

# MEDICAL POLICY

<b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b>	<b>EFFECTIVE DATE: 10/18/01</b> <b>REVISED DATE: 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</b>
<b>POLICY NUMBER: 2.02.03</b> <b>CATEGORY: Laboratory Test</b>	<b>PAGE: 1 OF: 9</b>
<ul style="list-style-type: none"><li>• <i>If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.</i></li><li>• <i>If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit.</i></li><li>• <i>If a Medicare 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.</i></li></ul>	

## POLICY STATEMENT:

- I. Based upon our criteria and review of the peer-reviewed literature, genetic testing for inheritable diseases, 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, has been medically proven to be effective and therefore, **medically appropriate** when:
  - A. There is reasonable expectation, based on family history, pedigree analysis, risk factors, and / or signs or symptoms that a genetically inherited condition exists; and
  - B. The testing method is considered a proven method for the identification of a genetically-linked disease; and
  - C. The test results will influence decisions concerning disease treatment or prevention.
- II. Based upon our criteria and the lack of peer-reviewed literature, genetic testing for chronic fatigue or ADHD has not been proven to be medically effective and is considered **investigational**.
- III. Based upon our criteria and the lack of peer-reviewed literature, genetic testing using “direct-to-the-consumer” home testing kits is considered **investigational**.

*This policy is to be utilized ONLY when Health Plan medical policies do not exist for specified diseases or conditions. Refer to the following Medical Policies for the specified diseases indicated:*

*Genetic Testing for Hereditary Hemochromatosis - Policy #2.02.05,*

*Genetic Testing for Hereditary BRCA1 and BRCA2 Mutations - Policy # 2.02.06,*

*Genetic Testing for Germline Mutations of the RET Proto Oncogene in Medullary Carcinoma of the Thyroid - Policy #2.02.07,*

*Genetic Testing for Inherited Susceptibility to Colorectal Cancer - Policy #2.02.11,*

*Genetic Testing for Familial Alzheimer’s Disease - Policy #2.02.16,*

*Genetic Testing for Cystic Fibrosis – Policy #2.02.17,*

*Genetic Testing for Congenital Long QT Syndrome – Policy #2.02.38,*

*Array Comparative Genomic Hybridization (aCGH) for the Genetic Evaluation of Patients with Developmental Delay, Mental Retardation or Autism Spectrum Disorder – Policy #2.02.42,*

*Genetic Testing for Susceptibility to Hereditary Cancers – Policy #2.02.44, and*

*Preconception and Prenatal Genetic Testing/Counseling and Preimplantation Genetic Diagnosis (PGD) - Policy #4.01.03.*

## POLICY GUIDELINES:

- 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

<p><b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b></p> <p><b>POLICY NUMBER: 2.02.03</b></p> <p><b>CATEGORY: Laboratory Test</b></p>	<p><b>EFFECTIVE DATE: 10/18/01</b></p> <p><b>REVISED DATE: 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</b></p> <p><b>PAGE: 2 OF: 9</b></p>
---	---

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.

- II. Laboratories performing clinical tests must be certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).
- III. The following factors should 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). If the genetic test is being done for knowledge only and that knowledge will not alter management or treatment of the patient then the testing is **not medically appropriate**.
- IV. Coverage for genetic testing for specific diseases, as well as prior authorization, is contract dependent. Genetic testing done for occupation-associated risk is typically excluded from most contracts. Genetic testing as part of an organ donor search is excluded from most contracts. Please refer to your Customer (Member/Provider) Service Department for determination of contract benefits.

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 medically appropriate 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:

