

Department of Origin: Integrated Healthcare Services	Effective Date: 05/09/24
Approved by: Chief Medical Officer	Date Approved: 05/09/24
Clinical Policy Document: Genetic Testing, Hereditary and Somatic Conditions	Replaces Effective Clinical Policy Dated: 06/12/23
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PURPOSE:

The intent of this clinical policy is to provide coverage guidelines for genetic testing for inherited and somatic conditions when benefits are available. When there is a separate medical criterion or policy addressing a specific genetic test or clinical scenario, that document should be used to determine whether the test is clinically indicated.

Please refer to the member’s benefit document for specific information. To the extent there is any inconsistency between this policy and the terms of the member’s benefit plan or certificate of coverage, the terms of the member’s benefit plan document will govern.

POLICY:

Benefits must be available for health care services. Health care services must be ordered by a provider. Licensed Genetic Counselors may also order genetic tests if it is within the scope of practice of their state licensure. Health care services must be medically necessary, applicable conservative treatments must have been tried, and the most cost-effective alternative must be requested for coverage consideration.

COVERAGE:

- I. Requests for genetic testing - must satisfy the following: A - C
 - A. Member (includes embryo or fetus) displays clinical features (symptomatic), or is at direct risk of inheriting the mutation in question (presymptomatic)

[Note: this includes family history of *autosomal dominant* disorders such as, but not limited to, Huntington’s disease, Marfan syndrome, neurofibromatosis, polycystic kidney disease. This also includes preimplantation genetic diagnosis [PGD]]
 - B. A *health care professional trained in genetics*, independent of the laboratory performing the testing, has reviewed and documented family history, advised the member of the potential harms/benefits of the testing and implications of the test results, and obtained written formal consent

[Note: Members who have no knowledge of their genetic family history (such as, members who are adopted) will be considered to be at high risk.]
 - C. After history, physical examination and completion of conventional diagnostic studies, a definitive diagnosis remains uncertain and a valid specific test exists for the suspected condition – as evidenced by all of the following: 1 - 3
 1. Each test has been approved for its intended use by the appropriate regulatory/oversight body (implies analytic validity); and
 2. Each test has sufficient sensitivity or specificity (*clinical validity*) for targeting the member’s specific clinical condition; and
 3. The results of each test will directly impact clinical decision-making and clinical care (*clinical utility*) for the individual, such as, but not limited to the following: a - c
 - a. Guiding surveillance for complications (eg, increase in frequency of colonoscopies for members with hereditary non-polyposis colorectal cancer [HNPCC] gene mutation).
 - b. Employing direct risk reduction strategies (eg, prophylactic mastectomy and/or oophorectomy for breast cancer [BRCA] gene mutation or decision to not implant affected embryo).

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- c. Determining avenues of medical therapy (eg, children with congenital deafness due to connexin 26 gene mutations tend to respond better to cochlear implants than those with deafness due to other causes).
- II. Known gene mutation of a moderate or high-risk gene associated with an inherited condition/ syndrome in a biologically *close blood relative*
 - A. There is a known familial variant (ie, the location of the mutation is known), single site testing should be performed.
 - B. There is a known gene mutation and the specific location of the mutation is not known – full sequence analysis, full duplication analysis, and/or common and uncommon deletion testing may be performed.
- III. The request is for confirmatory testing (ie, member paid out of pocket for a genetic test [GT], eg, 23andMe or other non-covered GT) - single site testing should be performed.
- IV. Request for genetic testing meets either of the following
 - A. An internally developed clinical policy; or
 - B. Another designated criterion, eg, Genetic Testing Registry <https://www.ncbi.nlm.nih.gov/gtr/>
- V. Multi-gene Testing (panels)
 - A. For testing panels including but not limited to multiple genes or multiple conditions, and in cases where a tiered approach/method is clinically available, testing should target the gene variant with the highest disease-causing penetrance, first.
 - B. The member’s personal and/or family history is suggestive of a syndrome that can be explained by more than one gene mutation.
- VI. Request for comprehensive genetic analysis on multiple family members that are members of the Plan, are initially covered for one affected family member only.
 - A. If a variant is identified, the other family members can then be tested for that specific variant.
 - B. If a variant is not found in the affected individual, testing other family members would have no benefit given that the familial variant is unknown.

EXCLUSIONS (not limited to):

Refer to member’s Certificate of Coverage or Summary Plan Description.

