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## Subject: Genetic Testing

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### DESCRIPTION:

A genetic or genomic test involves an analysis of human chromosomes, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), or gene products (e.g., enzymes and other types of proteins) to detect heritable or somatic variants, genotypes, or phenotypes related to disease and health.

There are several different types of genetic tests available today, including:

- **Carrier testing:** Carrier testing is used to identify people who carry one copy of a gene mutation that, when present in two copies, causes a genetic disorder. This type of testing is offered to individuals who have a family history of a genetic disorder and to people in certain ethnic groups with an increased risk of specific genetic conditions. If both parents are tested, the test can provide information about a couple's risk of having a child with a genetic condition.
- **Diagnostic testing:** Diagnostic testing is used to identify or rule out a specific genetic or chromosomal condition. In many cases, genetic testing is used to confirm a diagnosis when a particular condition is suspected based on physical signs and symptoms. Diagnostic testing can be performed before birth or at any time during a person's life, but is not available for all genes or all genetic conditions.
- **Newborn screening:** Newborn screening is used just after birth to identify genetic disorders that can be treated early in life. Millions of babies are tested each year in the United States. All states currently test infants for phenylketonuria (a genetic disorder that causes intellectual disability if left untreated) and congenital hypothyroidism (a disorder of the thyroid gland). Most states also test for other genetic disorders.
- **Predictive and presymptomatic testing:** Predictive and presymptomatic types of testing are used to detect gene variants associated with disorders that appear after birth, often later in life. These tests can be helpful to people who have a family member with a genetic disorder, but

who have no features of the disorder themselves at the time of testing. Predictive testing can identify variants that increase a person's risk of developing disorders with a genetic basis, such as certain types of cancer. Presymptomatic testing can determine whether a person will develop a genetic disorder before any signs or symptoms appear.

- **Preimplantation testing:** Preimplantation testing, also called preimplantation genetic diagnosis (PGD), is a specialized technique that can reduce the risk of having a child with a particular genetic or chromosomal disorder. It is used to detect genetic changes in embryos that were created using assisted reproductive techniques such as in-vitro fertilization. To perform preimplantation testing, a small number of cells are taken from these embryos and tested for certain genetic changes.
- **Prenatal testing:** Prenatal testing is used to detect changes in a fetus's genes or chromosomes before birth. This type of testing is offered during pregnancy if there is an increased risk that the baby will have a genetic or chromosomal disorder. In some cases, prenatal testing can lessen a couple's uncertainty or help them make decisions about a pregnancy. However, it cannot identify all possible inherited disorders and birth defects.

Cytogenetics is a branch of genetics that is involved with heredity and the cellular components, particularly chromosomes, associated with heredity. Cytogenetic testing involves the determination of chromosome number and structure. Variations in either the chromosome number or structure can produce numerous abnormalities that may lead to cancer, syndromes, or birth defects.

## POSITION STATEMENT:

**NOTE:** Coverage for genetic testing, screening, and counseling are applicable only under those contracts that include benefits for genetic testing, preventive health services, screening services, and medical counseling. Coverage may be governed by state or federal mandates.

### GENETIC TESTING TO ESTABLISH A DIAGNOSIS OF INHERITABLE DISEASE

Genetic testing **meets the definition of medical necessity** when used to establish a molecular diagnosis of an inheritable disease when the following criteria are met:

- The member displays clinical features, or is at direct risk of inheriting the [mutation](#) in question (presymptomatic); **AND**
- The result of the test will directly impact the treatment being delivered to the member; **AND**
- After history, physical examination, pedigree analysis, genetic counseling, and completion of conventional diagnostic studies, a definitive diagnosis remains uncertain, and one of the diagnoses listed in the table below may be suspected (the list is not all-inclusive)

**OR**

- For assisted reproductive technology (also known as preimplantation genetic testing [PGT] or preimplantation genetic diagnosis [PGD]) cases (i.e. in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), artificial insemination) where either parent is known to have a chromosomal abnormality. Results of testing must impact reproductive treatment and planning.  
**NOTE:** applicable only under those contracts that include infertility benefits.

### Diagnosis Table:

Albinism (albino)	Cystic Fibrosis (CF) <b>(see criteria below)</b>	Hemochromatosis (gene sequence analysis)	Retinoblastoma
Angelman Syndrome (see criteria below)	Duchenne Muscular Dystrophy (DMD) or Becker Muscular Dystrophy (BMD) <b>(see criteria below)</b>	Huntington's Chorea (see criteria below)	Sickle Cell Anemia
Canavan Disease	Fabry Disease	Myotonic Dystrophy (see criteria below)	Spinal Muscular Atrophy
Chromosome 22q11.2 Deletion Syndrome <b>(see criteria below)</b>	Fragile X Syndrome (see criteria below)	Niemann-Pick (enzyme or mutation analysis)	Tuberous Sclerosis (see criteria below)
Charcot-Marie-Tooth Disease	Gaucher Disease (see criteria below)	Prader-Willi Syndrome <b>(see criteria below)</b>	Von Hippel-Lindau Syndrome

The following test list includes, but is not limited to, specific indications for testing that may **meet the definition of medical necessity** and those for which testing is considered **experimental or investigational**.

Diagnosis	Criteria
<b>Angelman Syndrome</b>	Genetic testing for Angelman Syndrome <b>meets the definition of medical necessity</b> for <b>ONE</b> of the following: <ul style="list-style-type: none"> <li>• Cytogenic deletion is suspected on chorionic villus sampling (CVS) or amniocentesis</li> <li>• Previous child diagnosed with Angelman Syndrome caused by a UBE3A mutation.</li> </ul>
<b>Carrier Screening for Genetic Diseases</b>  Targeted carrier screening is performed in individuals having an increased risk based on population carrier prevalence, or personal or family history.	Targeted carrier screening for X-linked and autosomal recessive genetic diseases (also called risk-based or ethnic-based testing) <b>meets the definition of medical necessity</b> for members who are pregnant or are considering pregnancy and are at increased risk of having offspring with an X-linked or autosomal recessive disease when one of the following criteria is met: <ul style="list-style-type: none"> <li>• One or both individuals have a first- or second-degree relative who is affected <b>OR</b></li> <li>• One individual is known to be a carrier <b>OR</b></li> <li>• One or both individuals are members of a population known to have a carrier rate that exceeds a threshold</li> </ul>

<p>Non-targeted carrier screening involves screening individuals or couples for disorders in many genes by next-generation sequencing.</p>	<p>considered appropriate for testing for a particular condition.</p> <p>(First-degree relatives include a biological parent, brother, sister, or child; second-degree relatives include biologic grandparent, aunt, uncle, niece, nephew, grandchildren, and half-sibling.)</p> <p><b>AND ALL</b> of the following criteria are met:</p> <ul style="list-style-type: none"> <li>• The natural history of the disease is well understood and there is a reasonable likelihood that the disease is one with high morbidity in the homozygous or compound heterozygous state</li> <li>• Alternative biochemical or other clinical tests to definitively diagnose carrier status are not available, or, if available, provide an indeterminate result or are individually less efficacious than genetic testing</li> <li>• The genetic test has adequate clinical validity to guide clinical decision making and residual risk is understood;</li> <li>• If targeted testing is performed by a panel, the panel meets the minimum number of recommended gene variants but does not exceed the maximum (see note below)</li> <li>• Previous carrier screening or individual targeted gene testing for the gene variant(s) of interest has not been performed; <b>AND</b></li> <li>• An association of the marker with the disorder has been established.</li> </ul> <p>All targeted screening not meeting any of the above criteria <b>does not meet the definition of medical necessity.</b></p> <p>Non-targeted carrier screening panels for autosomal recessive and X-linked genetic disorders <b>meets the definition of medical necessity</b> as an alternative to testing of individual genes (eg, SMN1 gene and CFTR gene) for members who are pregnant or are considering pregnancy at any risk level including high risk and average risk when all of the following criteria are met:</p> <ul style="list-style-type: none"> <li>• The natural history of each disease is well understood and there is reasonable likelihood that the disease is one with high morbidity or early mortality in the homozygous or compound homozygous state;</li> </ul>
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	<ul style="list-style-type: none"> <li>•Alternative biochemical or other clinical tests to definitively diagnose carrier status are not available, or, if available, provide an indeterminate result or are individually less efficacious than genetic testing;</li> <li>•The genetic test has adequate clinical validity to guide clinical decision-making and residual risk is understood;</li> <li>•An association of the markers with the disorders has been established;</li> <li>•If testing is performed by a panel, the panel meets the minimum number of recommended gene variants but does not exceed the maximum (see note below); <b>AND</b></li> <li>•Previous carrier screening has not been performed.</li> </ul> <p>Non-targeted carrier screening panels are considered <b>experimental or investigational</b> in all other situations when above criteria are not met. There is insufficient clinical evidence to permit conclusions on net health outcomes.</p> <p><b>Notes:</b></p> <p>The statements above only apply if there are no separate position statements that outline specific criteria for carrier screening. If a separate position statement exists, then criteria for medical necessity in that position statement supersedes these statements.</p> <p>Targeted carrier screening for autosomal recessive or X-linked conditions is also called risk-based test or ethnic-based testing. If targeted testing is performed by a panel, the most appropriate panel code available should be used. The panel and the panel billing code should include CFTR and SMN1. If the carrier screening test is a panel less than 15 genes and does not include CFTR or SMN1, but would be 15 or more genes if including CFTR or SMN1, then it should be coded with 81443. Panels closely resembling 81443 should be billed using 81443 rather than billing individually (ie, unbundling).</p> <p>Non-targeted carrier screening applies to persons of any risk including average risk. Any panel using 81443 for non-targeted carrier screening must include the CFTR and SMN1 genes. Non-targeted carrier screening panels should include the minimum number of genes but not exceed the</p>
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	<p>maximum number of genes recommended by professional guidelines from the American College of Obstetricians and Gynecologists (ACOG; 2-22 conditions) or the American College of Medical Genetics and Genomics (ACMG; 113 genes).</p> <p>In 2021, the ACMG recommended that the phrase “expanded carrier screening” be replaced by “carrier screening” as expanded carrier screening is not well or precisely defined by professional organizations. Previously, ACMG defined expanded panels as those that use next-generation sequencing to screen for variants in many genes, as opposed to gene-by-gene screening (eg, ethnic-specific screening or panethnic testing for cystic fibrosis).</p> <p>The ACMG consensus group specified gene recommendations which include testing for 97 autosomal recessive genes and 16 X-linked genes, all of which associate with disorders of moderate, severe, or profound severity and are of 1/200 or greater carrier frequency. Non-targeted carrier screening panels that test for genes beyond this provide diminishingly small results, and pleiotropy, locus heterogeneity, variant interpretation, and poor genotype-phenotype correlation may disproportionately impact the ability to provide accurate prognostic information.</p> <p>(BCBSA 2.04.107 Carrier Screening for Genetic Diseases)Carrier screening should only be performed in adults.</p>
<p><b>Chromosomal Microarray Analysis (CMA)</b></p> <p>(Also referred to as genomic hybridization (CGH) or array comparative genomic hybridization (aCGH).)</p> <p><sup>1</sup>(Anora™ miscarriage test, CombiSNP™ Array for Pregnancy Loss, and CombiBAC™ Array)</p>	<p>Chromosome microarray (CMA) analysis <b>meets the definition of medical necessity</b> as an alternative to karyotyping in members who are undergoing invasive diagnostic prenatal (fetal) testing,</p> <p><sup>1</sup>Chromosomal microarray analysis of fetal tissue <b>meets the definition of medical necessity</b> for the evaluation of pregnancy loss in cases of pregnancy loss at 20 weeks of gestation or earlier when there is a maternal history of recurrent miscarriage (defined as a history of 2 or more failed pregnancies); or in all cases of pregnancy loss after 20 weeks of gestation.</p>