<ul style="list-style-type: none"> <li>• Alpha-1-antitrypsin deficiency (AAT; emphysema and liver disease);</li> </ul>	<ul style="list-style-type: none"> <li>• Hemophilia A and B (HEMA and HEMB; bleeding disorders);</li> </ul>
<ul style="list-style-type: none"> <li>• Amyotrophic lateral sclerosis (ALS; Lou Gehrig's Disease; progressive motor function loss leading to paralysis and death);</li> </ul>	<ul style="list-style-type: none"> <li>• Huntington's disease (HD; usually midlife onset; progressive, lethal, degenerative neurological disease);</li> </ul>
<ul style="list-style-type: none"> <li>• Canavan Disease (cerebral degenerative diseases of infancy)</li> </ul>	<ul style="list-style-type: none"> <li>• Myotonic dystrophy (MD; progressive muscle weakness; most common form of adult muscular dystrophy);</li> </ul>
<ul style="list-style-type: none"> <li>• Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL);</li> </ul>	<ul style="list-style-type: none"> <li>• Neurofibromatosis type 1 (NF1; multiple benign nervous system tumors that can be disfiguring; cancers);</li> </ul>
<ul style="list-style-type: none"> <li>• Charcot-Marie-Tooth (CMT; loss of feeling in ends of limbs);</li> </ul>	<ul style="list-style-type: none"> <li>• Niemann-Pick Disease (faulty lipid metabolism causes harmful amounts of lipids to accumulate in the spleen, liver, lungs, bone marrow &amp; brain)</li> </ul>
<ul style="list-style-type: none"> <li>• Congenital adrenal hyperplasia (CAH; hormone deficiency; ambiguous genitalia and male pseudohermaphroditism);</li> </ul>	<ul style="list-style-type: none"> <li>• Phenylketonuria (PKU; progressive mental retardation due to missing enzyme; correctable by diet);</li> </ul>
<ul style="list-style-type: none"> <li>• Congenital, Profound Deafness (DFNB1; GJB2 - Connexin 26 nonsyndromic, prelingual deafness)</li> </ul>	<ul style="list-style-type: none"> <li>• Prader Willi/Angelman syndromes (PW/A; decreased motor skills, cognitive impairment, early death);</li> </ul>
<ul style="list-style-type: none"> <li>• Duchenne muscular dystrophy/Becker muscular dystrophy (DMD; severe to mild muscle wasting, deterioration, weakness);</li> </ul>	<ul style="list-style-type: none"> <li>• Retinoblastoma (RB1 mutation; inherited, intraocular neoplasm)</li> </ul>
<ul style="list-style-type: none"> <li>• Dystonia (DYT; muscle rigidity, repetitive twisting movements);</li> </ul>	<ul style="list-style-type: none"> <li>• Sickle cell disease (SS; blood cell disorder; chronic pain and infections);</li> </ul>
<ul style="list-style-type: none"> <li>• Fanconi anemia, group C (FA; anemia, leukemia, skeletal deformities);</li> </ul>	<ul style="list-style-type: none"> <li>• Thalassemias (THAL; anemias - reduced red blood cell levels);</li> </ul>

<p><b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b></p> <p><b>POLICY NUMBER: 2.02.03</b></p> <p><b>CATEGORY: Laboratory Test</b></p>	<p><b>EFFECTIVE DATE: 10/18/01</b></p> <p><b>REVISED DATE: 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</b></p> <p><b>PAGE: 3 OF: 9</b></p>
---	---

<ul style="list-style-type: none"> <li>• Fragile X syndrome (FRAX; leading cause of inherited mental retardation);</li> </ul>	<ul style="list-style-type: none"> <li>• Tay-Sachs Disease (TS; fatal neurological disease of early childhood; seizures, paralysis)</li> </ul>
<ul style="list-style-type: none"> <li>• Gaucher disease (GD; enlarged liver and spleen, bone degeneration);</li> </ul>	<ul style="list-style-type: none"> <li>• Von Hippel-Lindau disease (hemangioblastomas of brain, spinal cord &amp; retinas; renal cysts &amp; carcinomas; pheochromocytomas; &amp; endolymphatic sac tumors.)</li> </ul>

**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)” (Gene Tests, 2006).

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 underlies 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 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, poses issues related to appropriateness of test utilization, interpretation of results, lack of pre- and post-test counseling and follow-up.

**RATIONALE:**

The rationale for this policy is based on the recommendations in the Final Report of the Task Force on Genetic Testing and the Secretary’s Advisory Committee on Genetic Testing.

Medically appropriate genetic testing requires that there must 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, and it is made up of three components: analytical sensitivity, analytical specificity and reliability.