- Direct-to-consumer testing

DEFINITIONS:

Allele:

An allele is one of two or more versions of a gene. An individual inherits two alleles for each gene, one from each parent. If the two alleles are the same, the individual is homozygous for that gene. If the alleles

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are different, the individual is heterozygous. Though the term allele was originally used to describe variation among genes, it now also refers to variation among non-coding DNA sequences.

Analytic Validity:

How accurately and reliably the test measures the genotype of interest. A major component in the validation of an analytical technique is the technique's ability to accurately determine the presence of the substance it is seeking. It must measure the target substance without a great range of variation over a number of trials. The technique also must be proven to work reliably at multiple labs to be validated by this testing.

Autosomal:

Pertaining to a chromosome that is not a sex chromosome. People normally have 22 pairs of autosomes (44 autosomes) in each cell, together with 2 sex chromosomes, X and Y in a male and X and X in a female.

Autosomal dominant:

A pattern of inheritance in which an affected individual has one copy of a mutant gene and one normal gene on a pair of autosomal chromosomes. Individuals with autosomal dominant diseases have a 50% chance of passing the mutant gene and therefore the disorder onto each of their children. Examples of autosomal dominant diseases include Huntington disease, neurofibromatosis, and polycystic kidney disease.

Autosomal recessive:

A genetic condition that appears only in individuals who have received two copies of an autosomal gene, one copy from each parent. The gene is on an autosome, a nonsex chromosome. The parents are carriers who have only one copy of the gene and do not exhibit the trait because the gene is recessive to its normal counterpart gene. If both parents are carriers, there is a 25% chance of a child inheriting both abnormal genes and, consequently, developing the disease. There is a 50% chance of a child inheriting only one abnormal gene and of being a carrier, like the parents, and there is a 25% chance of the child inheriting both normal genes. Cystic fibrosis (CF) is an example of an autosomal recessive disorder. A child with CF has the CF gene on both chromosome 7s and so is said to be homozygous for CF. The parents each have one CF and one normal paired gene and so are said to be heterozygous for CF.

Chromosome:

In the nucleus of each cell, the DNA molecule is packaged into thread-like structures called chromosomes. Each chromosome is made up of DNA tightly coiled many times around proteins called histones that support its structure.

Clinical Utility:

The evidence of improved measurable clinical outcomes, and its usefulness and added value to patient management decision-making compared with current management without the testing.

Clinical Validity:

How consistently and accurately the test detects or predicts the intermediate or final outcomes of interest.

First-degree relative:

A blood relative who shares 50% of the individual's genes (parents, full siblings, and children)

Genetic Disease:

A disease, such as cystic fibrosis, that has its origin in changes to the genetic material, DNA.

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Genetic Test:

A genetic test involves the analysis of chromosomes, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), genes, or gene products (eg, enzymes and other proteins) to detect heritable or somatic variations related to disease or health. Whether a laboratory method is considered a genetic test also depends on the intended use, claim or purpose of a test.

Genome:

Life is specified by genomes. Every organism, including humans, has a genome that contains all of the biological information needed to build and maintain a living example of that organism. The biological information contained in a genome is encoded in its deoxyribonucleic acid (DNA) and is divided into discrete units called genes. Genes code for proteins that attach to the genome at the appropriate positions and switch on a series of reactions called gene expression.

Health care professionals trained in genetics:

A genetics professional has experience and an educational background in genetics, counseling, and hereditary syndromes to provide accurate risk assessment and empathetic genetic counseling to patients and their families. Genetics professionals include people certified in any of the following ways:

- American Board of Genetic Counseling (ABGC) or American Board of Medical Genetics and Genomics (ABMGG) board certified/board eligible⁹ or a licensed genetic counselor
- Advanced Genetics Nursing Certification (AGN-BC)⁹
- Advanced Clinical Genomics Nurse (ACGN) credential⁹
- Clinical Genomics Nurse (CGN) certification⁹
- Cancer Genetic Risk Assessment (CGRA) certification⁹
- Advanced practice oncology nurse or physician assistant with specialized education in cancer genetics and hereditary cancer predisposition syndromes. The Advanced Oncology Certified Nurse Practitioner (AOCNP) credentials, or equivalent certification from the Oncology Nursing Certification Corporation (ONCC) is preferred.⁹
- Board-certified/board-eligible physician with experience in cancer genetics (defined as education resulting in a certification and undergoing ongoing continuing medical education in cancer genetics and hereditary cancer predisposition syndromes)⁹
- A registered nurse with specialized education in cancer genetics and hereditary cancer predisposition syndromes (defined as education resulting in a certification and undergoing ongoing continuing medical education in cancer genetics and hereditary cancer predisposition syndromes)⁹
- Board-certified specialty care physician with experience in the diagnosis and treatment of the hereditary condition, eg, cardiologist ordering genetic testing for hypertrophic cardiomyopathy