	<p>Chromosomal microarray analysis of fetal tissue in cases of miscarriage or intrauterine fetal demise is considered <b>experimental or investigational</b> in all other situations. There is insufficient clinical evidence to permit conclusions on net health outcomes.</p> <p>The use of next generation sequencing in the setting of invasive prenatal testing is considered <b>experimental or investigational</b>. There is a lack of clinical data to permit conclusions on efficacy and net health outcomes.</p>
<b>Chromosome 22q11.2 Deletion Syndrome</b>	Genetic testing for chromosome 22q11.2 deletion syndrome <b>meets the definition of medical necessity</b> in an at-risk fetus based on ultrasound findings or family history.
<b>Cystic Fibrosis (CF)</b>	<p>Genetic carrier testing for cystic fibrosis <b>meets the definition of medical necessity</b> for <b>ONE</b> of the following:</p> <ul style="list-style-type: none"> <li>• Individuals with a <u>positive</u> family history of CF</li> <li>• Either parent has a diagnosis of CF</li> <li>• Fetal echogenic bowel has been identified on ultrasound</li> <li>• Couples currently planning a pregnancy or seeking prenatal testing.</li> </ul>
<b>Duchenne Muscular Dystrophy (DMD) and Becker Muscular Dystrophy (BMD)</b>	<p>Genetic testing for DMD gene variants <b>meets the definition of medical necessity</b> for the following conditions:</p> <ul style="list-style-type: none"> <li>• In a male with signs and symptoms of a dystrophinopathy in order to confirm the diagnosis and direct treatment.</li> <li>• For at-risk female* relatives: <ul style="list-style-type: none"> <li>○ To confirm or exclude the need for cardiac surveillance</li> <li>○ For preconception testing to determine the likelihood of an affected offspring in a woman considering a pregnancy.</li> </ul> </li> <li>• For at-risk male** offspring to confirm or exclude the need for medical and cardiac surveillance.</li> </ul> <p>*(At-risk female: first- and second-degree female relatives and include the proband's mother, female siblings of the proband, female offspring of the proband, the proband's</p>

	<p>maternal grandmother, maternal aunts, and their offspring).</p> <p><b>**</b>(At-risk male: an asymptomatic male offspring of a female carrier or an asymptomatic male sibling of a patient with a DMD-associated dystrophinopathy).</p> <p>Genetic testing for DMD gene variants is considered <b>experimental or investigational</b> in all other situations. There is a lack of clinical data to permit conclusions on health outcomes.</p>
<p><b>Fetal RHD</b></p> <p>(SensiGene™ Fetal RHD)</p>	<p>Noninvasive fetal RHD genotyping using cell-free fetal DNA is considered <b>experimental or investigational</b>. It is uncertain whether this testing will lead to improved health outcomes and the evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>FMR1 Variants (Including Fragile X Syndrome)</b></p>	<p>See below.</p>
<p><b>Gaucher Disease</b></p>	<p>Genetic testing for Gaucher Disease <b>meets the definition of medical necessity</b> for <b>ONE</b> of the following:</p> <ul style="list-style-type: none"> <li>• There is an affected family member who has an identified GBA mutation or Gaucher disease</li> <li>• Either parents or a previously affected sibling have an identified GBA mutation or Gaucher disease.</li> </ul>
<p><b>Huntington's Chorea</b></p>	<p>Genetic testing for Huntington's chorea <b>meets the definition of medical necessity</b> when there is a confirmed diagnosis of Huntington's chorea in the family.</p>
<p><b>Myotonic Dystrophy</b></p>	<p>Genetic testing for myotonic dystrophy (Types 1 or 2) <b>meets the definition of medical necessity</b> for <b>ONE</b> of the following:</p> <ul style="list-style-type: none"> <li>• At least one parent has a confirmed diagnosis of myotonic dystrophy</li> <li>• At least one parent has been diagnosed as a presymptomatic carrier of myotonic dystrophy.</li> </ul>
<p><b>Prader-Willi Syndrome</b></p>	<p>Genetic testing for Prader-Willi Syndrome <b>meets the definition of medical necessity</b> when <b>ONE</b> of the following:</p>



	<ul style="list-style-type: none"> <li>• Previous child diagnosed with Prader-Willi Syndrome</li> <li>• Cytogenic deletion is suspected on chorionic villus sampling (CVS) or amniocentesis.</li> </ul>
<b>Single-Gene Disorders</b>	<p>Invasive diagnostic prenatal (fetal) testing for molecular analysis for single-gene disorders <b>meets the definition of medical necessity</b> when a pregnancy has been identified as being at high risk for:</p> <ol style="list-style-type: none"> <li>1. Autosomal dominant conditions, at least 1 of the parents has a known pathogenic variant.</li> <li>2. Autosomal recessive conditions: <ul style="list-style-type: none"> <li>• Both parents are suspected to be carriers or are known to be carriers, <b>OR</b></li> <li>• One parent is clinically affected and the other parent is suspected to be or is a known carrier.</li> </ul> </li> <li>3. X-linked conditions: A parent is suspected to be or is a known carrier.</li> </ol> <p><b>AND ALL</b> of the following are met:</p> <ul style="list-style-type: none"> <li>• The natural history of the disease is well understood, and there is a reasonable likelihood that the disease is one with high morbidity in the homozygous or compound heterozygous state</li> <li>• Any variants have a high penetrance</li> <li>• The genetic test has adequate sensitivity and specificity to guide clinical decision making and residual risk is understood, <b>AND</b></li> <li>• An association of the marker with the disorder has been established.</li> </ul> <p>Invasive diagnostic prenatal (fetal) testing for molecular analysis for single-gene disorders is considered <b>experimental or investigational</b> if the above criteria are not met. There is insufficient clinical evidence to permit conclusions on net health outcomes.</p>
<b>Tuberous Sclerosis</b>	<p>Genetic testing for Tuberous Sclerosis <b>meets the definition of medical necessity</b> for <b>ONE</b> of the following:</p> <ul style="list-style-type: none"> <li>• Family history of Tuberous Sclerosis</li> </ul>

	<ul style="list-style-type: none"> <li>A specific mutation in the TSC1 and TSC2 gene has been identified in an affected family member.</li> </ul>
<b>Whole Exome Sequencing</b> <b>Whole Genome Sequencing</b>	Prenatal diagnosis, screening, or preimplantation testing of an embryo using whole exome or whole genome sequencing is considered <b>experimental or investigational</b> . There is insufficient clinical evidence to permit conclusions on net health outcomes.

Genetic testing for screening the general population, other than conditions noted above, is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes.

Genetic testing of children to predict adult onset diseases **does not meet the definition of medical necessity** unless test results will guide current decisions concerning prevention and this benefit would be lost by waiting until the child has reached adulthood.

## NEWBORN SCREENING

See U.S. Preventive Services Task Force (USPSTF) Recommendations at [uspreventiveservicestaskforce.org](http://uspreventiveservicestaskforce.org).

## POSTNATAL AND OTHER GENETIC TESTS

**NOTE:** Coverage for genetic testing, screening, and counseling are applicable only under those contracts that include benefits for genetic testing, preventive health services, screening services, and medical counseling.

To be considered genetic testing (vs. [genetic screening](#)) for indications other than to establish a diagnosis of inheritable disease, **ALL** of the following criteria must be met:

Diagnostic results from conventional testing and physical examination are inconclusive; **AND**

Results of molecular diagnostic testing are necessary to guide treatment decisions.

The following test list includes, but is not limited to, specific indications for testing that may **meet the definition of medical necessity** and those for which testing is considered **experimental or investigational**.

TEST	CRITERIA
<b>5-Fluorouracil (5-FU)</b>  (My5-FU™; TheraGuide®)	My5-FU™ assay testing or other types of assays for determining 5-fluorouracil (5-FU) area under the curve in order to adjust 5-FU dose for members with colorectal cancer or other cancers is considered <b>experimental or</b>

	<p><b>investigational.</b> The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>Testing for genetic variants in dipyrimidine dehydrogenase (DPYD) or thymidylate synthase (TYMS) genes to guide 5-FU dosing and/or treatment choice in members with cancer is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Cytogenetically Normal Acute Myeloid Leukemia</b></p>	<p>Genetic testing for FLT3 internal tandem duplication (FLT3-ITD), NPM1, and CEBPA variants <b>meets the definition of medical necessity</b> in cytogenetically normal acute myeloid leukemia when testing will be used to guide management decisions in members who would receive treatment other than low-dose chemotherapy or best supportive care.</p> <p>Genetic testing for FLT3 internal tandem duplication (FLT3-ITD), NPM1, and CEBPA variants is considered <b>experimental or investigational</b> in all other situations. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>Genetic testing for FLT3 tyrosine kinase domain variants is considered <b>experimental or investigational</b> for all indications. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>Genetic testing for FLT3, NPM1, and CEBPA variants to detect minimal residual disease is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Alzheimer Disease</b></p> <p><b>Note:</b> Genetic testing for Alzheimer disease may be offered along with analysis of cerebral spinal fluid levels of the tau protein and amyloid-b peptide 1-42 (see MCG 05-86000-22). This group of tests may be collectively referred to as the Admark™ Profile, offered by Athena Diagnostics.</p>	<p>Targeted genetic testing for a known familial variant in the presenilin genes (PSEN) or amyloid-beta precursor protein (APP) gene associated with autosomal dominant early-onset Alzheimer disease <b>meets the definition of medical necessity</b> in an asymptomatic member to determine future risk of disease when the following criteria are met:</p> <ul style="list-style-type: none"> <li>• The member has a close relative (ie, first- or second-degree relative) with a known familial variant associated with autosomal dominant early-onset Alzheimer disease <b>AND</b></li> </ul>

	<ul style="list-style-type: none"> <li>• Results of testing will inform reproductive decision making.</li> </ul> <p>Genetic testing for variants in presenilin genes (PSEN) or amyloid-beta precursor protein (APP) gene associated with autosomal dominant early-onset Alzheimer disease <b>meets the definition of medical necessity</b> in an asymptomatic member to determine future risk of disease when the following criteria are met:</p> <ul style="list-style-type: none"> <li>• The member has a family history of dementia consistent with autosomal dominant Alzheimer disease for whom the genetic status of the affected family members is unavailable AND</li> <li>• Results of testing will inform reproductive decision making.</li> </ul> <p>Genetic testing for the risk assessment of Alzheimer disease in asymptomatic members is considered <b>experimental or investigational</b> in all other situations. Genetic testing includes, but is not limited to, testing for the apolipoprotein E (APOE) epsilon 4 allele or triggering receptor expressed on myeloid cells 2 (TREM2). There is insufficient clinical evidence to permit conclusions on health outcomes.</p> <p>Genetic testing to guide initiation or management of a U.S. Food and Drug Administration-approved amyloid-beta targeting therapy (eg, aducanumab) is considered <b>experimental or investigational</b>. Genetic testing includes but is not limited to, testing for the APOE epsilon 4 allele. There is insufficient clinical evidence to permit conclusions on health outcomes.</p>
<p><b>Assessment of Measurable Residual Disease (MRD)</b></p>	<p>Next-generation sequencing (eg, clonoSEQ) to detect MRD at a threshold of <math>10^{-4}</math> as an alternative test in members with acute lymphoblastic leukemia or chronic lymphocytic leukemia <b>meets the definition of medical necessity</b>.</p> <p>Next-generation sequencing (eg, clonoSEQ) to detect MRD at a threshold of <i>less</i> than <math>10^{-4}</math> in members with acute lymphoblastic leukemia or chronic lymphocytic leukemia is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>