<p><b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b></p> <p><b>POLICY NUMBER: 2.02.03</b></p> <p><b>CATEGORY: Laboratory Test</b></p>	<p><b>EFFECTIVE DATE: 10/18/01</b></p> <p><b>REVISED DATE: 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</b></p> <p><b>PAGE: 4 OF: 9</b></p>
---	---

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, e.g., 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. In the absence of such interventions, the benefits of testing are limited, and in fact, can cause psychological harm.

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 for him- or herself. 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 (2008) believes that it is critical for the public to realize that genetic testing is only one part of a complex process which has the potential for both positive and negative impact on health and well-being. The College believes that the following should be considered minimum requirements for any genetic testing protocol: A knowledgeable professional should be involved in the process of ordering and interpreting a genetic test. The consumer should be fully informed regarding what the test can and cannot say about his or her health. The scientific evidence on which a test is based should be clearly stated. The clinical testing laboratory must be accredited by CLIA, the State and/or other applicable accrediting agencies.

**CODES:**      Number      Description

*Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*

**CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.**

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

<b><u>CPT:</u></b>	81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
	81200	ASPA (aspartoacylase) (e.g., Canavan disease) gene analysis, common variants (e.g., E285A, Y231X)
	81205	BCKDHB (branched-chain keto acid dehydrongenase 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,

<b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b>  <b>POLICY NUMBER: 2.02.03</b> <b>CATEGORY: Laboratory Test</b>	<b>EFFECTIVE DATE: 10/18/01</b> <b>REVISED DATE: 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</b>  <b>PAGE: 5 OF: 9</b>
--	--

- 2281DEL6INS7 variant
- 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 mental retardation 1 (e.g., fragile X mental retardation) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles
- 81244 FMR1 (fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; characterization of alleles (e.g., expended size and 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)
- 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, for common deletions or variant (e.g., southeast Asian, Thai, Filipino, Mediterranean, alpha 3.7, alpha 4.2, alpha 20.5, and constant spring)
- 81260 IKBKAP 9inhibitor 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)
- 81290 MCOLN1 (mucolipin 1) (e.g. mucopolipidosis, 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
- 81324 PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis
- 81325 PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence analysis
- 81326 PMP22 (peripheral myelin protein 22) (eg, 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

<p><b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b></p> <p><b>POLICY NUMBER: 2.02.03</b></p> <p><b>CATEGORY: Laboratory Test</b></p>	<p><b>EFFECTIVE DATE: 10/18/01</b></p> <p><b>REVISED DATE: 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</b></p> <p><b>PAGE: 6 OF: 9</b></p>
---	---

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)
- 81410 Aortic dysfunction or dilation (e.g., Marfan Syndrome, Loeys-Dietz Syndrome, Ehler-Danlos Syndrome type IV, arterial tortuosity syndrome); genomic sequence analysis panel, must include sequencing of at least 9 genes, including FBN1, TGFBR1, TGFBR2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, and MYLK
- 81411 Aortic dysfunction or dilation (e.g., Marfan Syndrome, Loeys-Dietz Syndrome, Ehler-Danlos Syndrome type IV, arterial tortuosity syndrome); duplication/deletion analysis panel, must include analyses for TGFBR1, TGFBR2, MYH11, AND COL3A1
- 81412 Ashkenazi Jewish associated disorders (eg, 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
- 81448 Hereditary peripheral neuropathies (eg, Charcot-Marie-Tooth, spastic paraplegia), genomic sequence analysis panel, must include sequencing of at least 5 peripheral neuropathy-related genes (eg, BSCL2, GJB1, MFN2, MPZ, REEP1, SPAST, SPG11, SPTLC1) (*effective 1/1/2018*)
- 81479 Unlisted molecular pathology procedure  
*Copyright © 2018 American Medical Association, Chicago, IL*

**HCPCS:**

- S3800 Genetic testing for amyotrophic lateral sclerosis (ALS)
- S3841 Genetic testing for retinoblastoma
- S3842 Genetic testing for von Hippel-Lindau disease
- S3844 DNA analysis of the connexin26 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

**ICD10:**

Numerous diagnoses

**REFERENCES:**

\*American Academy of Pediatrics. Ethical Issues with Genetic Testing in Pediatrics. Jun 6, 2001. Reaffirmed May 1, 2005 [http://pediatrics.aappublications.org/content/107/6/1451.full.pdf+html?sid=37ba53f6-bd21-4482-bf25-ad1d4c8c37e8] accessed 5/18/18.