Heterozygous:

Possessing two different forms of a particular gene, one inherited from each parent.

Homozygous:

Possessing two identical forms of a particular gene, one inherited from each parent.

Karyotype (G-banded) analysis:

A conventional cytogenetic evaluation that can detect larger chromosomal abnormalities (eg, loss or gain of an entire chromosome or of large parts of chromosomes), or chromosomal rearrangements such as translocations (ie, when a portion of a chromosome breaks off and rejoins with another chromosome). Cells from blood, tissue, or body fluid (eg, bone marrow, amniotic fluid) are cultured so that the

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chromosomes are visible; these cells are then treated to reveal banding patterns that are specific to each chromosome. Examination of these cells by standard light microscopy permits trained technologists and cytogeneticists to examine the chromosomes for abnormalities of number or structure. Examples of constitutional conditions (ie, those present at birth) detectable by karyotype analysis include Down Syndrome (trisomy 21), Turner Syndrome (monosomy X), and Klinefelter syndrome (XXY). Acquired conditions (ie, those that develop after birth, typically associated with malignancy) can also be detected.

Penetrance:

The likelihood that a given gene will result in disease.

Second-degree relative:

A blood relative who shares 25% of the individual’s genes (grandparents, grandchildren, aunts, uncles, nephews, nieces, and half siblings).

Sex chromosome:

The X or Y chromosome in humans.

X-linked Disorder:

In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

BACKGROUND:

Genetic tests look for abnormalities in a person’s genes (DNA, RNA, chromosomes), or the presence/absence of key proteins whose production is directed by specific genes. Abnormalities in either could indicate an inherited disposition to a disorder.

A gene mutation is a permanent change in the DNA sequence that makes up a gene. Mutations range in size from a single DNA building block (DNA base) to a large segment of a chromosome.

Gene mutations occur in two ways: they can be inherited from a parent or acquired during a person’s lifetime. Mutations that are passed from parent to child are called hereditary mutations or germline mutations (because they are present in the egg and sperm cells, which are also called germ cells). This type of mutation is present throughout a person’s life in virtually every cell in the body and is the focus of this policy.

Mutations that occur only in an egg or sperm cell, or those that occur just after fertilization, are called new (de novo) mutations. De novo mutations may explain genetic disorders in which an affected child has a mutation in every cell, but has no family history of the disorder.

Mutations may also occur in a single cell within an early embryo. As all the cells divide during growth and development, the individual will have some cells with the mutation and some cells without the genetic change. This situation is called mosaicism.

Some genetic changes are very rare; others are common in the population. Genetic changes that occur in more than 1 percent of the population are called polymorphisms. They are common enough to be considered a normal variation in the DNA. Polymorphisms are responsible for many of the normal differences between people such as eye color, hair color, and blood type. Although many polymorphisms

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have no negative effects on a person's health, some of these variations may influence the risk of developing certain disorders.

CODING:

CPT® or HCPCS

- 81161 DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
- 81171 AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
- 81172 AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; characterization of alleles (eg, expanded size and methylation status)
- 81173 AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence
- 81174 AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; known familial variant
- 81177 ATN1 (atrophin 1) (eg, dentatorubral-pallidoluyian atrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
- 81178 ATXN1 (ataxin 1) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
- 81179 ATXN2 (ataxin 2) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
- 81180 ATXN3 (ataxin 3) (eg, spinocerebellar ataxia, Machado-Joseph disease) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
- 81181 ATXN7 (ataxin 7) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
- 81182 ATXN8OS (ATXN8 opposite strand [non-protein coding]) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
- 81183 ATXN10 (ataxin 10) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
- 81184 CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
- 81185 CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; full gene sequence
- 81186 CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; known familial variant
- 81187 CNBP (CCHC-type zinc finger nucleic acid binding protein) (eg, myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
- 81188 CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
- 81189 CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; full gene sequence
- 81190 CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; known familial variant(s)
- 81200 ASPA (aspartoacylase) (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X)
- 81204 AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; characterization of alleles (eg, expanded size or methylation status)
- 81205 BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (eg, maple syrup urine disease) gene analysis, common variants (eg, R183P, G278S, E422X)
- 81209 BLM (Bloom syndrome, RecQ helicase-like)(eg, Bloom syndrome) gene analysis, 2281 del6ins7 variant

