MEDICAL POLICY

Excellus
An independent licensee of the Blue Cross Blue Shield Association

Medical Policy Title	**Genetic Testing for Inherited Disorders**
Policy Number	**2.02.03**
Current Effective Date	**December 18, 2025**
Next Review Date	**December 2026**

Our medical policies are based on the assessment of evidence based, peer-reviewed literature, and professional guidelines. Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. (Link to Product Disclaimer)

This policy is to be utilized ONLY when Health Plan medical policies do not exist for specified diseases or conditions.

POLICY STATEMENT(S)

I. Genetic testing for inheritable conditions is considered **medically appropriate** when **ALL** of the following are met:

   A. There is reasonable expectation, based on family history, pedigree analysis, risk factors, and/or signs or symptoms that a genetically inherited condition exists;

   B. The testing method is considered a proven method for the identification of a genetically linked disease;

   C. Documentation of how the test results will influence decisions concerning disease treatment or prevention;

   D. When offered in a setting with adequately trained health care professionals to provide appropriate pre- and post-test counseling and performed by a qualified laboratory.

II. Testing for the specific known familial pathogenic variant (rather than full panel testing) in an individual from a family in which there is a known pathogenic variant is considered **medically necessary**.

III. The following are considered **investigational:**

   A. Genetic testing for chronic fatigue;

   B. Genetic testing for Attention Deficit/Hyperactivity Disorder (ADHD);

   C. Genetic testing using "direct-to-the-consumer" home testing kits.

RELATED POLICIES

Corporate Medical Policy

2.02.16 Lab Testing for Alzheimer's Disease

2.02.17 Genetic Testing for Cystic Fibrosis

2.02.30 Pharmacogenetics

2.02.38 Genetic Testing for Cardiac Ion Channelopathies

2.02.42 Chromosomal Microarray (CMA) for Prenatal Evaluation and Evaluation of Patients with Developmental Delay/Intellectual Disability or Autism Spectrum Disorder

2.02.46 Whole Exome and Whole Genome Sequencing for Diagnosis of Genetic Disorders

2.02.60 Germline Genetic Testing for Hereditary Cancer

2.02.61 Genetic Testing for Thoracic Aortic Aneurysms/ Dissections and Connective Tissue Related Disorders

4.01.03 Prenatal Genetic Testing

11.01.03 Experimental or Investigational Services

POLICY GUIDELINE(S)

I. The Health Plan and its employees adhere to all State and Federal laws concerning the confidentiality of genetic testing and the results of genetic testing. All records, findings and results of any genetic test performed on any person shall be deemed confidential and shall not be disclosed without the written informed consent of the person to whom such genetic test relates. This information shall not be released to any person or organization not specifically authorized by the individual subject of the test or in compliance with applicable law.

II. Genetic testing is appropriate only when performed by a qualified laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and offered in a setting with adequately trained health care professionals who are qualified to provide appropriate pre- and post-test counseling.

III. Genetic testing is contract dependent. Coverage only applies to members with a valid contract; coverage is not provided for family members without a valid contract.

IV. Supporting documentation required:

The following factors will be considered when determining the medical appropriateness of a genetic test:

A. There must be reasonable expectation based on family history, pedigree analysis, risk factors, and/or symptomatology that a genetically inherited condition exists. Autosomal recessive disorders may be present without a family history.

B. The genotypes to be detected by a genetic test must be shown by scientifically valid methods to be associated with the occurrence of the disease, and the analytical and clinical validity of the test must be established.

C. The clinical utility of the test must be established (e.g., test results will influence decisions concerning disease treatment or prevention).

D. Genetic testing should be performed for management or treatment of the patient and not only for knowledge purposes. Documentation should demonstrate how test results will impact treatment or medical management.

E. When there is family history or phenotype suggestive of a specific syndrome, results of

targeted testing for the mutation associated with the syndrome should be documented prior to any panel testing. If targeted testing has not been performed, rationale as to why panel testing is medically necessary should be documented.