<p><b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b></p> <p><b>POLICY NUMBER: 2.02.03</b></p> <p><b>CATEGORY: Laboratory Test</b></p>	<p><b>EFFECTIVE DATE: 10/18/01</b></p> <p><b>REVISED DATE: 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</b></p> <p><b>PAGE: 7 OF: 9</b></p>
---	---

\*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. 2008 Apr 7. [[https://www.acmg.net/docs/ACMG\\_Statement\\_on\\_DTC\\_4.07.08.pdf](https://www.acmg.net/docs/ACMG_Statement_on_DTC_4.07.08.pdf)] accessed 5/18/18.

\*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. Reaffirmed 2015 [[http://www.acog.org/Resources\\_And\\_Publications/Committee\\_Opinions/Committee\\_on\\_Ethics/Patient\\_Testing\\_Ethical\\_Issues\\_in\\_Selection\\_and\\_Counseling](http://www.acog.org/Resources_And_Publications/Committee_Opinions/Committee_on_Ethics/Patient_Testing_Ethical_Issues_in_Selection_and_Counseling)] accessed 5/18/18.

\*American Society of Clinical Oncology. Policy statement update: genetic testing for cancer susceptibility. J Clin Oncol 2003 Jun 15;21(12):2397-406.

Ballana E, et al. Connexins and deafness homepage. Updated: 2014 Jun 15 [<http://davinci.crg.es/deafness/>] accessed 5/18/18.

Bender MA, et al. Sickle cell disease. Gene Reviews. Initial Posting: 15 Sep 2003, updated 2017 Aug 17. Funded by the NIH [<https://www.ncbi.nlm.nih.gov/books/NBK1377/>] accessed 5/18/18.

Bird TD. Myotonic dystrophy type 1. Gene Reviews. Funded by the NIH. Initial posting: 1999 Sep 17. Last update: 2015 Oct 22 [<http://www.ncbi.nlm.nih.gov/books/NBK1165/>] accessed 5/18/18.

Blue Cross BlueShield Association. General approach to genetic testing. Medical Policy Reference Manual. Policy #2.04.91. 2017 Dec 14.

Blue Cross BlueShield Association. Genetic testing for alpha<sub>1</sub>-antitrypsin deficiency. Medical Policy Reference Manual. Policy #2.04.79. 2018 Jan 11.

Blue Cross BlueShield Association. Genetic testing for Duchenne and Becker muscular deficiency. Medical Policy Reference Manual. Policy #2.04.86. 2018 Mar 08.

Blue Cross BlueShield Association. Genetic testing for Fanconi anemia. Medical Policy Reference Manual. Policy #2.04.128. 2017 Dec 14.

Blue Cross BlueShield Association. Genetic testing for FMR1 mutations. Medical Policy Reference Manual. Policy #2.04.83. 2018 Jan 11.

Blue Cross BlueShield Association. Genetic testing for hereditary hearing loss. Medical Policy Reference Manual. Policy #2.04.87. 2018 Apr 12.

Blue Cross BlueShield Association. Genetic testing for hereditary hemochromatosis. Medical Policy Reference Manual. Policy #2.04.80. 2018 May 04.

Blue Cross BlueShield Association. Genetic testing for limb-girdle muscular dystrophies. Medical Policy Reference Manual. Policy #2.04.132. 2018 Apr 12.

Blue Cross BlueShield Association. Genetic testing for Marfan syndrome. Medical Policy Reference Manual. Policy #2.04.129. 2018 Feb 08.

Blue Cross BlueShield Association. Genetic testing for mitochondrial disorders. Medical Policy Reference Manual. Policy #2.04.117. 2017 Jun 08.

Blue Cross BlueShield Association. Genetic testing for Rett syndrome. Medical Policy Reference Manual. Policy #2.04.81. 2018 May 04.