	<p>Next-generation sequencing (eg. clonoSEQ) to detect MRD at a threshold of <math>10^{-5}</math> as an alternative test in members with multiple myeloma <b>meets the definition of medical necessity</b>.</p> <p>Next-generation sequencing (eg. clonoSEQ) to detect MRD at a threshold of less than <math>10^{-5}</math> in members with multiple myeloma is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>Next-generation sequencing to detect MRD in all other situations is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<b>A-Thalassemia</b>	<p>Preconception (carrier) testing for <math>\alpha</math>-thalassemia in prospective parents <b>meets the definition of medical necessity</b> when both parents have evidence of possible <math>\alpha</math>-thalassemia (including <math>\alpha</math>-thalassemia minor, hemoglobin H disease [<math>\alpha</math>-thalassemia intermedia], or <math>\alpha</math>-thalassemia minima [silent carrier]) based on biochemical testing.</p> <p>Genetic testing to confirm a diagnosis of <math>\alpha</math>-thalassemia <b>does not meet the definition of medical necessity</b>. The diagnosis of <math>\alpha</math>-thalassemia can be made without genetic testing.</p> <p>Genetic testing of members with hemoglobin H disease (<math>\alpha</math>-thalassemia intermedia) to determine prognosis is considered <b>experimental or investigational</b>. There is insufficient clinical evidence to permit conclusions on health outcomes.</p> <p>Genetic testing for <math>\alpha</math>-thalassemia in other clinical situations is considered <b>experimental or investigational</b>. There is insufficient clinical evidence to permit conclusions on health outcomes.</p> <p>(Prenatal testing is not addressed in the position statements above.)</p>
<b>Biallelic RPE65 Inherited Retinal Dystrophies</b>	<p>Genetic testing to detect the presence of pathogenic variants in the RPE65 gene <b>meets the definition of medical necessity</b> to establish a diagnosis of inherited retinal dystrophy.</p>

## CADASIL Syndrome

Genetic testing for a NOTCH3 variant to confirm the diagnosis of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) syndrome in a member **meets the definition of medical necessity** under the following conditions:

- Clinical signs, symptoms, and imaging results are consistent with CADASIL, indicating that the pretest probability of CADASIL is at least in the moderate-to-high range (score of 14 or greater\*); **AND**
- The diagnosis of CADASIL is inconclusive following alternative methods of testing, including magnetic resonance imaging.

For individuals who are asymptomatic with a family member with a diagnosis of CADASIL syndrome:

- If there is a family member (first- and second-degree relative) with a known variant, targeted genetic testing of the known NOTCH3 familial variant **meets the definition of medical necessity**.
- If the family member's genetic status is unknown, genetic testing of NOTCH3 **meets the definition of medical necessity**.

Genetic testing for a NOTCH3 variant to confirm the diagnosis of CADASIL syndrome in all other situations is considered **experimental or investigational**. There is insufficient clinical evidence to permit conclusions on health outcomes.

### \*Screening Tool to Select Patients for NOTCH3 Gene:

Features	No. With NOTCH3 Variant	Percent With NOTCH3 Variant	Points
<b>Clinical:</b>			
Migraine	239/463	52%	1
Migraine with aura	65/85	76%	3
Transient ischemic attack/stroke	380/526	72%	1 (2 if <50 y)
Psychiatric disturbance	106/380	28%	1

	Cognitive decline	188/434	43%	3
	<b>Radiologic:</b>			
	LE	277/277	100%	3
	LE extended to temporal pole	174/235	74%	1
	LE extended to external capsule	228/303	75%	5
	Subcortical infarcts	210/254	83%	2
<b>Cardiovascular Disease or Aneurysm</b>  (9p21-EarlyMICheck™ Genotype Test, deCODE MI™)	The use of genotyping for 9p21 single nucleotide polymorphisms is considered <b>experimental or investigational</b> , including but not limited to, identification of members who may be at increased risk of cardiovascular disease or its manifestations (e.g., MI, ischemic stroke, peripheral arterial disease, coronary artery calcification), or identification of members who may be at increased risk for aneurysmal disease (abdominal aortic aneurysms, intracranial aneurysms, polypoidal choroidal vasculopathy). There is insufficient evidence regarding the clinical utility of this testing to permit conclusions on health outcomes.			
<b>Cardiovascular Risk and/or Effectiveness of Statin Therapy</b>  (Cardio IQ™ KIF6 Genotype, KIF6 StatinCheck™ Genotype)	KIF6 Genotyping is considered <b>experimental or investigational</b> for predicting cardiovascular risk and/or the effectiveness of statin therapy. There is insufficient evidence on the clinical validity of the testing to permit conclusions on health outcomes.			
<b>Celiac Disease</b>  (HLA Typing; PROMETHEUS® Celiac PLUS)	<p>HLA-DQ2 and HLA-DQ8 testing <b>meets the definition of medical necessity</b> to rule out celiac disease in individuals with discordant serologic and histologic (biopsy) findings or individuals with persistent symptoms despite negative serology and histology.</p> <p>HLA-DQ2 and HLA-DQ8 testing for celiac disease is considered <b>experimental or investigational</b> in all other situations. There is insufficient clinical evidence to permit conclusions on net health outcomes.</p>			

<p><b>Chromosomal Microarray Analysis (CMA)</b></p> <p>(Also referred to as genomic hybridization (CGH) or array comparative genomic hybridization (aCGH).)</p> <p>(Affymetrix CytoScan® Dx; FirstStepDx PLUS; Reveal® SNP Microarray Pediatric)</p>	<p>Chromosomal microarray analysis <b>meets the definition of medical necessity</b> as first line testing in the initial postnatal evaluation of members with any of the following:</p> <ul style="list-style-type: none"> <li>• Apparent nonsyndromic developmental delay/intellectual disability</li> <li>• Autism spectrum disorder <b>OR</b></li> <li>• Multiple congenital anomalies not specific to a well-delineated genetic syndrome.</li> </ul> <p>Chromosomal microarray analysis is considered <b>experimental or investigational</b> for the evaluation of all other conditions of delayed development, including but not limited to idiopathic growth or language delay. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>Panel testing using next-generation sequencing (NGS) is considered <b>experimental or investigational</b> in all cases of suspected genetic abnormality in children with developmental delay/intellectual disability, autism spectrum disorder or congenital anomalies. The evidence is insufficient to permit conclusions whether NGS panel testing improves outcomes.</p>
<p><b>Cardiac Ion Channelopathies</b></p> <p>[Includes QT syndrome (LQTS), catecholaminergic polymorphic ventricular tachycardia (CPVT), Brugada syndrome (BrS), and short QT syndrome (SQTS)]</p> <p>(FAMILION® Test)</p>	<p><b>Long QT Syndrome (LQTS)</b></p> <p>Genetic testing to confirm a diagnosis of congenital LQTS <b>meets the definition of medical necessity</b> when signs and/or symptoms of LQTS are present but a definitive diagnosis cannot be made without genetic testing. This includes:</p> <ul style="list-style-type: none"> <li>• Members who do not meet the clinical criteria for LQTS (i.e., those with a Schwartz score less than 4), but who have a moderate-to-high pretest probability based on the Schwartz score and/or clinical criteria.</li> </ul> <p>Note: Determining the pretest probability of LQTS is not standardized. An example of a member with a moderate-to-high pretest probability of LQTS is a member with a Schwartz score of 2 – 3. Refer to Diagnostic Scoring System* for LQTS below.</p>



	<p>Genetic testing of asymptomatic members to determine future risk of LQTS <b>meets the definition of medical necessity</b> when at least one of the following criteria is met:</p> <ul style="list-style-type: none"> <li>• A close relative (ie, first-, second-, or third-degree relative) with a known LQTS mutation; <b>OR</b></li> <li>• A close relative diagnosed with LQTS by clinical means whose genetic status is unavailable.</li> </ul> <p>Genetic testing for LQTS for all other situations not meeting criteria above, including but not limited to determining prognosis and/or directing therapy in members with known LQTS is considered <b>experimental or investigational</b>. There is insufficient clinical evidence to permit conclusions on net health outcomes.</p> <p><b>Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)</b></p> <p>Genetic testing to confirm a diagnosis of CPVT <b>meets the definition of medical necessity</b> when signs and/or symptoms of CPVT are present, but a definitive diagnosis cannot be made without genetic testing.</p> <p>Genetic testing of asymptomatic members to determine future risk of CPVT <b>meets the definition of medical necessity</b> when at least one of the following criteria is met:</p> <ul style="list-style-type: none"> <li>• A close relative (ie, first-, second-, or third-degree relative) with a known CPVT mutation; <b>OR</b></li> <li>• A close relative diagnosed with CPVT by clinical means whose genetic status is unavailable.</li> </ul> <p>Genetic testing for CPVT for all other situations not meeting the criteria above is considered <b>experimental or investigational</b>. There is insufficient clinical evidence to permit conclusions on net health outcomes.</p> <p><b>Brugada Syndrome (BrS)</b></p> <p>Genetic testing to confirm a diagnosis of BrS <b>meets the definition of medical necessity</b> when signs and/or symptoms consistent with BrS are present but a definitive diagnosis cannot be made without genetic testing.</p> <p>Genetic testing of asymptomatic members to determine future risk of BrS <b>meets the definition of medical necessity</b></p>
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	<p>when members have a close relative (ie, first-, second-, or third-degree relative) with a known BrS mutation.</p> <p>Genetic testing for BrS for all other situations not meeting the criteria above is considered <b>experimental or investigational</b>. There is insufficient clinical evidence to permit conclusions on net health outcomes.</p> <p><b>Short QT Syndrome (SQTS)</b></p> <p>Genetic testing of asymptomatic members to determine future risk of SQTS <b>meets the definition of medical necessity</b> when members have a close relative (ie, first-, second-, or third-degree relative) with a known SQTS mutation.</p> <p>Genetic testing for SQTS for all other situations not meeting the criteria above is considered <b>experimental or investigational</b>. There is insufficient clinical evidence to permit conclusions on net health outcomes.</p> <p><b>NOTE:</b> First-degree relatives: children, brothers, sisters and parents. Second-degree relatives: grandparents, aunts, uncles, nieces, nephews, half-siblings, and grandchildren. Third-degree relatives: great-grandparents, great-aunts, great-uncles, great-grandchildren, and first cousins.</p>
<b>CHARGE Syndrome</b>	<p>Genetic testing for CHARGE syndrome <b>meets the definition of medical necessity</b> to confirm a diagnosis in a member with signs/symptoms of CHARGE syndrome when a definitive diagnosis cannot be made with clinical criteria.</p> <p>Genetic testing for CHARGE syndrome is considered <b>experimental or investigational</b> in all other situations. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<b>Evaluation of Stable Ischemic Heart Disease</b>	<p>Gene expression testing in the evaluation of members with stable ischemic heart disease is considered <b>experimental or investigational</b> for all indications, including but not limited to prediction of coronary artery disease in stable, nondiabetic members. There is a lack of clinical data to permit conclusions on net health outcomes.</p>
<b>Cutaneous Malignant Melanoma</b>	<p>Genetic testing for genes associated with familial cutaneous malignant melanoma or associated with</p>