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81220 CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)

81221 CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants

81222 CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants

81223 CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence

81224 CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)

81234 DMPK (DM1 protein kinase (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles

81239 DMPK (DM1 protein kinase (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)

81242 FANCC (Fanconi anemia, complementation group C) (eg, Fanconi anemia, type C) gene analysis, common variant (eg, IVS4+4A>T)

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 promoter methylation status)

81247 G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, A, A-)

81248 G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; known familial variant(s)

81249 G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; full gene sequence

81250 G6PC (glucose-6-phosphatase, catalytic subunit) (eg, Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (eg, R83C, Q347X)

81251 GBA (glucosidase, beta, acid) (eg, Gaucher disease) gene analysis, common variants (eg, N370S, 84GG, L444P, IVS2+1G>A)

81252 GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; full gene sequence

81253 Hearing loss (eg, 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 GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; known familial variants GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; known familial variants

81254 GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (eg, nonsyndromic hearing loss) gene analysis, common variants

81256 HFE (hemochromatosis) (hereditary hemochromatosis) gene analysis, common variants (eg C282Y, H63D)

81271 HTT (huntingtin) (eg, Huntington disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles

81277 Cytogenomic neoplasia (genome-wide) microarray analysis, interrogation of genomic regions for copy number and loss-of-heterozygosity variants for chromosomal abnormalities

81284 FXN (frataxin) (eg, Friedreich ataxia) gene analysis; evaluation to detect expanded alleles

81285 FXN (frataxin) (eg, Friedreich ataxia) gene analysis; characterization of alleles (eg, expanded size)

81286 FXN (frataxin) (eg, Friedreich ataxia) gene analysis; full gene sequence

81289 FXN (frataxin) (eg, Friedreich ataxia) gene analysis; known familial variants

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81290 MCOLN1 (mucopolin 1) (eg, Mucopolidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb)

81302 MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; full sequence analysis

81303 MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; known familial variant

81304 MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; duplication/deletion variants

81312 PABPN1 (poly[A] binding protein nuclear 1) (eg, oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles

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) (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330)

81331 SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (eg, Prader-Willi syndrome and/or Angelman syndrome), methylation analysis

81332 SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, Member 1) (eg, alpha-1-antitrypsin deficiency), gene analysis, common variants (eg, *S and *Z)

81333 TGFBI (transforming growth factor beta-induced) (eg, corneal dystrophy) gene analysis, common variants (eg, R124H, R124C, R124L, R555W, R555Q)

81334 RUNX1 (runt related transcription factor 1) (eg, acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (eg, exons 3-8)

81343 PPP2R2B (protein phosphatase 2 regulatory subunit beta) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles

81344 TBP (TATA box binding protein) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles

81400 Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg, SNP], by techniques such as restriction enzyme digestion or melt curve analysis)

81401 Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using non-sequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)

81402 Molecular pathology procedure, Level 3 (eg, >10 SNPs, 2-10 methylated variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene arrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD])

81403 Molecular pathology procedure, Level 4 (eg, 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 (eg, 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 (eg, 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 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)

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81407 Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of > 50 exons, sequence analysis of multiple genes on 1 platform)

81408 Molecular pathology procedure, Level 9 (eg, analysis of > 50 exons in a single gene by DNA sequence analysis, full gene sequence)

81410 Aortic dysfunction or dilation (eg, 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 (eg, 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

81413 Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A

81414 Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); duplication/deletion gene analysis panel, must include analysis of at least 2 genes, including KCNH2 and KCNQ1

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 (eg, 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 (eg, 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

81434 Hereditary retinal disorders (eg, retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy), genomic sequence analysis panel, must include sequencing of at least 15 genes, including ABCA4, CNGA1, CRB1, EYS, PDE6A, PDE6B, PRPF31, PRPH2, RDH12, RHO, RP1, RP2, RPE65, RPGR, and USH2A