<p><b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b></p> <p><b>POLICY NUMBER: 2.02.03</b></p> <p><b>CATEGORY: Laboratory Test</b></p>	<p><b>EFFECTIVE DATE: 10/18/01</b></p> <p><b>REVISED DATE: 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</b></p> <p><b>PAGE: 8 OF: 9</b></p>
---	---

\*Dong Y, et al. Yield of screening for CADASIL mutations in lacunar stroke and leukoaraiosis. Stroke 2003 Jan;34(1):203-5.

Frantzen C, et al. Von Hippel-Lindau syndrome. Seattle, WA: GeneReviews, University of Washington; 2015 Aug 6. Update 2012 Jun 21 [http://www.ncbi.nlm.nih.gov/books/NBK1463/] accessed 5/18/18.

\*Frayling TM, et al. A genome-wide scan in families with maturity-onset diabetes of the young. Diabetes 2003 Mar;52(3):872-81.

Galanello R, Cao A. Alpha-Thalassemia. Gene Reviews. Initial Posting 2005 Nov 1; Last update: 2016 Dec 29. Funded by the NIH. [http://www.ncbi.nlm.nih.gov/books/NBK1435/] accessed 5/18/18.

\*Garber KB, et al. Fragile X syndrome. Eur J Hum Genet 2008 Jun;16(6):666-72.

Gatheridge MA, et al. Identifying non-Duchenne muscular dystrophy-positive and false negative results in prior Duchenne muscular dystrophy newborn screening programs: a review. JAMA Neurol 2016 Jan;73(1):111-6.

GeneTests [http://www.ncbi.nlm.nih.gov/sites/GeneTests/?db=GeneTests] accessed 5/18/18.

\*Ganalez-Porras JR, et al. Risk of recurrent venous thrombosis in patients with G20210A mutation in the prothrombin gene or factor V Leiden mutation. Blood Coagul Fibrinolysis 2006 Jan;17(1):23-8.

\*Glueck CJ, et al. Factor V Leiden mutation: a treatable etiology for sporadic and recurrent pregnancy loss. Fertil Steril 2008 Feb;89(2):410-6.

\*Grody WW, et al. American College of Medical Genetics Consensus Statement on Factor V Leiden Mutation Testing. Mar/Apr 2001; reaffirmed 2007 May 14 [http://www.acmg.net/StaticContent/StaticPages/Factor\_V.pdf] accessed 5/18/18.

Kaback M. Hexoaminidase A deficiency. Posted: 1999 Mar 11. Funded by the NIH. Developed at the University of Washington, Seattle. Gene Reviews. Update 2011 Aug 11 [http://www.ncbi.nlm.nih.gov/books/NBK1218/] accessed 5/18/18.

\*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.

Kujovich J. Thrombophilia. Updated 2018 Jan 04. Funded by the NIH [http://www.ncbi.nlm.nih.gov/books/NBK1368/] accessed 5/18/18.

\*Laukaitis CM. Genetics for the general internist. Am J Med 2012 Jan;125(1):7-13.

\*Lindgren ML, et al. Applying public health strategies to primary immunodeficiency diseases: a potential approach to genetic disorders. MMWR Recomm Rep 2004 Jan 16;53(RR-1):1-29.

Lohmann D and Gallie B. Retinoblastoma. Gene Reviews. Funded by the NIH. Developed at the University of Washington, Seattle. Initial posting: 2000 Jul 18. Last update: 2015 Nov 19. [http://www.ncbi.nlm.nih.gov/books/NBK1452/] accessed 5/18/18.

Long S and Goldblatt J. MTHFR genetic testing: controversy and clinical implications. Aust Fam Physician 2016 Apr;45(4):237-40.

Majidi S, et al. Can Biomarkers Help Target Maturity-Onset Diabetes of the Young Genetic Testing in Antibody-Negative Diabetes? Diabetes Technol Ther. 2018 Feb;20(2):106-112.

Matalon R. Canavan disease. Gene Reviews, University of Washington. Initial posting: 1999 Sep 16. Last updated 2011 Aug 11. [http://www.ncbi.nlm.nih.gov/books/NBK1234/] accessed 5/18/18.



