MASSACHUSETTS

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Medical Policy

Genetic Testing for FMR1 mutations - including Fragile X Syndrome

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Policy Number: 907

BCBSA Reference Number:2.04.83

Related Policies

- Array Comparative Genomic Hybridization (aCGH) for the Genetic Evaluation of Patients with Developmental Delay, #228

Policy

Genetic testing for FMR1 mutations may be considered **MEDICALLY NECESSARY** for the following patient populations:

- Individuals of either sex with mental retardation, developmental delay, or autism spectrum disorder.
- Individuals seeking reproductive counseling who have a family history of fragile X syndrome or a family history of undiagnosed mental retardation.
- Prenatal testing of fetuses of known carrier mothers.
- Affected individuals or their relatives who have had a positive cytogenetic fragile X test result who are seeking further counseling related to the risk of carrier status among themselves or their relatives.

Prior Authorization Information

Commercial Members: Managed Care (HMO and POS)

Prior authorization is **NOT** required.

Commercial Members: PPO, and Indemnity

Prior authorization is **NOT** required.

Medicare Members: HMO Blue℠

Prior authorization is **NOT** required.

Medicare Members: PPO Blue℠

Prior authorization is **NOT** required.

CPT Codes / HCPCS Codes / ICD-9 Codes

The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's

contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member. A draft of future ICD-10 Coding related to this document, as it might look today, is included below for your reference

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

CPT codes:	Code Description
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)

ICD-9 Diagnosis Codes

ICD-9-CM diagnosis codes:	Code Description
299.00	Autistic disorder
299.01	Autistic disorder, residual state
299.10	Childhood disintegrative disorder, current or active state
299.11	Childhood disintegrative disorder, residual state
299.80	Other specified pervasive developmental disorders, current or active state
299.81	Other specified pervasive developmental disorders, residual state
299.90	Unspecified pervasive developmental disorder, current or active state
299.91	Unspecified pervasive developmental disorder, residual state
315.00	Developmental reading disorder, unspecified
315.01	Alexia
315.02	Developmental dyslexia
315.09	Other specific developmental reading disorder
315.1	Mathematics disorder
315.2	Other specific developmental learning difficulties
315.31	Expressive language disorder
315.32	Mixed receptive-expressive language disorder
315.34	Speech and language developmental delay due to hearing loss
315.35	Childhood onset fluency disorder
315.39	Other developmental speech or language disorder
315.4	Developmental coordination disorder
315.5	Mixed development disorder
315.8	Other specified delays in development
315.9	Unspecified delay in development
317	Mild intellectual disabilities
318.0	Moderate intellectual disabilities
318.1	Severe intellectual disabilities
318.2	Profound intellectual disabilities
319	Unspecified intellectual disabilities
759.83	Fragile X syndrome

V18.4	Family history of intellectual disabilities
V26.31	Testing of female for genetic disease carrier status
V28.89	Other specified antenatal screening

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
F70	Mild intellectual disabilities
F71	Moderate intellectual disabilities
F72	Severe intellectual disabilities
F73	Profound intellectual disabilities
F78	Other intellectual disabilities
F79	Unspecified intellectual disabilities
F80.0	Phonological disorder
F80.1	Expressive language disorder
F80.2	Mixed receptive-expressive language disorder
F80.4	Speech and language development delay due to hearing loss
F80.81	Childhood onset fluency disorder
F80.89	Other developmental disorders of speech and language
F80.9	Developmental disorder of speech and language, unspecified
F81.0	Specific reading disorder
F81.2	Mathematics disorder
F81.81	Disorder of written expression
F81.89	Other developmental disorders of scholastic skills
F81.9	Developmental disorder of scholastic skills, unspecified
F82	Specific developmental disorder of motor function
F84.0	Autistic disorder
F84.3	Other childhood disintegrative disorder
F84.5	Asperger's syndrome
F84.8	Other pervasive developmental disorders
F84.9	Pervasive developmental disorder, unspecified
F88	Other disorders of psychological development
F89	Unspecified disorder of psychological development
H93.25	Central auditory processing disorder
Q99.2	Fragile X chromosome
R48.0	Dyslexia and alexia
Z31.430	Encounter of female for testing for genetic disease carrier status for procreative management
Z36	Encounter for antenatal screening of mother
Z81.0	Family history of intellectual disabilities

Description

Fragile X syndrome (FXS) is the most common inherited form of mental disability and known genetic cause of autism. The diagnosis includes use of a genetic test that determines the number of CGG repeats in the fragile X gene.

Patients may show behavioral problems including autism spectrum disorders, sleeping problems, social anxiety, poor eye contact, mood disorders and hand-flapping or biting. Another prominent feature of the disorder is neuronal hyperexcitability, manifested by hyperactivity, increased sensitivity to sensory stimuli and a high incidence of epileptic seizures.

Diagnosis of FXS may include using a genetic test that determines the number of CGG repeats in the fragile X gene. The patient is classified as normal, intermediate (or “gray zone”), premutation or full mutation based on the number of CGG repeats.Patients with a full mutation are associated with FXS.

Women with a premutation are at risk of premature ovarian insufficiency and at small risk of FXTAS; they carry a 50% risk of transmitting an abnormal gene, which either contains a premutation copy number (55-200) or a full mutation (>200) in each pregnancy.

Men who are premutation carriers are referred to as transmitting males. All of their daughters will inherit a premutation, but their sons will not inherit the premutation. Males with a full mutation usually have mental retardation and decreased fertility.

Summary

Fragile X syndrome is the most common inherited cause of intellectual disabilities and the most common genetic cause of autism. A thorough family history, patient assessment and genetic counseling should guide testing for individuals affected by the many manifestations of these mutations. Analytic sensitivity and specificity for diagnosing these disorders has been demonstrated to be sufficiently high.

Evidence on the impact on health outcomes of documenting FMR1 gene mutations is largely anecdotal but may end the need for additional testing in the etiologic workup of an intellectual disability, aid in management of psychopharmacologic interventions, and assist in reproductive decision making. Therefore, genetic testing for FMR1 mutations may be considered medically necessary in individuals of either sex with mental retardation, developmental delay, or autism spectrum disorder, and for the other clinical scenarios as outlined in the policy statements.

Policy History

Date	Action
6/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
2/04/2013	New policy describing coverage

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

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3. Hawkins M, Boyle J, Wright KE et al. Preparation and validation of the first WHO international genetic reference panel for Fragile X syndrome. Eur J Hum Genet 2011; 19(1):10-7.
4. Hersh JH, Saul RA. Health supervision for children with fragile X syndrome. Pediatrics 2011; 127(5):994-1006.
5. Sherman S, Pletcher BA, Driscoll DA. Fragile X syndrome: diagnostic and carrier testing. Genet Med 2005; 7(8):584-7.
6. Schaefer GB, Mendelsohn NJ. Genetics evaluation for the etiologic diagnosis of autism spectrum disorders. Genet Med 2008; 10(1):4-12.