V. The following are some conditions for which there are genetics tests available from clinical genetics laboratories that are not addressed in other medical policies. Genetic testing for these conditions may be considered if after history, physical examination, pedigree analysis, genetic counseling, and completion of conventional diagnostic studies, a definitive diagnosis remains uncertain. These include, but are not limited to:

• Alpha-1-antitrypsin deficiency (AAT; emphysema and liver disease);	• Hemophilia A and B (HEMA and HEMB; bleeding disorders);
• Amyotrophic lateral sclerosis (ALS; Lou Gehrig's Disease; progressive motor function loss leading to paralysis and death);	• Huntington's disease (HD; usually midlife onset; progressive, lethal, degenerative neurological disease);
• Canavan Disease (cerebral degenerative diseases of infancy)	• Myotonic dystrophy (MD; progressive muscle weakness; most common form of adult muscular dystrophy);
• Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL);	• Neurofibromatosis type 1 (NF1; multiple benign nervous system tumors that can be disfiguring; cancers);
• Charcot-Marie-Tooth (CMT; loss of feeling in ends of limbs);	• Niemann-Pick Disease (faulty lipid metabolism causes harmful amounts of lipids to accumulate in the spleen, liver, lungs, bone marrow & brain)
• Congenital adrenal hyperplasia (CAH; hormone deficiency; ambiguous genitalia and male pseudohermaphroditism);	• Phenylketonuria (PKU; progressive mental retardation due to missing enzyme; correctable by diet);
• Congenital, Profound Deafness and Nonsyndromic Hearing Loss (DFNB1; GJB2 - Connexin 26 nonsyndromic, prelingual deafness)	• Prader Willi/Angelman syndromes (PW/A; decreased motor skills, cognitive impairment, early death);
• Duchenne muscular dystrophy/Becker muscular dystrophy (DMD; severe to mild muscle wasting, deterioration, weakness);	• Retinoblastoma (RB1 mutation; inherited, intraocular neoplasm)
• Dystonia (DYT; muscle rigidity, repetitive	• Rett syndrome

twisting movements);	
• Familial hypercholesterolemia (homozygous and heterozygous);	• Sickle cell disease (SS; blood cell disorder; chronic pain and infections);
• Fanconi anemia, group C (FA; anemia, leukemia, skeletal deformities);	• Thalassemias (THAL; anemias - reduced red blood cell levels);
• Fragile X syndrome (FRAX; leading cause of inherited mental retardation);	• Tay-Sachs Disease (TS; fatal neurological disease of early childhood; seizures, paralysis)
• Gaucher disease (GD; enlarged liver and spleen, bone degeneration);	• Von Hipple-Lindau disease (hemangioblastomas of brain, spinal cord & retinas; renal cysts & carcinomas; pheochromocytomas; & endolymphatic sac tumors.)

DESCRIPTION

A genetic test is defined as the analysis of human DNA, ribonucleic acid (RNA), chromosomes, proteins, and certain metabolites in order to detect alterations related to a heritable disorder. This can be accomplished by directly examining the DNA or RNA that makes up a gene (e.g., direct testing) looking at markers co-inherited with a disease-causing gene (e.g., linkage testing) assaying certain metabolites (e.g., biochemical testing) or examining the chromosomes (cytogenetics testing).

"Genetic disease" is defined as a morbid disorder that is caused by a variation in human genetic material. In some cases, merely the presence of the variation will cause illness. It is estimated that genetic mutations are responsible for 3,000-4,000 hereditary disorders. Genetic defects find their most varied expression in disruptions of the intricate chemistry that underlie human structure and metabolism. These manifestations range from such well-known conditions as Down syndrome and Phenylketonuria (PKU) to very rare conditions. Some genetic disorders are caused by the mutation of a single gene (e.g., sickle cell anemia, cystic fibrosis, Tay-Sachs disease), while chromosomal disorders are caused by an excess or deficiency of a number of genes (e.g., Down syndrome). Other heritable conditions are considered multifactorial inheritance disorders (e.g., heart disease and many cancers), arising from a combination of genetic and environmental factors.

Genetic tests are used for several reasons, including:

I. Carrier screening, which involves identifying unaffected individuals who carry one copy of a gene for a disease that requires two copies for the disease to be expressed;

II. Prenatal diagnostic testing;

III. Newborn screening, such as for Phenylketonuria (PKU);

IV. Presymptomatic testing for predicting adult-onset disorders such as Huntington's disease;

V. Presymptomatic testing for estimating the risk of developing adult-onset diseases; and

VI. Confirmational diagnosis of a symptomatic individual.

Direct-to-consumer marketing of genetic testing, frequently using "home testing" kits, pose issues related to appropriateness of test utilization, interpretation of results, and lack of pre- and post-test counseling and follow-up.

SUPPORTIVE LITERATURE

Ebert et al (2024) conducted a study to examine the clinical utility and diagnostic yield of genetic testing for neuromuscular diseases (NMDs). Genetic testing results were reviewed for all patients who underwent testing through a single, large neuromuscular center from 2015 to 2020. Retrospective chart reviews were performed to determine whether genetic testing results conferred a specific NMD diagnosis, including cases where a variant of uncertain significance (VUS) was identified. Genetic testing was pursued for 192 patients. A positive result, defined as a pathogenic mutation, a VUS, or both, was found in 77.1%. A definitive diagnosis was conferred in 35.9%. The most common testing indication was suspected neuropathy (53.3%), and the indication with the highest diagnostic yield was suspected myopathy (48.7%). The authors conclude this study provides further evidence of the clinical utility of genetic testing for NMDs in a real-world setting with over one-third of patients tested receiving a definitive diagnosis.