<p><b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b></p> <p><b>POLICY NUMBER: 2.02.03</b></p> <p><b>CATEGORY: Laboratory Test</b></p>	<p><b>EFFECTIVE DATE: 10/18/01</b></p> <p><b>REVISED DATE: 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</b></p> <p><b>PAGE: 9 OF: 9</b></p>
---	---

\*McGovern MM and Schuchman EH. Acid Sphingomyelinase Deficiency. Gene Reviews. Posted: Dec 7, 2006. Last update: 2015 Jun 18 [<http://www.ncbi.nlm.nih.gov/books/NBK1370/>] accessed 5/18/18.

McKusick V. GBA gene map: Gaucher Disease. GD I, Gaucher disease, noncerebral juvenile glucocerebrosidase deficiency, acid beta-glycosidase deficiency, GBA deficiency. In Web site: OMIM™. Online Mendelian inheritance in man™. Johns Hopkins University. 1986. Edited 2017 Aug 08 [<http://www.ncbi.nlm.nih.gov/omim/230800>] accessed 5/18/18.

National Cancer Institute (NCI). U.S. National Institutes of Health (NIH). Retinoblastoma (PDQ®): treatment. Last modified: 2016 Nov 30 [<http://www.cancer.gov/cancertopics/pdq/treatment/retinoblastoma/healthprofessional>] accessed 5/18/18.

\*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.

Nielsen DE, et al. Diet and exercise changes following direct-to-consumer personal genomic testing. BMC Med Genomics 2017 May 2;10(1):24.

Pastores G. Gaucher Disease. Gene Review. Funded by the NIH. Developed at the University of Washington, Seattle. Initial posting: 2000 Jul 27. Last update: 2015 Feb 26 [<http://www.ncbi.nlm.nih.gov/books/NBK1269/>] accessed 5/18/18.

\*Richter S, et al. Sensitive and efficient detection of RB1 gene mutations enhances care for families with retinoblastoma. Am J Hum Genet 2003 Feb;72(2):253-69.

\*Ruttum MS, et al. Application of genetic approaches to ocular disease. Pediatr Clin North Am 2006 Aug;53(4):751-65.

Schaefer GB, et al. Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions. Genet Med 2013 May;15(5):399-407.

Smith J, et al. Nonsyndromic hearing loss and deafness, DFNB1. Gene Review. Initial Posting: 1998, Last update: 2017 Jul 27 [<http://www.ncbi.nlm.nih.gov/books/NBK1434/>] accessed 5/18/18.

\*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.

\*Task Force on Genetic Testing. Final Report - last reviewed 2006 Apr [<http://www.genome.gov/10002393#%20EXECUTIVE>] accessed 5/18/18.

\*Thapar A, et al. What have we learnt about the causes of ADHD? J Child Psychol Psychiatry 2013 Jan;54(1):3-16.

\*Trent RJ, et al. Complex phenotypes in the haemoglobinopathies: recommendations on screening and DNA testing. Pathology 2006 Dec;38(6):507-19.

\*Vanier M. Prenatal diagnosis of Niemann-Pick diseases types A, B and C. Prenat Diag 2002 Jul;22(7):630-2.

\*Wu O, et al. Screening for thrombophilia in high-risk situations: systematic review and cost-effectiveness analysis. The Thrombosis: Risk and Economic Assessment of Thrombophilia Screening (TREATS) study. Health Technol Assess 2006 Apr;10(11):1-110

\*key article

**KEY WORDS:**

Carrier screening, genetic analysis, inherited disease.

<b>SUBJECT: GENETIC TESTING FOR INHERITED DISORDERS</b>	<b>EFFECTIVE DATE: 10/18/01</b>
<b>POLICY NUMBER: 2.02.03</b>	<b>REVISED DATE: 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</b>
<b>CATEGORY: Laboratory Test</b>	<b>PAGE: 10 OF: 9</b>

---

---

## CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

---

---

There is currently a Local Coverage Determination (LCD) for Molecular Pathology Procedures. Please refer to the following LCD website for Medicare Members: [https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35000&ver=79&CtrctrSelected=298\\*1&Ctrctr=298&s=41&DocType=Active&bc=AggAAAIBA AAA&](https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35000&ver=79&CtrctrSelected=298*1&Ctrctr=298&s=41&DocType=Active&bc=AggAAAIBA AAA&)