(Mellaris®)	<p>susceptibility to cutaneous malignant melanoma is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Cytochrome P450 Genotype-Guided Treatment Strategy</b></p>	<p>CYP2D6 genotyping to determine drug metabolizer status <b>meets the definition of medical necessity</b> for members with:</p> <ul style="list-style-type: none"> <li>• Gaucher disease being considered for treatment with eliglustat; <b>OR</b></li> <li>• Huntington disease being considered for treatment with tetrabenazine in a dosage greater than 50 mg per day.</li> </ul> <p>CYP2C9 genotyping to determine drug metabolizer status <b>meets the definition of medical necessity</b> for members with relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, being considered for treatment with Siponimod.</p> <p>CYP450 genotyping for the purpose of aiding in the choice of drug or dose to increase efficacy and/or avoid toxicity for the following drugs is considered <b>experimental or investigational</b> (If a separate position statement exists, then criteria for medical necessity in that position statement supersedes this statement):</p> <ul style="list-style-type: none"> <li>• selection or dosage of codeine</li> <li>• dosing of efavirenz and other antiretroviral therapies for HIV infection</li> <li>• dosing of immunosuppressants for organ transplantation</li> <li>• selection or dosing of <math>\beta</math>-blockers (eg, metoprolol)</li> <li>• dosing and management of antitubercular medications.</li> </ul> <p>The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>CYP450 genotyping for the purpose of aiding in the choice of clopidogrel vs alternative antiplatelet agents, or in decisions on the optimal dosing for clopidogrel, is</p>

	<p>considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>The use of genetic testing panels that include multiple CYP450 variants is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<b>Dilated Cardiomyopathy</b>	<p>Comprehensive genetic testing for members with signs or symptoms of dilated cardiomyopathy (ie, heart failure or arrhythmias, frequently presenting as dyspnea on exertion and peripheral edema) which is considered idiopathic after a negative workup for secondary causes <b>meets the definition of medical necessity</b>.</p> <p>Targeted genetic testing for asymptomatic members with a first-degree relative* who has dilated cardiomyopathy and a known familial variant <b>meets the definition of medical necessity</b>.</p> <p>*First-degree relative- child, brother, sister, parent.</p> <p>Genetic testing for dilated cardiomyopathy is considered <b>experimental or investigational</b> in all other situations. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<b>Duchenne and Becker Muscular Dystrophy</b>	<p>Genetic testing for DMD gene <b>meets the definition of medical necessity</b> for the following conditions:</p> <ul style="list-style-type: none"> <li>• In a male with signs and symptoms of a dystrophinopathy in order to confirm the diagnosis and direct treatment.</li> <li>• For at-risk female relatives (first- and second-degree female relatives and include the proband's mother, female siblings of the proband, female offspring of the proband, the proband's maternal grandmother, maternal aunts, and their offspring): <ul style="list-style-type: none"> <li>○ To confirm or exclude the need for cardiac surveillance</li> <li>○ For preconception testing to determine the likelihood of an affected offspring in a woman considering a pregnancy.</li> </ul> </li> </ul>

	<ul style="list-style-type: none"> <li>For at-risk male offspring (asymptomatic male offspring of a female carrier or an asymptomatic male sibling of a member with a DMD-associated dystrophinopathy) to confirm or exclude the need for medical and cardiac surveillance.</li> </ul> <p>Genetic testing for DMD gene variants is considered <b>experimental or investigational</b> in all other postnatal situations. There is a lack of clinical data to permit conclusions on health outcomes.</p>
<b>FMR1 Variants (Including Fragile X Syndrome)</b>	<p>Genetic testing for FMR1 variants <b>meets the definition of medical necessity</b> for the following member populations:</p> <p>Members who have a personal or family history of fragile X syndrome who are seeking reproductive counseling, including:</p> <ul style="list-style-type: none"> <li>Prenatal testing of fetuses of known carrier mothers;</li> <li>Affected members or relatives of affected members who have had a positive cytogenetic fragile X test result who are seeking information on carrier status;</li> <li>Members who have a family history of fragile X syndrome or a family history of undiagnosed intellectual disability.</li> </ul> <p>Members with characteristics of fragile X syndrome or a fragile X–associated disorder, including:</p> <ul style="list-style-type: none"> <li>Member with intellectual disability, developmental delay, or autism spectrum disorder;</li> <li>Members with neurologic symptoms consistent with fragile X-associated tremor or ataxia syndrome;</li> <li>Women with primary ovarian insufficiency under the age of 40 in whom fragile X-associated primary ovarian insufficiency is suspected.</li> </ul> <p>Genetic testing for FMR1 variants is considered <b>experimental or investigational</b> for all other uses. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<b>Hereditary Pancreatitis</b>	<p>Genetic testing for hereditary pancreatitis <b>meets the definition of medical necessity</b> for members aged 18 years and younger with unexplained acute recurrent (greater</p>

	<p>than 1 episode) or chronic pancreatitis with documented elevated amylase or lipase levels.</p> <p>Genetic testing for hereditary pancreatitis is considered <b>experimental or investigational</b> in all other situations. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Germline Variants of the RET Proto-Oncogene in Medullary Carcinoma of the Thyroid</b></p>	<p>Genetic testing for RET proto-oncogene point variants <b>meets the definition of medical necessity</b> for the following indications:</p> <ul style="list-style-type: none"> <li>• Asymptomatic members of families with defined RET gene variants</li> <li>• Members of families known to be affected by inherited medullary thyroid cancer, but not previously evaluated for RET variants</li> <li>• Members with sporadic medullary thyroid cancer.</li> </ul> <p>Genetic testing for RET proto-oncogene point variants is considered <b>experimental or investigational</b>, as there is insufficient clinical evidence to support the use of genetic testing for screening the general population. There is a lack of clinical data to permit conclusions on efficacy and net health outcomes.</p>
<p><b>Mental Health Conditions</b></p> <p>(GeneSightRX®, PROOVE Drug Metabolism Profile, PHARMAchip, SureGene, MD Tox Expanded Comprehensive Profile; MD Tox Psychiatry &amp; Risk Factors Profile; Idgenetix panels.)</p>	<p>Genetic testing for diagnosis and management of mental health disorders is considered <b>experimental or investigational</b> in all situations, including but not limited to:</p> <ul style="list-style-type: none"> <li>• To confirm a diagnosis of a mental health disorder in an individual with symptoms.</li> <li>• To predict future risk of a mental health disorder in an asymptomatic individual.</li> <li>• To inform the selection or dose of medications used to treat mental health disorders, including but not limited to the following medications: <ul style="list-style-type: none"> <li>○ selective serotonin reuptake inhibitors</li> <li>○ selective norepinephrine reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors</li> <li>○ tricyclic antidepressants</li> <li>○ antipsychotic drugs.</li> </ul> </li> </ul>

	<p>The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>Genetic testing panels for mental health disorders, including but not limited to the Genecept Assay, STA<sup>2</sup>R test, the GeneSight Psychotropic panel, the Proove Opioid Risk assay, and the Mental Health DNA Insight panel, are considered <b>experimental or investigational</b> for all indications. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Helicobacter pylori (H. pylori) Treatment</b></p> <p>(AmHPR H. pylori AB Resistance NGS Panel)</p>	<p>Genotyping to determine cytochrome p450 (CYP2C19) genetic polymorphisms is considered <b>experimental or investigational</b> for the purpose of managing the treatment of H. pylori infection. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Hereditary Cardiomyopathies</b></p>	<p>Genetic testing for predisposition to hypertrophic cardiomyopathy (HCM) <b>meets the definition of medical necessity</b> for individuals who are at risk for development of HCM, defined as having a first-degree relative with established HCM, when there is a known pathogenic gene variant present in that affected relative.</p> <p>Genetic testing for predisposition to HCM <b>does not meet the definition of medical necessity</b> for members with a family history of HCM in which a first-degree relative with established HCM has tested negative for pathogenic variants.</p> <p>Genetic testing for predisposition to HCM is considered <b>experimental or investigational</b> for all other member populations, including but not limited to individuals who have a first-degree relative with clinical HCM, but in whom genetic testing is unavailable. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>* <b>(First-degree relatives:</b> children, brothers, sisters and parents.)</p> <p>Genetic testing to determine the diagnosis or management of all other hereditary cardiomyopathies, including but not limited to, arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C), restrictive, and left</p>

	ventricular noncompaction cardiomyopathies, is considered <b>experimental or investigational</b> . There is a lack of clinical data to permit conclusions on net health outcomes.
<b>Inherited Peripheral Neuropathy</b>	<p>Genetic testing <b>meets the definition of medical necessity</b> when the diagnosis of an inherited peripheral motor or sensory neuropathy is suspected due to signs and/or symptoms but a definitive diagnosis cannot be made without genetic testing.</p> <p>Genetic testing for an inherited peripheral neuropathy is considered <b>experimental or investigational</b> for all other indications. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<b>Inflammatory Bowel Disease</b>  (Prometheus® IBD sgi Diagnostic™; Prometheus® Crohn's Prognostic; Prometheus® IBD Serology 7)	Determination of anti-neutrophil cytoplasmic antibody (ANCA), anti-Saccharomyces cerevisiae antibody (ASCA), OmpC antibodies, and I2 antibodies is considered <b>experimental or investigational</b> . The evidence is insufficient to determine the effects of the technology on health outcomes.
<b>Lactase Insufficiency</b>  (LactoType®)	The use of targeted MCM6 -13910C>T variant analysis for the prediction of lactase insufficiency is considered <b>experimental or investigational</b> . There is insufficient evidence that the testing would affect medical management or improve clinical outcomes.
<b>Lipoprotein(a) Variant(s) as a Decision Aid for Aspirin Treatment</b>  (LPA-Aspirin Genotype )	The use of genetic testing for the LPArs3798220 allele (LPA-Aspirin Genotype) is considered <b>experimental or investigational</b> in members who are being considered for treatment with aspirin to reduce risk of cardiovascular events. There is insufficient evidence to permit conclusions on how this testing would change medical management and improve health outcomes.
<b>Macular Degeneration</b>  (Macula Risk®; Macula Risk®PGx; RetnaGene™, Vita Risk®)	Genetic testing for macular degeneration is considered <b>experimental or investigational</b> for all indications. The evidence is insufficient to determine the effects of the technology on health outcomes.