PROFESSIONAL GUIDELINE(S)

The National Human Genome Research Institute Task Force on Genetic Testing (NHGRI) published recommendations to ensure the safety and effectiveness of genetic tests (Holtzman and Watson 1998). Their recommendations include:

- "The genotypes to be detected by a genetic test must be shown by scientifically valid methods to be associated with the occurrence of a disease, independently replicated and subject to peer review."
- "Analytical sensitivity and specificity of a genetic test must be determined before it is made available in clinical practice."
- "Data to establish the clinical validity of genetic tests (clinical sensitivity, specificity, and predictive value) must be collected under investigative protocols. In clinical validation, the study sample must be drawn from a group of subjects representative of the population for whom the test is intended. Formal validation for each intended use of a genetic test is needed."
- "Before a genetic test can be generally accepted in clinical practice, data must be collected to demonstrate the benefits and risks that accrue from both positive and negative results."
- "Tests under development must be conducted in CLIA-certified laboratories if the results will be reported to patients or their providers."

Medically appropriate genetic testing requires that there be reasonable expectation based on family history, pedigree analysis, risk factors, and/or symptomatology that a genetically inherited condition exists. With a few limited exceptions (e.g., PKU testing and other newborn screenings), general

screening of populations for diseases that can be attributed to genetic mutations is not advocated in scientific literature.

The genotypes to be detected by a genetic test must be shown by scientifically valid methods to be associated with the occurrence of the disease, and the analytical and clinical validity of the test must be established. Analytical validity is an indicator of how well a test measures the property or characteristic it is intended to measure. It is made up of three components: analytical sensitivity, analytical specificity, and reliability.

Clinical validity in genetic testing is a measurement of the accuracy with which a test identifies or predicts a clinical condition and involves the following: clinical sensitivity, clinical specificity, positive predictive value, negative predictive value, heterogeneity, and penetrance.

The clinical utility of a genetic test must be established, i.e., test results will influence decisions concerning disease treatment or prevention. The development of genetic tests that can diagnose or predict disease occurrence has far outpaced the development of interventions to treat, ameliorate or prevent those same diseases. Clinical utility refers to the ability of genetic test results, either positive or negative, to provide information that is of value in the clinical setting. Specifically for positive test results, this could involve instituting treatments or surveillance measures, making decisions concerning future conception, or avoiding harmful treatments. Negative test results can have clinical utility in that unnecessary treatments or surveillance can be avoided.

Information on the risks and benefits of genetic testing must be presented fully and objectively without coercion to persons contemplating genetic testing. The patient must give fully informed consent for the test with appropriate pre-test counseling. When appropriate, there should be a plan for post-test counseling.

Genetic testing of children to confirm current symptomatology or predict adult-onset diseases is not considered medically necessary unless direct medical benefit would be lost by waiting until the child has reached adulthood. It is generally accepted in the published literature that unless useful medical intervention can be offered to children as a result of testing, formal testing should wait until the child is old enough to understand the consequences of testing and request it personally. Ethical concerns related to the testing of children include the breach of confidentiality that is required by revealing test results to parents, the lack of ability to counsel the child in a meaningful way regarding the risks and benefits of testing, the impact a positive test could have in terms of discrimination, and the potential psychological damage that could occur from distorting a family's perception of the child.

Direct-to-consumer genetic testing has been marketed to the public as a method of identifying the presence of or susceptibility to disease. The American College of Medical Genetics (ACMG) (2016) expressed the view that it is critical for the public to realize that genetic testing is only one part of a complex process and has the potential for both positive and negative impact on health and well-being. The ACMG asserted that the following should be considered minimum requirements for any genetic testing protocol: (1) A knowledgeable professional should be involved in the process of ordering and interpreting a genetic test; (2) The patient should be fully informed regarding what the test can and cannot say about the patient's health; (3) The scientific evidence on which a test is based should be clearly stated; and (4) The clinical testing laboratory must be accredited under the

CLIA, and by the state in which it is located and/or other applicable accrediting agencies.