81437 Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL

81438 Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL

81439 Inherited cardiomyopathy (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy) genomic sequence analysis panel, must include sequencing of at least 5 genes, including DSG2, MYBPC3, MYH7, PKP2, and TTN

81440 Nuclear encoded mitochondrial genes (eg, neurologic or myopathic phenotypes), genomic Nuclear encoded mitochondrial genes (eg, neurologic or myopathic phenotypes), genomic sequence panel, must include analysis of at least 100 genes, including BCS1L, C10orf2, COQ2, COX10, DGUOK, MPV17,

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OPA1, PDSS2, POLG, POLG2, RRM2B, SCO1, SCO2, SLC25A4, SUCLA2, SUCLG1, TAZ, TK2, and TYMP

81441 Inherited bone marrow failure syndromes (IBMFS) (eg, 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 (eg, 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, NRAS, PTPN11, RAF1, RIT1, SHOC2, and SOS1

81443 Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucopolidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (eg, ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH

81448 Hereditary peripheral neuropathies (eg, Charco-Marie-Tooth, spastic paraplegia), genomic sequence analysis panel, must include sequencing of at least 5 peripheral

81460 Whole mitochondrial genome (eg, Leigh syndrome, mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes [MELAS], myoclonic epilepsy with ragged-red fibers [

81465 Whole mitochondrial genome large deletion analysis panel (eg, Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed

81470 X-linked intellectual disability (XLID) (eg, 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) (eg, 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

S3800 Genetic testing for amyotrophic lateral sclerosis (ALS)

S3840 DNA analysis for germline mutations of the RET-oncogene for susceptibility to multiple neuroendocrine neoplasia type 2

S3841 Genetic testing for retinoblastoma

S3842 Genetic testing for Von Hippel-Lindau disease

S3844 DNA analysis of the connexin 26 (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

S3852 DNA analysis for APOE epsilon 4 allele for susceptibility to Alzheimer's disease

S3853 Genetic testing for myotonic muscular dystrophy

S3861 Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada Syndrome

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

0156U Copy number (eg, intellectual disability, dysmorphism), sequence analysis

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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

0229U Gene analysis (branched chain amino acid transaminase 1 and IKAROS family zinc finger 1), promoter methylation analysis

0230U AR (androgen receptor) (eg, 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

0231U CACNA1A (calcium voltage-gated channel subunit alpha 1A) (eg, 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

0232U CSTB (cystatin B) (eg, 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

0233U FXN (frataxin) (eg, 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

0234U MECP2 (methyl CpG binding protein 2) (eg, 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

0236U SMN1 (survival of motor neuron 1, telomeric) and SMN2 (survival of motor neuron 2, centromeric) (eg, spinal muscular atrophy) full gene analysis, including small sequence changes in exonic and intronic regions, duplications and deletions, and mobile element insertions

0237U Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia), genomic sequence analysis panel including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions

0355U APOL1 (apolipoprotein L1) (eg, chronic kidney disease), risk variants (G1, G2)

0378U RFC1 (replication factor C subunit 1), repeat expansion variant analysis by traditional and repeat-primed PCR, blood, saliva, or buccal swab

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2. Clinical Policy: Coverage Determination Guidelines (MP/C009)
3. Clinical Policy: Laboratory Tests (MP/L001)
4. Clinical Policy: Genetic Testing, Hereditary Cancer Syndromes (MC/L010)

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Clinical Policy Document: Genetic Testing, Hereditary and Somatic Conditions	Replaces Effective Clinical Policy Dated: 06/12/23
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Nondiscrimination & Language Access Policy



Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:

Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If you need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If you believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If you need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitmi shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë. Telefononi në 1-800-332-6501 (TTY: 711).

Arabic: تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف 1-800-332-6501 (رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: यान द : य द आप िहंदी बोलते ह तो आपके िलए मु त म भाषा सहायता सेवाएं उपल थ ह 1-800-332-6501 (TTY: 711) पर कॉल कर ।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1-800-332-6501 (TTY: 711) 번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer 1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzsch, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ ໂດຍບໍ່ເສັຽຄ່າ, ຈະມີມື້ອມໃຫ້ທ່ານ. ໂທສ 1-800-332-6501 (TTY: 711).