<p><b>Neurofibromatosis (NF)</b></p>	<p>Genetic testing for neurofibromatosis (NF1 or NF2) variants <b>meets the definition of medical necessity</b> when a diagnosis of neurofibromatosis is clinically suspected due to signs of disease, but a definitive diagnosis cannot be made without genetic testing.</p> <p>Genetic testing for neurofibromatosis (NF1 or NF2) variants in at-risk relatives with no signs of disease <b>meets the definition of medical necessity</b> when a definitive diagnosis cannot be made without genetic testing <b>AND</b> at least one of the following criteria is met:</p> <ul style="list-style-type: none"> <li>• A close relative (ie, first-, second-, or third-degree relative) has a known NF1 or NF2 variant; <b>or</b></li> <li>• A close relative has been diagnosed with neurofibromatosis but whose genetic status is unavailable.</li> </ul> <p>Genetic testing for neurofibromatosis for all other situations not meeting the criteria outlined above is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Nonfamilial Breast Cancer</b></p> <p>(City of Hope Breast Cancer Susceptibility Assay, deCODE BreastCancer™, &amp; deCODEme Complete Scan,)</p>	<p>Testing for one or more single nucleotide variants to predict an individual's risk of breast cancer is considered <b>experimental or investigational</b>.</p> <p>The GeneType® breast cancer risk test (previously known as BREVAGenplus) is considered <b>experimental or investigational</b> for all indications, including but not limited to use as a method of estimating individual member risk for developing breast cancer.</p> <p>The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Molecular Testing for Germline Variants Associated with Ovarian Cancer</b></p>	<p>Testing for germline BRIP1, RAD51C, and RAD51D variants for ovarian cancer risk assessment in adults <b>meets the definition of medical necessity</b> when the following criteria are met (1 or 2):</p> <ol style="list-style-type: none"> <li>1. The member has a diagnosis of epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer; <b>AND</b></li> </ol>

	<ul style="list-style-type: none"> <li>• The member has not previously been tested for these gene variants; AND</li> <li>• The member is thought to be the most informative member of a family (proband) to have genetic testing; AND</li> <li>• The member has closely related (1<sup>st</sup>- or 2<sup>nd</sup>-degree*) relatives who are considering genetic testing for these gene variants to inform prophylactic decision-making or who have test results that cannot be fully interpreted without testing an affected relative.</li> </ul> <p>2. The member has not been diagnosed with epithelial ovarian cancer; <b>AND</b></p> <ul style="list-style-type: none"> <li>• The member has a blood relative* with a known pathogenic/likely pathogenic germline BRIP1, RAD51C, or RAD51D variant; <b>OR</b></li> <li>• The member has a 1<sup>st</sup>- or 2<sup>nd</sup>-degree relative* diagnosed with ovarian cancer.</li> </ul> <p>Testing for BRIP1, RAD51C, and RAD51D variants for ovarian cancer risk assessment in adults who do not meet the criteria above is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>Testing for germline NBN variants for ovarian cancer risk assessment is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>Testing for germline BRIP1, RAD51C, RAD51D, and NBN variants in members diagnosed with epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer to guide treatment is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>*(For familial assessment, 1<sup>st</sup>- and 2<sup>nd</sup>-degree relatives are blood relatives on the same side of the family (maternal or paternal): 1<sup>st</sup>-degree relatives: parents, siblings, and children 2<sup>nd</sup>-degree relatives: grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings.)</p>
<b>Pain Management</b>	Genetic testing for pain management is considered <b>experimental or investigational</b> for all indications. The

<p>(GeneSight Analgesic; Idgenetix Pain; MD Tox Comprehensive Profile; MD Tox Comprehensive &amp; Risk Factors Profile; MD Tox Pain Profile; Pain Management Panel; PersonaGene Genetic; Proove<sup>®</sup> Narcotic Risk; Proove<sup>®</sup> Opioid Risk; Proove<sup>®</sup> Pain Perception; Pain Medication DNA Insight<sup>™</sup>; Millennium PGT<sup>SM</sup>; YouScript<sup>®</sup>.)</p>	<p>evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Germline Genetic Testing for Gene Variants Associated With Breast Cancer in Individuals at High Breast Cancer Risk</b></p>	<p>Testing for CHEK2, BARD1, and ATM variants in the assessment of breast cancer risk is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Prostate Cancer</b></p>	<p>The following genetic and protein biomarkers for the diagnosis of prostate cancer are considered <b>experimental or investigational</b>:</p> <ul style="list-style-type: none"> <li>• Autoantibodies ARF 6, NKX3-1, 5'-UTR-BMI1, CEP 164, 3'-UTR-Ropporin, Desmocollin, AURKAIP-1, CSNK2A2 (eg, Apinify<sup>®</sup>)</li> <li>• Candidate gene panels</li> <li>• Gene hypermethylation testing (e.g., ConfirmMDx<sup>®</sup>)</li> <li>• HOXC6 and DLX1 testing (e.g., SelectMDx<sup>®</sup>)</li> <li>• IsoPSA<sup>®</sup></li> <li>• Kallikrein markers (e.g., 4Kscore<sup>™</sup> Test)</li> <li>• Mitochondrial DNA variant testing (e.g., Prostate Core Mitomics Test<sup>™</sup>)</li> <li>• PCA3, ERG, and SPDEF RNA expression in exosomes (e.g., ExoDx<sup>™</sup> Prostate IntelliScore)</li> <li>• PCA3 testing (e.g. Progenisa<sup>®</sup> PCA3 Assay)</li> <li>• Prostate Health Index (phi)</li> <li>• TMPRSS:ERG fusion genes (e.g., MyProstateScore).</li> </ul> <p>The evidence is insufficient to determine the effects of the technology on health outcomes.</p>

<p><sup>1</sup> (Decipher<sup>®</sup>; Ki-67, Oncotype Dx<sup>®</sup> Prostate, Oncotype DX<sup>®</sup> AR-V7 Nuclear Detect; Prolaris<sup>®</sup>, PTEN, ProMark<sup>™</sup>)</p>	<p>Single nucleotide variant testing (e.g., 23and me, deCODE) for cancer risk assessment of prostate cancer is considered <b>experimental or investigational</b>. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p><sup>1</sup> Use of gene expression analysis and protein biomarkers to guide management of prostate cancer is considered <b>experimental or investigational</b> for all indications. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>PTEN Hamartoma Tumor Syndrome (PHTS)</b></p>	<p>Genetic testing for PTEN <b>meets the definition of medical necessity</b> to confirm the diagnosis when a member has clinical signs of a PTEN hamartoma tumor syndrome.</p> <p>Targeted genetic testing for a PTEN familial variant <b>meets the definition of medical necessity</b> in a first-degree relative of a proband with a known PTEN pathogenic variant.</p> <p>Genetic testing for PTEN is considered <b>experimental or investigational</b> for all other indications. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
<p><b>Rett Syndrome</b></p>	<p>Genetic testing for Rett syndrome associated genes (eg, MECP2, FOXP1, or CDKL5) <b>meets the definition of medical necessity</b> to confirm a diagnosis of Rett syndrome in a child with developmental delay and signs/symptoms of Rett syndrome when a definitive diagnosis cannot be made without genetic testing.</p> <p>Targeted genetic testing for a known familial Rett syndrome associated variant <b>meets the definition of medical necessity</b> to determine carrier status of first-degree female relatives of an individual with Rett syndrome.</p> <p>All other indications for genetic testing for Rett syndrome associated genes, including routine carrier testing (prenatal or preconception) in members with negative family history, and testing of asymptomatic family members to determine future risk of disease, are considered <b>experimental or investigational</b>. The evidence is insufficient to determine that the technology results in a meaningful improvement in the net health outcome.</p>

<b>ScoliScore™</b>	DNA-based prognostic testing for adolescent idiopathic scoliosis is considered <b>experimental or investigational</b> . There is insufficient clinical evidence in peer-reviewed literature to permit conclusions on net health outcomes.
<b>Statin-Induced Myopathy</b>  (Statin Induced Myopathy (SLCO1B1) Genotype, SLCO1B1 Variants)	Genetic testing for the presence of variants in the SLCO1B1 gene to identify members at risk of statin-induced myopathy is considered <b>experimental or investigational</b> . There is insufficient clinical evidence to permit conclusions on health outcomes.
<b>Tamoxifen Treatment</b>	Genotyping to determine cytochrome p450 (CYP2D6) genetic variants is considered <b>experimental or investigational</b> for the purpose of managing treatment with tamoxifen for members at high risk for or with breast cancer. The evidence is insufficient to determine the effects of the technology on health outcomes.
<b>Warfarin Dosing</b>  (eQ-PCR™ LightCycle; eSensor® Warfarin Plus; eSensor® Warfarin Sensitivity; INFINITI 2C9-VKORC1 Multiplex Assay; Rapid Genotyping Assay; Verigence Warfarin Metabolism Nucleic Acid Test®)	Genotyping to determine cytochrome p450 2C9 (CYP2C9), P450 4F2 (CYP4F2), and vitamin K epoxide reductase subunit C1 (VKORC1) genetic variants is considered <b>experimental or investigational</b> for the purpose of managing the administration and dosing of warfarin, including use in guiding the initial warfarin dose to decrease time to stable INR and reduce the risk of serious bleeding. The evidence is insufficient to determine the effects of the technology on health outcomes.
<b>Whole Exome Sequencing</b>  <b>Whole Genome Sequencing</b>  (ExaCT-1, ExomeNext, ExomeNext-Rapid, TruGenome tests, XomeDx)	Standard whole exome sequencing, with trio testing (testing of child and both parents) when possible, <b>meets the definition of medical necessity</b> for the evaluation of unexplained congenital or neurodevelopmental disorder in children when <b>ALL</b> of the following criteria are met: <ul style="list-style-type: none"> <li>• The member has been evaluated by a clinician with expertise in clinical genetics, including at minimum a family history and phenotype description, and counseled about the potential risks of genetic testing</li> <li>• There is potential for a change in management and clinical outcome for the member being tested</li> <li>• A genetic etiology is considered the most likely explanation for the phenotype despite previous genetic testing (eg, chromosomal microarray</li> </ul>

	<p>analysis and/or targeted single-gene testing), <b>OR</b> when previous genetic testing has failed to yield a diagnosis and the affected member is faced with invasive procedures or testing as the next diagnostic step (eg, muscle biopsy).</p> <p>Rapid whole exome sequencing or rapid whole genome sequencing, with trio testing when possible, <b>meets the definition of medical necessity</b> for the evaluation of critically ill infants in neonatal or pediatric intensive care with a suspected genetic disorder of unknown etiology when <b>both (1 &amp; 2)</b> of the following criteria are met:</p> <ol style="list-style-type: none"> <li>1. <b>At least one</b> of the following criteria is met: <ol style="list-style-type: none"> <li>a. Multiple congenital anomalies (e.g. persistent seizures, abnormal ECG, hypotonia);</li> <li>b. An abnormal laboratory test or clinical features suggests a genetic disease or complex metabolic phenotype (e.g, abnormal newborn screen, hyperammonemia, lactic acidosis not due to poor perfusion); <b>or</b></li> <li>c. An abnormal response to standard therapy for a major underlying condition.</li> </ol> </li> <li>2. <b>None</b> of the following criteria apply regarding the reason for admission to intensive care: <ol style="list-style-type: none"> <li>a. An infection with normal response to therapy;</li> <li>b. Isolated prematurity;</li> <li>c. Isolated unconjugated hyperbilirubinemia;</li> <li>d. Hypoxic Ischemic Encephalopathy;</li> <li>e. Confirmed genetic diagnosis explains illness;</li> <li>f. Isolated Transient Neonatal Tachypnea;</li> <li>g. Nonviable neonates.</li> </ol> </li> </ol> <p>Whole exome sequencing is considered <b>experimental or investigational</b> for the diagnosis of genetic disorders in all other situations. The evidence is insufficient to determine the effects of the technology on health outcomes.</p> <p>Whole genome sequencing is considered <b>experimental or investigational</b> for the diagnosis of genetic disorders in all other situations. The evidence is insufficient to determine the effects of the technology on health outcomes.</p>
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	Whole exome sequencing and whole genome sequencing are considered <b>experimental or investigational</b> for screening for genetic disorders. The evidence is insufficient to determine the effects of the technology on health outcomes.
<b>X Chromosome Abnormality Test (XCAT) for Turner Syndrome (XCAT-TS)</b>	The use of the XCAT-TS test to detect Classic and Mosaic Turner Syndrome is considered <b>experimental or investigational</b> as there is insufficient clinical evidence in peer-reviewed literature to permit conclusions the test is as beneficial as the established alternatives and on net health outcomes

**\*Diagnostic Scoring System for LQTS**

Criteria	Points
<b>Electrocardiographic findings</b>	
* QTc >480 msec	3
* QTc 460-470 msec	2
* QTc <450 msec	1
History of torsades de pointes	2
<b>T-wave alternans</b>	1
Notched T-waves in three leads	1
Low heart rate for age	0.5
<b>Clinical history</b>	
* Syncope brought on by stress	2
* Syncope without stress	1
* Congenital deafness	0.5
<b>Family history</b>	
* Family members with definite LQTS	1
* Unexplained sudden death in immediate family members younger than 30 years of age	0.5

Genetic Counseling: Genetic counseling is covered in accordance to the member's contract benefits for medical counseling. Pre and post genetic counseling **meets the definition of medical necessity** as an adjunct to the genetic test(s).