The National Society of Genetic Counselors (Miller 2025) evidence-based practice for genetic testing and counseling for hypertrophic cardiomyopathy recommendations include:

- "Genetic testing should be offered to all individuals with a suspected or confirmed clinical diagnosis of HCM in the setting of appropriate genetic counseling."
- "Genetic tests should be selected, ordered, and interpreted in the setting of appropriate genetic counseling."
- "Family screening, including cardiac screening and cascade genetic testing, as appropriate, should be offered to at-risk relatives. Cascade genetic testing should be offered in the setting of appropriate genetic counseling without limitation of age."

The American College of Medical Genetics and Genomics (ACMG) clinical practice resource for the clinical evaluation and etiologic diagnosis of hearing loss (Li 2022) state, "identifying the etiology of hearing loss may affect clinical management, improve prognostic accuracy, and refine genetic counseling and assessment of the likelihood of recurrence for relatives of deaf and hard-of-hearing individuals." This clinical practice resource offers information about the frequency, causes, and presentations of hearing loss and suggests approaches to the clinical and genetic evaluation of deaf and hard-of-hearing individuals aimed at identifying an etiologic diagnosis and providing informative and effective patient education and genetic counseling.

The National Society of Genetic Counselors published a practice guideline on genetic testing and counseling for unexplained epilepsies (Smith 2023). Their recommendations include:

- "We strongly recommend that individuals with unexplained epilepsy be offered genetic testing, without limitation of age."
- "We strongly recommend comprehensive, multi-gene testing, such as exome/genome sequencing or multi-gene panel as a first-tier test."
- "We conditionally recommend exome/genome sequencing over multi-gene panel as the first-tier test."
- "The multi-gene panel should have a minimum of 25 genes and include copy number analysis."

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing.

More information is available at: Clinical Laboratory Improvement Amendments (CLIA) | FDA [accessed 2025 Nov 6]

CODE(S)

- Codes may not be covered under all circumstances.

- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational
- (NMN)=Not medically necessary/appropriate

CPT Codes

Code	Description
The following codes are not all inclusive and various other codes may apply to the policy criteria	
81161	DMD (dystrophin) (e.g., Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81177	ATN1 (atrophin 1) (e.g., dentatorubral-pallidoluysian atrophy) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81178	ATXN1 (ataxin 1) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81179	ATXN2 (ataxin 2) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81180	ATXN3 (ataxin 3) (e.g., spinocerebellar ataxia, Machado-Joseph disease) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81181	ATXN7 (ataxin 7) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81182	ATXN8OS (ATXN8 opposite strand [non-protein coding]) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81183	ATXN10 (ataxin 10) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81184	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (e.g., spinocerebellar ataxia) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles
81185	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (e.g., spinocerebellar ataxia) gene analysis; full gene sequence
81186	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (e.g., spinocerebellar ataxia) gene analysis; known familial variant
81187	CNBP (CCHC-type zinc finger nucleic acid binding protein) (e.g., myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81188	CSTB (cystatin B) (e.g., Unverricht-Lundborg disease) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles

Code	Description
The following codes are not all inclusive and various other codes may apply to the policy criteria	
81189	CSTB (cystatin B) (e.g., Unverricht-Lundborg disease) gene analysis; full gene sequence
81190	CSTB (cystatin B) (e.g., Unverricht-Lundborg disease) gene analysis; known familial variant(s)
81200	ASPA (aspartoacylase) (e.g., Canavan disease) gene analysis, common variants (e.g., E285A, Y231X)
81205	BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (e.g., maple syrup urine disease) gene analysis, common variants (e.g., R183P, G278S, E422X)
81209	BLM (Bloom syndrome, RecQ helicase-like) (e.g., Bloom syndrome) gene analysis, 2281del6ins7 variant
81234	DMPK (DM1 protein kinase) (e.g., myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles
81239	DMPK (DM1 protein kinase) (e.g., myotonic dystrophy type 1) gene analysis; characterization of alleles (e.g., expanded size)
81242	FANCC (Fanconi anemia, complementation group C) (e.g., Fanconi anemia, type C) gene analysis, common variant (e.g., IVS4+4A>T)
81243	FMR1 (fragile X messenger ribonucleoprotein 1) (e.g., fragile X syndrome, X-linked intellectual disability [XLID]) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles
81244	FMR1 (fragile X messenger ribonucleoprotein 1) (e.g., fragile X syndrome, X-linked intellectual disability [XLID]) gene analysis; characterization of alleles (e.g., expanded size and promoter methylation status)
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (e.g., Glycogen storage disease, type 1A, von Gierke disease) gene analysis, common variants (e.g., R83C, Q347X)
81251	GBA (glucosidase, beta, acid) (e.g., Gaucher disease) gene analysis, common variants (e.g., N370S, 84GG, L444P, IVS2+1G>A)
81252	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (e.g., nonsyndromic hearing loss) gene analysis; full gene sequence
81253	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (e.g., nonsyndromic hearing loss) gene analysis; known familial variants

