely affected than females. Affected females generally have milder intellectual disability and more variable physical features than affected males.

Males with fragile X syndrome often exhibit intellectual disability, generally in the moderate range, with characteristic features including an elongated face with a prominent forehead, protruding jaw, and large ears. Connective tissue anomalies may include hyperextensible finger and thumb joints, hand calluses, velvet-like skin, flat feet and mitral valve prolapse. Hyperactivity, increased sensitivity to sensory stimuli, and seizures also occur in some individuals with fragile X syndrome.

Individuals with fragile X syndrome may exhibit behaviors associated with attention deficit disorder which includes an impaired ability to maintain attention and difficulty focusing on specific tasks. They may also have features of autism spectrum disorder including social anxiety, poor eye contact, and mood disorders.

Other conditions caused by mutations of the *FMR1* gene include fragile X-associated primary ovarian syndrome and fragile X-associated tremor/ataxia syndrome. Presence of fragile X-associated primary ovarian syndrome in women is characterized by irregular menstrual cycles, infertility and elevated levels of follicle stimulating hormone. Fragile X-associated tremor/ataxia syndrome occurs in males and less often in females. The syndrome is characterized by progressive movement limitations with tremor, memory loss, peripheral neuropathy, mental and behavioral changes. The disorder usually develops late in life and worsens over time.

**Definitions:**

**Carrier status**

Carrier testing refers to DNA analysis for mutations that may be passed from either one or both parents to a child.

**Relative:** for the purposes of this policy, a relative is someone who is related by blood; a first-, second-, or third-degree relative.

- **First degree relative:** A family member who shares about 50 percent of their genes with a particular individual in a family. First degree relatives include parents, offspring, and siblings.
- **Second degree relative:** A family member who shares about 25 percent of their genes with a particular individual in a family. Second degree relatives include grandparents, grandchildren, uncles, aunts, nephews, nieces, and half-siblings.
- **Third degree relative:** A family member who shares about one eighth of their genes, such as first cousins, great-grandparents, great-aunts, great-uncles.

**X-linked**

X-linked conditions are those that are due to mutations in genes located on the X chromosome. In most instances a daughter, who has two X chromosomes in each cell, is not affected by the disease or may experience a milder form of the disease than a son, who has an X chromosome and a Y chromosome in each cell.

**Policy:**

- I. Genetic testing for *FMR1* mutations may be considered **MEDICALLY NECESSARY** for the following patient populations:
  - A. Individuals of either sex with mental retardation, developmental delay, or autism spectrum disorder; **OR**
  - B. Individuals seeking reproductive counseling who have a family history of fragile X syndrome or a family history of undiagnosed mental retardation; **OR**
  - C. Prenatal testing of fetuses of known carrier mothers; **OR**
  - D. Affected individuals or their relatives who have had a positive cytogenetic fragile X test results who are seeking further counseling related to the risk of carrier status among themselves or their relatives.
- II. Population-based screening for *FMR1* mutations in individuals not meeting one or more of the criteria above is **INVESTIGATIVE** due to the lack of clinical evidence demonstrating its impact on improved health outcomes.

**Coverage:**

Blue Cross and Blue Shield of Minnesota medical policies apply generally to all Blue Cross and Blue Plus plans and products. Benefit plans vary in coverage and some plans may not provide coverage for certain services addressed in the medical policies.

Medicaid products and some self-insured plans may have additional policies and prior authorization requirements. Receipt of benefits is subject to all terms and conditions of the member's summary plan

description (SPD). As applicable, review the provisions relating to a specific coverage determination, including exclusions and limitations. Blue Cross reserves the right to revise, update and/or add to its medical policies at any time without notice.

For Medicare NCD and/or Medicare LCD, please consult CMS or National Government Services websites.

Refer to the Pre-Certification/Pre-Authorization section of the Medical Behavioral Health Policy Manual for the full list of services, procedures, prescription drugs, and medical devices that require Pre-certification/Pre-Authorization. Note that services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial of claims may result if criteria are not met.

**Coding:**

*The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.*

**CPT:**

81243 FMR1 (Fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; evaluation to detect abnormal (eg, expanded) alleles

81244 FMR1 (Fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; characterization of alleles (eg, expanded size and methylation status)

**Policy History:**

**Developed February 13, 2013**

**Most recent history:**

Reviewed March 12, 2014

**Cross Reference:**

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