Genetic testing for screening the general population, other than conditions noted above, is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes. Home testing (including self-testing home kits) is considered **experimental or investigational** as the clinical validity of the tests have not been established. The evidence is insufficient to determine the effects of the technology on health outcomes.

The following tests are considered **experimental or investigational**, as there is insufficient evidence to support the use of these tests for all indications. Although there are ongoing clinical studies the current data are inadequate to permit scientific conclusions on net health outcomes:

BRCaPlus®

BreastNext™

+RNAinsight for BreastNext

BreastSentry

BROCA Cancer Risk Panel

CancerNext™

+RNAinsight for CancerNext

CardioPredict™

ColoNext™

+RNAinsight for ColoNext

ColoSeq™

Comprehensive Cancer Panel

Counsyl Reliant Cancer Screen

CustomNext®

+RNAinsight for CustomNext

DetoxiGenomic® Profile Test

Ehlers-Danlos Syndrome Panel

epiSEEK™

GenArray™

Gene Trails Genotyping Panels

GeneSeq®:Cardio

Genoptix® MDS Molecular Profile

GYNPlus®

+RNAinsight for GYNPlusHCM Sequencing Panel

Heart Cholesterol Balance™

Heart HDL Map™



High/Moderate Risk Panel

MD Tox Cardiac & Risk Factors Profile

Mitochondrial Disorders Panel

MitoMED-Autism™

Monogenic Hypertension Evaluation Panel

MVL Vision Panel

myRisk®

Nemaline Myopathy Panel

nucSEEK™

OneOme RightMed Tests

OvaNext™

+RNAinsight for OvaNext

Pan Cardiomyopathy Panel

PancNext™

Panexia™

Periodic Fever Syndromes Panel

ProstateNext

+RNAinsight for ProstateNext

RenalNext™

TumorNext

X-linked Intellectual Disability Panel.

## **CYTOGENETIC STUDIES (CHROMOSOMAL STUDIES)**

**NOTE:** Coverage for cytogenetic studies and counseling are applicable only under those contracts that include benefits for cytogenetic testing, genetic testing, preventive health services, screening services, and medical counseling.

Cytogenetic studies **meet the definition of medical necessity** for the diagnosis and treatment of the following conditions (the list is not all-inclusive):

- Genetic disorders (e.g., Down's Syndrome) in a fetus
- Failure of sexual development
- Chronic myelogenous leukemia

- Acute leukemias lymphoid, acute leukemias myeloid
- Acute leukemias unclassified; **or**
- Myelodysplasia.

## BILLING/CODING INFORMATION:

### CPT Coding:

81161	DMD (dystrophin) (e.g., Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81171	AFF2 (ALF transcription elongation factor 2 [FMR2]) (eg, fragile X intellectual disability 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81172	AFF2 (ALF transcription elongation factor 2 [FMR2]) (eg, fragile X intellectual disability 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
81200	ASPA (aspartoacylase) (e.g. Canavan disease) gene analysis, common variants (e.g. 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) (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
81218	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (eg, acute myeloid leukemia), gene analysis, full gene sequence
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g. cystic fibrosis) gene analysis; common variants (e.g. ACMG/ACOG guidelines)
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g. cystic fibrosis) gene analysis; known familial variants
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g. cystic fibrosis) gene analysis; duplication/deletion variants
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g. cystic fibrosis) gene analysis; full gene sequence
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g. cystic fibrosis) gene analysis; intron 8 poly-T analysis (e.g. male infertility)
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (e.g. drug metabolism), gene analysis, common variants (e.g. *2, *3, *4, *8, *17) ( <b>Investigational</b> )

81226	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g. drug metabolism), gene analysis, common variants (e.g. *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (e.g. drug metabolism), gene analysis, common variants (e.g. *2, *3, *5, *6)
81228	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis
81229	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants, comparative genomic hybridization (CGH) microarray analysis
81230	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism) gene analysis, common variant(s) (eg, *2, *22) ( <b>Investigational</b> )
81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism) gene analysis, common variants (eg, *2, *3, *4, *5 *6, *7) ( <b>Investigational</b> )
81232	DPYD (dihydropyrimidine dehydrogenase) (eg, 5-fluorouracil/5-FU and capecitabine drug metabolism) gene analysis, common variant(s) (eg, *2A, *4, *5, *6) ( <b>Investigational</b> )
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) (eg, fragile X syndrome, X-linked intellectual disability [XLID]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81244	FMR1 (fragile X messenger ribonucleoprotein 1) (eg, fragile X syndrome, X-linked intellectual disability [XLID]) gene analysis; characterization of alleles (eg, expanded size and promoter methylation status)
81245	FLT3 (fms-related tyrosine kinase 3) (e.g. acute myeloid leukemia), gene analysis, internal tandem duplication (ITD) variants (ie, exons 14, 15)
81246	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (eg, D835, I836) ( <b>Investigational</b> )
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, alpha3.7, alpha4.2, alpha20.5, Constant Spring)
81258	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant

81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, 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) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants
81277	Cytogenomic neoplasia (genome-wide) microarray analysis, interrogation of genomic regions for copy number and loss-of-heterozygosity variants for chromosomal abnormalities
81290	MCOLN1 (mucolipin 1) (e.g. Mucopolidosis, type IV) gene analysis, common variants (e.g. IVS3-2A>G, del6.4kb)
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (e.g. hereditary hypercoagulability) gene analysis, common variants (e.g. 677T, 1298C) <b>(Investigational)</b>
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
81310	NPM1 (nucleophosmin) (e.g. acute myeloid leukemia) gene analysis, exon 12 variants
81313	PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer) <b>(Investigational)</b>
81321	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
81322	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant
81323	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant
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
81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (eg, adverse drug reaction) gene analysis, common variant(s) (eg, *5) <b>(Investigational)</b>
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)

81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism) gene analysis, common variant(s) (eg, tandem repeat variant) <b>(Investigational)</b>
81349	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and loss-of-heterozygosity variants, low-pass sequencing analysis
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (e.g. warfarin metabolism), gene analysis, common variants (e.g. -1639G>A, c.173+1000C>T) <b>(Investigational)</b>
81370	HLA Class I and II typing, low resolution (e.g. antigen equivalents); HLA-A, -B, -C, -DRB1/3/4/5, and DQB1
81371	HLA Class I and II typing, low resolution (e.g. antigen equivalents); HLA-A, -B, and DRB1 (e.g. verification typing)
81372	HLA Class I typing, low resolution (e.g. antigen equivalents); complete (ie, HLA-A, -B, and C)
81373	HLA Class I typing, low resolution (e.g. antigen equivalents); 1 locus (e.g. HLA-A, -B, or C), each
81374	HLA Class I typing, low resolution (e.g. antigen equivalents); 1 antigen equivalent (e.g. B*27), each
81375	HLA Class II typing, low resolution (e.g. antigen equivalents); HLA-DRB1/3/4/5 and DQB1
81376	HLA Class II typing, low resolution (e.g. antigen equivalents); 1 locus (e.g. HLA-DRB1, DRB3/4/5, -DQB1, -DQA1, -DPB1, or DPA1), each
81377	HLA Class II typing, low resolution (e.g. antigen equivalents); 1 antigen equivalent, each
81378	HLA Class I and II typing, high resolution (ie, alleles or allele groups), HLA-A, -B, -C, and DRB1
81379	HLA Class I typing, high resolution (ie, alleles or allele groups); complete (ie, HLA-A, -B, and C)
81380	HLA Class I typing, high resolution (ie, alleles or allele groups); 1 locus (e.g. HLA-A, -B, or C), each
81381	HLA Class I typing, high resolution (ie, alleles or allele groups); 1 allele or allele group (e.g. B*57:01P), each
81382	HLA Class II typing, high resolution (ie, alleles or allele groups); 1 locus (e.g. HLA-DRB1, -DRB3, -DRB4, -DRB5, -DQB1, -DQA1, -DPB1, or DPA1), each
81383	HLA Class II typing, high resolution (ie, alleles or allele groups); 1 allele or allele group (e.g. HLA-DQB1*06:02P), each
81400	MOLECULAR PATHOLOGY PROCEDURE LEVEL 1
81401	MOLECULAR PATHOLOGY PROCEDURE LEVEL 2
81402	MOLECULAR PATHOLOGY PROCEDURE LEVEL 3
81403	MOLECULAR PATHOLOGY PROCEDURE LEVEL 4
81404	MOLECULAR PATHOLOGY PROCEDURE LEVEL 5
81405	MOLECULAR PATHOLOGY PROCEDURE LEVEL 6
81406	MOLECULAR PATHOLOGY PROCEDURE LEVEL 7
81407	MOLECULAR PATHOLOGY PROCEDURE LEVEL 8
81408	MOLECULAR PATHOLOGY PROCEDURE LEVEL 9

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, TGFB1, TGFB2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, and MYLK ( <b>Investigational</b> )
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 TGFB1, TGFB2, MYH11, and COL3A1 ( <b>Investigational</b> )
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
81415	Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis
81416	Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (eg, parents, siblings) (List separately in addition to code for primary procedure)
81417	Exome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (eg, updated knowledge or unrelated condition/syndrome)
81418	Drug metabolism (eg, pharmacogenomics) genomic sequence analysis panel, must include testing of at least 6 genes, including CYP2C19, CYP2D6, and CYP2D6 duplication/deletion analysis ( <b>Investigational</b> )
81425	Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis
81426	Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (eg, parents, siblings) (List separately in addition to code for primary procedure)
81427	Genome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (eg, updated knowledge or unrelated condition/syndrome)
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 ( <b>Investigational</b> )

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 <b>(Investigational)</b>
81439	Hereditary cardiomyopathy (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy), genomic sequence analysis panel, must include sequencing of at least 5 cardiomyopathy-related genes (eg, DSG2, MYBPC3, MYH7, PKP2, TTN)
81440	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, OPA1, PDSS2, POLG, POLG2, RRM2B, SCO1, SCO2, SLC25A4, SUCLA2, SUCLG1, TAZ, TK2, and TYMP <b>(Investigational)</b>
81443	Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucopolipidosis 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 panel (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, and SPTLC1) <b>(Investigational)</b>
81460	Whole mitochondrial genome (eg, Leigh syndrome, mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes [MELAS], myoclonic epilepsy with ragged-red fibers [MERFF], neuropathy, ataxia, and retinitis pigmentosa [NARP], Leber hereditary optic neuropathy [LHON]), genomic sequence, must include sequence analysis of entire mitochondrial genome with heteroplasmy detection <b>(Investigational)</b>
81465	Whole mitochondrial genome large deletion analysis panel (eg, Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed <b>(Investigational)</b>
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 <b>(Investigational)</b>
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 <b>(Investigational)</b>
81493	Coronary artery disease, mRNA, gene expression profiling by real-time RT-PCR of 23 genes, utilizing whole peripheral blood, algorithm reported as a risk score <b>(investigational)</b> [Test no longer available]