Code	Description
The following codes are not all inclusive and various other codes may apply to the policy criteria	
81254	GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (e.g., nonsyndromic hearing loss) gene analysis, common variants (e.g., 309kb [del (GJB6-D13S1830)] and 232kb [del (GJB6-D13S1854)])
81255	HEXA (hexosaminidase A [alpha polypeptide]) (e.g., Tay-Sachs disease) gene analysis, common variants (e.g., 1278insTATC, 1421+1G>C, G269S)
81256	HFE (hemochromatosis) (e.g., hereditary hemochromatosis) gene analysis, common variants (e.g., C282Y, H63D)
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, common deletions or variant (e.g., Southeast Asian, Thai, Filipino, Mediterranean, alpha 3.7, alpha 4.2, alpha 20.5, Constant Spring)
81258	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant
81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; full gene sequence
81260	IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (e.g., familial dysautonomia) gene analysis, common variants (e.g., 2507+6T>C, R696P)
81269	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants
81271	HTT (huntingtin) (e.g., Huntington disease) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles
81274	HTT (huntingtin) (e.g., Huntington disease) gene analysis; characterization of alleles (e.g., expanded size)
81284	FXN (frataxin) (e.g., Friedreich ataxia) gene analysis; evaluation to detect abnormal (expanded) alleles
81285	FXN (frataxin) (e.g., Friedreich ataxia) gene analysis; characterization of alleles (e.g., expanded size)
81286	FXN (frataxin) (e.g., Friedreich ataxia) gene analysis; full gene sequence
81289	FXN (frataxin) (e.g., Friedreich ataxia) gene analysis; known familial variant(s)

Code	Description
The following codes are not all inclusive and various other codes may apply to the policy criteria	
81290	MCOLN1 (mucolipin 1) (e.g., Mucolipidosis, type IV) gene analysis, common variants (e.g., IVS3 2A>G, del 6.4kb)
81302	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; full sequence analysis
81303	MECP2 (methyl CPG binding protein 2) (e.g., Rett syndrome) gene analysis; known familial variant
81304	MECP2 (methyl CPG binding protein 2) (e.g., Rett syndrome) gene analysis; duplication/deletion variants
81312	PABPN1 (poly[A] binding protein nuclear 1) (e.g., oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81324	PMP22 (peripheral myelin protein 22) (e.g., Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis
81325	PMP22 (peripheral myelin protein 22) (e.g., Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence analysis
81326	PMP22 (peripheral myelin protein 22) (e.g., Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; known familial variant
81330	SMPD1 (sphingomyelin phosphodiesterase 1, acid lysosomal) (e.g., Neimann-Pick disease, type A) gene analysis; common variants (e.g., R496L, L302P, fsP330)
81331	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (e.g., Prader-Willi syndrome and/or Angelman syndrome), methylation analysis
81332	SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, member 1) (e.g., alpha-1-antitrypsin deficiency), gene analysis, common variants (e.g., *S and *Z)
81333	TGFBI (transforming growth factor beta-induced) (e.g., corneal dystrophy) gene analysis, common variants (e.g., R124H, R124C, R124L, R555W, R555Q)
81344	TBP (TATA box binding protein) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles
81361	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (e.g., HbS, HbC, HbE)

Code	Description
The following codes are not all inclusive and various other codes may apply to the policy criteria	
81362	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); known familial variant(s)
81363	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)
81364	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); full gene sequence
81401	Molecular pathology procedure, Level 2 (e.g., 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
81402	Molecular pathology procedure, Level 3 (e.g., >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD])
81403	Molecular pathology procedure, Level 4 (e.g., analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
81404	Molecular pathology procedure, Level 5 (e.g., analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
81405	Molecular pathology procedure, Level 6 (e.g., analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)
81406	Molecular pathology procedure, Level 7 (e.g., analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons)
81407	Molecular pathology procedure, Level 8 (e.g., analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)
81408	Molecular pathology procedure, Level 9 (e.g., analysis of >50 exons in a single gene by DNA sequence analysis)

Code	Description
The following codes are not all inclusive and various other codes may apply to the policy criteria	
81412	Ashkenazi Jewish associated disorders (e.g., Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1
81419	Epilepsy genomic sequence analysis panel, must include analyses for ALDH7A1, CACNA1A, CDKL5, CHD2, GABRG2, GRIN2A, KCNQ2, MECP2, PCDH19, POLG, PRRT2, SCN1A, SCN1B, SCN2A, SCN8A, SLC2A1, SLC9A6, STXBP1, SYNGAP1, TCF4, TPP1, TSC1, TSC2, and ZEB2
81430	Hearing loss (e.g., nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); genomic sequence analysis panel, must include sequencing of at least 60 genes, including CDH23, CLRN1, GJB2, GPR98, MTRNR1, MYO7A, MYO15A, PCDH15, OTOF, SLC26A4, TMC1, TMPRSS3, USH1C, USH1G, USH2A, and WFS1
81431	Hearing loss (e.g., nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); duplication/deletion analysis panel, must include copy number analyses for STRC and DFNB1 deletions in GJB2 and GJB6 genes
81439	Hereditary cardiomyopathy (e.g., hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy), genomic sequence analysis panel, must include sequencing of at least 5 cardiomyopathy-related genes (e.g., DSG2, MYBPC3, MYH7, PKP2, TTN)
81441	Inherited bone marrow failure syndromes (IBMFS) (e.g., Fanconi anemia, dyskeratosis congenita, Diamond-Blackfan anemia, Shwachman-Diamond syndrome, GATA2 deficiency syndrome, congenital amegakaryocytic thrombocytopenia) sequence analysis panel, must include sequencing of at least 30 genes, including BRCA2, BRIP1, DKC1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, GATA1, GATA2, MPL, NHP2, NOP10, PALB2, RAD51C, RPL11, RPL35A, RPL5, RPS10, RPS19, RPS24, RPS26, RPS7, SBDS, TERT, and TINF2
81442	Noonan spectrum disorders (e.g., Noonan syndrome, cardio-facio-cutaneous syndrome, Costello syndrome, LEOPARD syndrome, Noonan-like syndrome), genomic sequence analysis panel, must include sequencing of at least 12 genes, including BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NRAS, PTPN11, RAF1, RIT1, SHOC2, and SOS1

Code	Description
The following codes are not all inclusive and various other codes may apply to the policy criteria	
81448	Hereditary peripheral neuropathies (e.g., Charcot-Marie-Tooth, spastic paraplegia), genomic sequence analysis panel, must include sequencing of at least 5 peripheral neuropathy-related genes (e.g., BSCL2, GJB1, MFN2, MPZ, REEP1, SPAST, SPG11, SPTLC1)
81470	X-linked intellectual disability (XLID) (e.g., syndromic, and non-syndromic XLID); genomic sequence analysis panel, must include sequencing of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, AND SLC16A2
81471	X-linked intellectual disability (XLID) (e.g., syndromic, and non-syndromic XLID); duplication/deletion gene analysis, must include analysis of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2
81479	Unlisted molecular pathology procedure
0205U	Ophthalmology (age-related macular degeneration), analysis of 3 gene variants (2 CFH gene, 1 ARMS2 gene), using PCR and MALDI-TOF, buccal swab, reported as positive or negative for neovascular age related macular-degeneration risk associated with zinc supplements
0216U	Neurology (inherited ataxias), genomic DNA sequence analysis of 12 common genes including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants
0217U	Neurology (inherited ataxias), genomic DNA sequence analysis of 51 genes including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants
0218U	Neurology (muscular dystrophy), DMD gene sequence analysis, including small sequence changes, deletions, duplications, and variants in non-uniquely mappable regions, blood or saliva, identification, and characterization of genetic variants (Genomic Unity DMD Analysis, Variantyx Inc)
0230U	AR (androgen receptor) (e.g., spinal, and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation), full sequence analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) expansions, mobile element insertions, and variants in non-uniquely mappable regions (Genomic Unity AR Analysis, Variantyx, Inc)