81539	Oncology (high-grade prostate cancer), biochemical assay of four proteins (Total PSA, Free PSA, Intact PSA, and human kallikrein-2 [hK2]), utilizing plasma or serum, prognostic algorithm reported as a probability score <b>(Investigational)</b>
81541	Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin embedded tissue, algorithm reported as a disease-specific mortality risk score <b>(Investigational)</b>
81542	Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score <b>(Investigational)</b>
81551	Oncology (prostate), promoter methylation profiling by real-time PCR of 3 genes (GSTP1, APC, RASSF1), utilizing formalin-fixed paraffin embedded tissue, algorithm reported as a likelihood of prostate cancer detection on repeat biopsy <b>(Investigational)</b>
83080	Hemosiderin; b-Hexosaminidase, each assay
88230	Tissue culture for non-neoplastic disorders; lymphocyte
88233	Tissue culture for non-neoplastic disorders; skin or other solid tissue biopsy
88235	Tissue culture for non-neoplastic disorders; amniotic fluid or chorionic villus cells
88237	Tissue culture for neoplastic disorders; bone marrow, blood cells
88239	Tissue culture for neoplastic disorders; solid tumor
88240	Cryopreservation, freezing and storage of cells, each cell line
88241	Thawing and expansion of frozen cells, each aliquot
88245	Chromosome analysis for breakage syndromes; baseline Sister Chromatid Exchange (SCE), 20-25 cells
88248	Chromosome analysis for breakage syndromes; baseline breakage, score 50-100 cells, count 20 cells, 2 karyotypes (eg, for ataxia telangiectasia, Fanconi anemia, fragile X)
88249	Chromosome analysis for breakage syndromes; score 100 cells, clastogen stress (eg, diepoxybutane, mitomycin C, ionizing radiation, UV radiation)
88261	Chromosome analysis; count 5 cells, 1 karyotype, with banding
88262	Chromosome analysis; count 15-20 cells, 2 karyotypes, with banding
88263	Chromosome analysis; count 45 cells for mosaicism, 2 karyotypes, with banding
88264	Chromosome analysis; analyze 20-25 cells
88267	Chromosome analysis, amniotic fluid or chorionic villus, count 15 cells, 1 karyotype, with banding
88269	Chromosome analysis, in situ for amniotic fluid cells, count cells from 6-12 colonies, 1 karyotype, with banding
88271	Molecular cytogenetics; DNA probe, each (e.g., FISH-fluorescence in situ hybridization)
88272	Chromosomal in situ hybridization, analyze 3 – 5 cells (e.g., for derivatives and markers)
88273	Chromosomal in situ hybridization, analyze 10 – 30 cells (e.g., for microdeletions)
88274	Interphase in situ hybridization, analyze 25 – 99 cells
88275	Interphase in situ hybridization, analyze 100 – 300 cells
88280	Chromosome analysis; additional karyotypes, each study
88283	Chromosome analysis; additional specialized banding technique (eg, NOR, C-banding)
88285	Chromosome analysis; additional cells counted, each study
88289	Chromosome analysis; additional high resolution study



88291	Cytogenetics and molecular cytogenetics, interpretation and report
96040	Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family
0004M	Scoliosis, DNA analysis of 53 single nucleotide polymorphisms (SNPs), using saliva, prognostic algorithm reported as a risk score <b>(Investigational)</b>
0005U	Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score <b>(Investigational)</b>
0008U	Helicobacter pylori detection and antibiotic resistance, DNA, 16S and 23S rRNA, gyrA, pbp1, rdxA and rpoB, next generation sequencing, formalin-fixed paraffin embedded or fresh tissue or fecal sample, predictive, reported as positive or negative for resistance to clarithromycin, fluoroquinolones, metronidazole, amoxicillin, tetracycline, and rifabutin <b>(Investigational)</b>
0011M	Oncology, prostate cancer, mRNA expression assay of 12 genes (10 content and 2 housekeeping), RT-PCR test utilizing blood plasma and/or urine, algorithms to predict high-grade prostate cancer risk <b>(Investigational)</b>
0021U	Oncology (prostate), detection of 8 autoantibodies (ARF 6, NKX3-1, 5'-UTR-BMI1, CEP 164, 3'-UTR-Ropporin, Desmocollin, AURKAIP-1, CSNK2A2), multiplexed immunoassay and flow cytometry serum, algorithm reported as risk score <b>(Investigational)</b>
0023U	Oncology (acute myelogenous leukemia), DNA, genotyping of internal tandem duplication, p.D835, p.I836, using mononuclear cells, reported as detection or non-detection of FLT3 mutation and indication for or against the use of midostaurin
0029U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis (ie, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 and rs12777823) <b>(Investigational)</b>
0030U	Drug metabolism (warfarin drug response), targeted sequence analysis (ie, CYP2C9, CYP4F2, VKORC1, rs12777823) <b>(Investigational)</b>
0031U	CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7) <b>(Investigational)</b>
0032U	COMT (catechol-O-methyltransferase)(drug metabolism) gene analysis, c.472G>A (rs4680) variant <b>(Investigational)</b>
0033U	HTR2A (5-hydroxytryptamine receptor 2A), HTR2C (5-hydroxytryptamine receptor 2C) (eg, citalopram metabolism) gene analysis, common variants (ie, HTR2A rs7997012 [c.614-2211T>C], HTR2C rs3813929 [c.-759C>T] and rs1414334 [c.551-3008C>G]) <b>(Investigational)</b>
0036U	Exome (ie, somatic mutations), paired formalin-fixed paraffin-embedded tumor tissue and normal specimen, sequence analyses
0046U	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia) internal tandem duplication (ITD) variants, quantitative <b>(Investigational)</b>
0047U	Oncology (prostate), mRNA, gene expression profiling by real-time RT-PCR of 17 genes (12 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a risk score <b>(Investigational)</b>
0049U	NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, quantitative <b>(Investigational)</b>

0050U	Targeted genomic sequence analysis panel, acute myelogenous leukemia, DNA analysis, 194 genes, interrogation for sequence variants, copy number variants or rearrangements <b>(Investigational)</b>
0053U	Oncology (prostate cancer), FISH analysis of 4 genes (ASAP1, HDAC9, CHD1 and PTEN), needle biopsy specimen, algorithm reported as probability of higher tumor grade <b>(Investigational)</b>
0063U	Neurology (autism), 32 amines by LC-MS/MS, using plasma, algorithm reported as metabolic signature associated with autism spectrum disorder <b>(Investigational)</b>
0070U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, common and select rare variants (ie, *2, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14A, *14B, *15, *17, *29, *35, *36, *41, *57, *61, *63, *68, *83, *xN) <b>(Investigational)</b>
0071U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, full gene sequence (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0072U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D6-2D7 hybrid gene) (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0073U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D7-2D6 hybrid gene) (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0074U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, non-duplicated gene when duplication/multiplication is trans) (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0075U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 5' gene duplication/multiplication) (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0076U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 3' gene duplication/ multiplication) (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0078U	Pain management (opioid-use disorder) genotyping panel, 16 common variants (ie, ABCB1, COMT, DAT1, DBH, DOR, DRD1, DRD2, DRD4, GABA, GAL, HTR2A, HTTLPR, MTHFR, MUOR, OPRK1, OPRM1), buccal swab or other germline tissue sample, algorithm reported as positive or negative risk of opioid-use disorder <b>(Investigational)</b>
0094U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis
0101U	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated (15 genes [sequencing and deletion/duplication], EPCAM and GREM1 [deletion/duplication only]) <b>(Investigational)</b> [ColoNext]

0102U	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated [17 genes (sequencing and deletion/duplication)] <b>(Investigational)</b> [BreastNext]
0103U	Hereditary ovarian cancer (eg, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated [24 genes (sequencing and deletion/duplication); EPCAM (deletion/duplication only)] <b>(Investigational)</b> [OvaNext]
0113U	Oncology (prostate), measurement of PCA3 and TMPRSS2-ERG in urine and PSA in serum following prostatic massage, by RNA amplification and fluorescence-based detection, algorithm reported as risk score <b>(Investigational)</b>
0117U	Pain management, analysis of 11 endogenous analytes (methylmalonic acid, xanthurenic acid, homocysteine, pyroglutamic acid, vanilmandelate, 5-hydroxyindoleacetic acid, hydroxymethylglutarate, ethylmalonate, 3-hydroxypropyl mercapturic acid (3-HPMA), quinolinic acid, kynurenic acid), LC-MS/MS, urine, algorithm reported as a pain-index score with likelihood of atypical biochemical function associated with pain <b>(Investigational)</b>
0129U	Hereditary breast cancer–related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis and deletion/duplication analysis panel (ATM, BRCA1, BRCA2, CDH1, CHEK2, PALB2, PTEN, and TP53) <b>(Investigational)</b> [BRCAplus]
0130U	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), targeted mRNA sequence analysis panel (APC, CDH1, CHEK2, MLH1, MSH2, MSH6, MUTYH, PMS2, PTEN, and TP53) (List separately in addition to code for primary procedure) <b>(Investigational)</b> [+RNAinsight for ColoNext]
0131U	Hereditary breast cancer–related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (13 genes) (List separately in addition to code for primary procedure) <b>(Investigational)</b> [+RNAinsight for BreastNext]
0132U	Hereditary ovarian cancer–related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (17 genes) (List separately in addition to code for primary procedure) <b>(Investigational)</b> [+RNAinsight for OvaNext]
0133U	Hereditary prostate cancer–related disorders, targeted mRNA sequence analysis panel (11 genes) (List separately in addition to code for primary procedure) <b>(Investigational)</b> [+RNAinsight for ProstateNext]
0134U	Hereditary pan cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (18 genes) (List separately in addition to code for primary procedure) <b>(Investigational)</b> [+RNAinsight for CancerNext]

0135U	Hereditary gynecological cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (12 genes) (List separately in addition to code for primary procedure) <b>(Investigational)</b> [+RNAinsight for GYNPlus]
0136U	ATM (ataxia telangiectasia mutated) (eg, ataxia telangiectasia) <i>mRNA sequence analysis</i> (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0137U	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) <i>mRNA sequence analysis</i> (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0138U	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) mRNA sequence analysis (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0156U	Copy number (eg, intellectual disability, dysmorphism), sequence analysis <b>(Investigational)</b>
0157U	APC (APC regulator of WNT signaling pathway) (eg, familial adenomatosis polyposis [FAP]) mRNA sequence analysis (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0158U	MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0159U	MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0160U	MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0161U	PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary nonpolyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure) <b>(Investigational)</b>
0170U	Neurology (autism spectrum disorder [ASD]), RNA, next-generation sequencing, saliva, algorithmic analysis, and results reported as predictive probability of ASD diagnosis <b>(Investigational)</b>
0171U	Targeted genomic sequence analysis panel, acute myeloid leukemia, myelodysplastic syndrome, and myeloproliferative neoplasms, DNA analysis, 23 genes, interrogation for sequence variants, rearrangements and minimal residual disease, reported as presence/absence <b>(Investigational)</b>
0173U	Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes <b>(Investigational)</b>
0175U	Psychiatry (eg, depression, anxiety); genomic analysis panel, variant analysis of 15 genes <b>(Investigational)</b>

0203U	Autoimmune (inflammatory bowel disease), mRNA, gene expression profiling by quantitative RT-PCR, 17 genes (15 target and 2 reference genes), whole blood, reported as a continuous risk score and classification of inflammatory bowel disease aggressiveness <b>(Investigational)</b>
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 <b>(Investigational)</b>
0209U	Cytogenomic constitutional (genome-wide) analysis, interrogation of genomic regions for copy number, structural changes and areas of homozygosity for chromosomal abnormalities
0212U	Rare diseases (constitutional/heritable disorders), whole genome and mitochondrial DNA sequence analysis, 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, proband
0213U	Rare diseases (constitutional/heritable disorders), whole genome and mitochondrial DNA sequence analysis, 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, each comparator genome (eg, parent, sibling)
0214U	Rare diseases (constitutional/heritable disorders), whole exome and mitochondrial DNA sequence analysis, 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, proband
0215U	Rare diseases (constitutional/heritable disorders), whole exome and mitochondrial DNA sequence analysis, 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, each comparator exome (eg, parent, sibling)
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
0228U	Oncology (prostate), multianalyte molecular profile by photometric detection of macromolecules adsorbed on nanosponge array slides with machine learning, utilizing first morning voided urine, algorithm reported as likelihood of prostate cancer <b>(Investigational)</b>
0235U	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor 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