Code	Description
The following codes are not all inclusive and various other codes may apply to the policy criteria	
0231U	CACNA1A (calcium voltage-gated channel subunit alpha 1A) (e.g., spinocerebellar ataxia), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) gene expansions, mobile element insertions, and variants in non-uniquely mappable regions (Genomic Unity CACNA1A Analysis, Variantyx Inc)
0232U	CSTB (cystatin B) (e.g., progressive myoclonic epilepsy type 1A, Unverricht-Lundborg disease), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) expansions, mobile element insertions, and variants in non-uniquely mappable regions (Genomic Unity CSTB Analysis, Variantyx Inc)
0233U	FXN (frataxin) (e.g., Friedreich ataxia), gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) expansions, mobile element insertions, and variants in non-uniquely mappable regions (Genomic Unity FXN Analysis, Variantyx Inc)
0234U	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions (Genomic Unity MECP2 Analysis, Variantyx Inc)
0236U	SMN1 (survival of motor neuron 1, telomeric) and SMN2 (survival of motor neuron 2, centromeric) (e.g., spinal muscular atrophy) full gene analysis, including small sequence changes in exonic and intronic regions, duplications and deletions, and mobile element insertions (Genomic Unity SMN1/2 Analysis, Variantyx Inc)
0322U	Neurology (autism spectrum disorder [ASD]), quantitative measurements of 14 acyl carnitines and microbiome-derived metabolites, liquid chromatography with tandem mass spectrometry (LC-MS/MS), plasma, results reported as negative or positive for risk of metabolic subtypes associated with ASD (NPDX ASD Test Panel III, Stemina Biomarker Discovery d/b/a NeuroPointDX)
0378U	RFC1 (replication factor C subunit 1), repeat expansion variant analysis by traditional and repeat-primed PCR, blood, saliva, or buccal swab (UCGSL RFC1 Repeat Expansion Test, University of Chicago Genetic Services Laboratories)
0605U	Allergy and immunology (hereditary alpha tryptasemia), DNA, analysis of TPSAB1 gene copy number variation using digital PCR, whole blood, results reported with genotype-specific interpretation of alpha-tryptase copy number and algorithmic classification as normal or abnormal (Tryptase Gene Copy Number Analysis by dPCR, Virant Diagnostics, Inc.)

HCPCS Codes

Code	Description
S3800	Genetic testing for amyotrophic lateral sclerosis (ALS)
S3841	Genetic testing for retinoblastoma
S3842	Genetic testing for von Hipple-Lindau disease
S3844	DNA analysis of the connexin 26 gene (GJB2) for susceptibility to congenital, profound deafness
S3845	Genetic testing for alpha-thalassemia
S3846	Genetic testing for hemoglobin E beta-thalassemia
S3849	Genetic testing for Niemann-Pick disease
S3850	Genetic testing for sickle cell anemia
S3853	Genetic testing for myotonic muscular dystrophy
S3865	Comprehensive gene sequence analysis for hypertrophic cardiomyopathy
S3866	Genetic analysis for a specific gene mutation for hypertrophic cardiomyopathy (HCM) in an individual with a known HCM mutation in the family

ICD10 Codes

Code	Description
Multiple Codes	

REFERENCES

American Academy of Pediatrics Committee on Bioethics; Committee on Genetics, and American College of Medical Genetics and; Genomics Social; Ethical; Legal Issues Committee. Ethical and policy issues in genetic testing and screening of children. Pediatrics. 2013 Mar;131(3):620-2.

American College of Obstetrics and Gynecology (ACOG) Committee on Genetics. Opinion Number 318, Oct 2005. Screening for Tay-Sachs disease. Obstet Gynecol. 2005 Oct;106(4):893-4.

American College of Medical Genetics. Policy statement on direct-to-consumer genetic testing. Revised 2015 Dec 17. Genet Med. 2016 Feb;18(2):207-208.

American College of Obstetricians and Gynecologists (ACOG). Patient testing: Ethical issues in selection and counseling. ACOG Committee Opinion No. 363. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2007;109:1021–3.

American Society of Clinical Oncology. Policy statement update: genetic and genomic testing for cancer susceptibility. J Clin Oncol. 2015 Nov 1;33(31):3660-7.

Barbosa-Gouveia S, et al. Rapid molecular diagnosis of genetically inherited neuromuscular disorders using next-generation sequencing technologies. J Clin Med. 2022 May 12;11(10):2750.

Christian S, et al. Diagnostic validity, and clinical utility of genetic testing for hypertrophic cardiomyopathy: a systematic review and meta-analysis. Open Heart. 2022 Apr;9(1):e001815.

Ebert SE, et al. Clinical utility and diagnostic yield of genetic testing for inherited neuromuscular disorders in a single, large neuromuscular center. Neurol Clin Pract. 2024 Apr;14(2):e200268.

Emdin CA, et al. Genome-wide polygenic score and cardiovascular outcomes with Evacetrapib in patients with high-risk vascular disease: a nested case-control study. Circ Genom Precis Med. 2020 Feb;13(1):e002767.

Grody WW, et al. [Internet]. American College of Medical Genetics consensus statement on Factor V Leiden mutation testing. Mar/Apr 2001; reaffirmed 2007 May 14 [accessed 2025 Nov 6]. Available from: https://www.acmg.net/PDFLibrary/Factor-V-Ledien-Mutation-Testing.pdf

Hotzman N and Watson M. National Human Genome Research Institute [Internet]. Final report of the task force on genetic testing. Promoting safe and effective genetic testing in the United States. 1997 Sep [accessed 2025 Nov 6]. Available from: https://www.genome.gov/10001733/genetic-testing-report

Huml AM, et al. Consistency of direct-to-consumer genetic testing results among identical twins. Am J Med. 2020 Jan;133(1):143-146.

Kaye CI; Committee on Genetics, et al. Introduction to the newborn screening fact sheets. Pediatrics. 2006 Sep;118(3):1304-12.

Kaye CI; Committee on Genetics, et al. Newborn screening fact sheets. Pediatrics. 2006 Sep;118(3):e934-63.

Li MM, et al; ACMG Professional Practice and Guidelines Committee. Clinical evaluation and etiologic diagnosis of hearing loss: A clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2022 Jul;24(7):1392-1406.

McBenedict B, et al. Impact of genetic testing on the diagnosis, management, and prognosis of hypertrophic cardiomyopathy: a systematic review. Cureus. 2024 Oct 7;16(10): e70993.

Miller EM, et al. Genetic testing and counseling for hypertrophic cardiomyopathy: An evidence-based practice resource of the National Society of Genetic Counselors. J Genet Couns. 2025 Jun;34(3): e1993.

Nadkarni GN, et al. Effects of testing and disclosing ancestry-specific genetic risk for kidney failure on patients and health care professionals: a randomized clinical trial. JAMA Netw Open. 2022 Mar;5(3):e221048.

Narcisa V, et al. Parental interest in a genetic risk assessment for autism spectrum disorders. Clin Pediatr (Phila). 2013 Feb;52(2):139-46.

Nelson TN, et al. CMG Ethics and Public Policy Committee. CCMG statement on direct-to-consumer genetic testing. Clin Genet. 2012 Jan;81(1):1-3.

Patrick MT, et al. Shared genetic risk factors for multiple sclerosis/psoriasis suggest involvement of interleukin-17 and janus kinase-signal transducers and activators of transcription signaling. Ann Neurol. 2023 Aug;94(2):384-397.

Petersen LM and Lefferts JA. Lessons learned from direct-to-consumer genetic testing. Clin Lab Med. 2020 Mar;40(1):83-92.

Ross LF, et al.; American Academy of Pediatrics; American College of Medical Genetics and Genomics. Technical report: Ethical and policy issues in genetic testing and screening of children. Genet Med. 2013 Mar;15(3):234-45.

Smith L, et al. Genetic testing and counseling for the unexplained epilepsies: an evidence-based practice guideline of the National Society of Genetic Counselors. J Genet Couns. 2023 Apr;32(2):266-280.

Skirton H, et al. Direct to consumer genetic testing: a systematic review of position statements, policies, and recommendations. Clin Genet. 2012 Sep;82(3):210-8.

Trottier M, et al. Genetics healthcare providers' experiences counseling patients with results from consumer genomic testing. Mol Genet Genomic Med. 2024 Aug;12(8):e2508.

SEARCH TERMS

Genetic analysis, inherited disease.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Molecular Pathology Procedures (LCD L35000) [accessed 2025 Nov 6]

Billing and Coding: Molecular Pathology Procedures (Article A56199) [accessed 2025 Nov 6]

COVERAGE FOR NYS MEDICAID MANAGED CARE/HARP PRODUCT MEMBERS

The Department of Health (DOH) has mandated testing of the Duchenne muscular dystrophy (DMD) gene in individuals who are being considered for treatment with Exondys 51 (eteplirsen) be carved into the Medicaid managed care (MMC) and Health and Recovery Plan (HARP) benefit packages.

Duchenne muscular dystrophy is a genetic disorder characterized by progressive muscle degeneration and weakness. It is one of nine types of muscular dystrophy. Exondys 51 (eteplirsen) has been identified as the first disease-modifying drug for DMD.

Effective for dates of service on or after November 1, 2019, the Health Plan will cover DMD gene testing. DMD gene testing is reimbursable once in a lifetime.

PRODUCT DISCLAIMER

- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.

- If a commercial product (including an Essential Plan or Child Health Plus product) covers a specific service, medical policy criteria apply to the benefit.
- If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.
- If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.
- If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY HISTORY/REVISION	
Committee Approval Dates	
11/19/99, 12/20/01, 02/20/03, 04/15/04, 05/18/05, 05/18/06, 05/17/07, 06/19/08, 05/28/09, 05/27/10, 05/19/11, 05/24/12, 06/20/13, 07/17/14, 05/28/15, 06/16/16, 07/20/17, 06/21/18, 06/20/19, 07/16/20, 07/15/21, 12/16/21, 12/22/22, 12/21/23, 12/19/24, 12/18/25	
Date	**Summary of Changes**
12/18/25	• Annual review, policy intent unchanged.
01/01/25	• Summary of changes tracking implemented.
11/19/99	• Original effective date