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
0265U	Rare constitutional and other heritable disorders, whole genome and mitochondrial DNA sequence analysis, blood, frozen and formalin-fixed paraffinembedded (FFPE) tissue, saliva, buccal swabs or cell lines, identification of single nucleotide and copy number variants
0290U	Pain management, mRNA, gene expression profiling by RNA sequencing of 36 genes, whole blood, algorithm reported as predictive risk score <b>(Investigational)</b>
0291U	Psychiatry (mood disorders), mRNA, gene expression profiling by RNA sequencing of 144 genes, whole blood, algorithm reported as predictive risk score <b>(Investigational)</b>
0292U	Psychiatry (stress disorders), mRNA, gene expression profiling by RNA sequencing of 72 genes, whole blood, algorithm reported as predictive risk score <b>(Investigational)</b>
0293U	Psychiatry (suicidal ideation), mRNA, gene expression profiling by RNA sequencing of 54 genes, whole blood, algorithm reported as predictive risk score <b>(Investigational)</b>
0297U	Oncology (pan tumor), whole genome sequencing of paired malignant and normal DNA specimens, fresh or formalin-fixed paraffin-embedded (FFPE) tissue, blood or bone marrow, comparative sequence analyses and variant identification
0339U	Oncology (prostate), mRNA expression profiling of HOXC6 and DLX1, reverse transcription polymerase chain reaction (RT-PCR), first-void urine following digital rectal examination, algorithm reported as probability of high-grade cancer <b>(Investigational)</b>
0345U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6 <b>(Investigational)</b>
0347U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 16 gene report, with variant analysis and reported phenotypes <b>(Investigational)</b>
0348U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 25 gene report, with variant analysis and reported phenotypes <b>(Investigational)</b>
0349U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 27 gene report, with variant analysis, including reported phenotypes and impacted gene-drug interactions <b>(Investigational)</b>
0350U	Infectious disease (bacterial or viral), biochemical assays, tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), interferon gamma-induced protein-10 (IP-10), and C-reactive protein, serum, algorithm reported as likelihood of bacterial infection <b>(Investigational)</b>
0359U	Oncology (prostate cancer), analysis of all prostate-specific antigen (PSA) structural isoforms by phase separation and immunoassay, plasma, algorithm reports risk of cancer <b>(Investigational)</b>

0364U	Oncology (hematolymphoid neoplasm), genomic sequence analysis using multiplex (PCR) and next-generation sequencing with algorithm, quantification of dominant clonal sequence(s), reported as presence or absence of minimal residual disease (MRD) with quantitation of disease burden, when appropriate [clonoSEQ]
0392U	Drug metabolism (depression, anxiety, attention deficit hyperactivity disorder [ADHD]), gene-drug interactions, variant analysis of 16 genes, including deletion/duplication analysis of CYP2D6, reported as impact of gene-drug interaction for each drug <b>(Investigational)</b>
0400U	Obstetrics (expanded carrier screening), 145 genes by nextgeneration sequencing, fragment analysis and multiplex ligationdependent probe amplification, DNA, reported as carrier positive or negative
0403U	Oncology (prostate), mRNA, gene expression profiling of 18 genes, first-catch post-digital rectal examination urine (or processed first-catch urine), algorithm reported as percentage of likelihood of detecting clinically significant prostate cancer <b>(Investigational)</b>
0411U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6 <b>(Investigational)</b>
0425U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis, each comparator genome (eg, parents, siblings)
0426U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), ultra-rapid sequence analysis
0434U	Drug metabolism (adverse drug reactions and drug response), genomic analysis panel, variant analysis of 25 genes with reported phenotypes <b>(Investigational)</b>
0437U	Psychiatry (anxiety disorders), mRNA, gene expression profiling by RNA sequencing of 15 biomarkers, whole blood, algorithm reported as predictive risk score <b>(Investigational)</b>
0438U	Drug metabolism (adverse drug reactions and drug response), buccal specimen, gene-drug interactions, variant analysis of 33 genes, including deletion/duplication analysis of CYP2D6, including reported phenotypes and impacted genedrug interactions <b>(Investigational)</b>
0449U	Carrier screening for severe inherited conditions (eg, cystic fibrosis, spinal muscular atrophy, beta hemoglobinopathies [including sickle cell disease], alpha thalassemias) regardless of race or self-identified ancestry, genomic sequence analysis of 5 genes (CFTR, SMN1, HBB, HBA1, HBA2)

#### HCPCS Coding:

G9143	Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s) <b>(Investigational)</b>
S0265	Genetic counseling, under physician supervision, each 15 minutes
S3722	Dose optimization by area under the curve (AUC) analysis, for infusional 5-fluorouracil <b>(Investigational)</b>
S3841	Genetic testing for retinoblastoma
S3842	Genetic testing for Von Hippel-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
S3852	DNA analysis for APOE epsilon 4 allele for susceptibility to Alzheimer's disease <b>(Investigational)</b>
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
S3870	Comparative genomic hybridization (CGH) microarray testing for developmental delay, autism spectrum disorder and/or intellectual disability

## REIMBURSEMENT INFORMATION:

Florida Blue has adopted the U.S. Preventive Services Task Force (USPSTF) Recommendations. In order to be covered, Services shall be provided in accordance with prevailing medical standards consistent with the USPSTF Recommendations.

Codes 83080, 88230, 88233, 88235, 88237, 88239, 88240, 88241, 88245, 88248, 88249, 88261, 88262, 88263, 88264, 88267, 88269 are limited to four (4) tests within a 12-month period.

Code 88291 is limited to twenty-five (25) of each test within a 12-month period.

Code 88271 is limited to forty-one (41) tests within a 12-month period.

Code 88280 is limited to two (2) tests within a 12-month period.

Codes 88272, 88273, 88274, 88283, 88285, 88289, S3841, S3842, S3844, S3845, S3846, S3849, S3850, S3853 and S3861 are limited to one (1) of each test within a 12-month period.

The following information is required for services subject to medical review, including services in excess of reimbursement limitations: documentation to support medical necessity: reason for test(s), previous lab results, how the results of the test will be utilized, how the results of the test will contribute to improved health outcomes, or alters patient's treatment and or management.

## LOINC Codes:

Documentation Table	LOINC Codes	LOINC Time Frame Modifier Code	LOINC Time Frame Modifier Codes Narrative
Physician history and physical	28626-0	18805-2	Include all data of the selected type that represents observations made six months or



			fewer before starting date of service for the claim
Attending physician visit note	18733-6	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Attending physician progress note	18741-9	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Plan of treatment	18776-5	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Laboratory studies	26436-6	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim

## PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products:

The following National Coverage Determinations (NCDs) were reviewed on the last guideline reviewed date and are located at cms.gov: Next Generation Sequencing (NGS) (90.2), Pharmacogenomic Testing for Warfarin Response (90.1) and Cytogenetic Studies (190.3).

The following were reviewed on the last guideline reviewed date: Molecular Diagnostic Services (MoIDX) coverage determinations; located at cms.gov.

The following Local Coverage Determinations (LCD) are located at fcso.com: Molecular Pathology Procedures (L34519), 4Kscore Test Algorithm (L37798).

The following Local Coverage Determination (LCD) located at cms.gov was reviewed on the last guideline reviewed date: Prostate Cancer Detection with IsoPSA® (L39284).

The following Local Coverage Article is located at fcso.com: Billing and Coding: Molecular Pathology and Genetic Testing (A58918).

## DEFINITIONS:

**Carrier screening:** Genetic testing that is performed on an individual who does not have any symptoms of a particular genetic disorder but may have one abnormal allele for the gene that is associated with the disorder. (ACOG Committee Opinion No. 690, 2017)

**Compound Heterozygous:** The presence of 2 different mutant alleles at a particular gene locus, one on each chromosome of a pair.

**Expanded carrier screening:** Disease screening that evaluates an individual's carrier state for multiple conditions at once and regardless of ethnicity. (ACOG Committee Opinion No. 690, 2017)

**Homozygous:** Having the same alleles at a particular gene locus on homologous chromosomes (chromosome pairs).

**Panethnic screening:** Individuals are screened regardless of their ethnic background. (ACOG Committee Opinion No. 690, 2017)

**Penetrance:** The proportion of individuals with a variant that causes a disorder who exhibit clinical symptoms of that disorder.

**Residual Risk:** The risk that an individual is a carrier of a disease, but testing for carrier status of the disease is negative (eg, if the individual carries a pathogenic variant not included in the test assay).

## RELATED GUIDELINES:

[Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer, 05-86000-26](#)

[Genetic Testing for Hereditary Breast or Ovarian Cancer, 05-82000-30](#)

[Genetic Testing for Lynch Syndrome and Other Inherited Colon Cancer Syndromes , 05-82000-31](#)  
[Tumor/Genetic Markers, 05-86000-22](#)

## OTHER:

None applicable.

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22. Blue Cross Blue Shield Association Evidence Positioning System®. 2.04.13 Genetic Testing for Alzheimer Disease, 11/22.
23. Blue Cross Blue Shield Association Evidence Positioning System®. 2.04.33 Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer, 12/22.
24. Blue Cross Blue Shield Association Evidence Positioning System®. 2.04.38 Cytochrome P450 Genotype-Guided Treatment Strategy, 07/23.
25. Blue Cross Blue Shield Association Evidence Positioning System®. 2.04.43 Genetic Testing for Cardiac Ion Channelopathies, 02/23.

26. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.44 Genetic Testing for Familial Cutaneous Malignant Melanoma, 04/23.
27. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.48 Genotype-Guided Warfarin Dosing, 07/23.
28. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.51 Genotype-Guided Tamoxifen Treatment, 08/23.
29. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.59 Genetic Testing for Developmental Delay/Intellectual Disability, Autism Spectrum Disorder, and Congenital Anomalies, 11/22.
30. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.63 Use of Common Genetic Variants (Single Nucleotide Variants) to Predict Risk of Nonfamilial Breast Cancer, 11/22.
31. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.68 Laboratory and Genetic Testing for Use of 5-Fluorouracil in Patients with Cancer, 04/23.
32. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.75 Genetic Testing of CADASIL Syndrome, 05/23.
33. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.83 Genetic Testing for FMR1 Variants (Including Fragile X Syndrome), 02/23.
34. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.86 Genetic Testing for Duchenne and Becker Muscular Dystrophy, 04/23.
35. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.81 Genetic Testing for Rett Syndrome, 06/23.
36. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.88 Genetic Testing for PTEN Hamartoma Tumor Syndrome, 03/23.
37. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.89 Genetic Testing for the Diagnosis of Inherited Peripheral Neuropathies, 02/23.
38. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.93 Genetic Cancer Susceptibility Panels Using Next Generation Sequencing, 11/22.
39. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.94 Genetic Testing for Lactase Insufficiency, 06/23.
40. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.95, Human Leukocyte Antigen Testing for Celiac Disease, 12/22.
41. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.96 Genetic Testing for Statin-Induced Myopathy, 12/22.
42. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.99 Genetic Testing for Hereditary Pancreatitis, 03/23.
43. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.102 Whole Exome and Whole Genome Sequencing for Diagnosis of Genetic Disorders, 04/23.
44. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.103 Genetic Testing for Macular Degeneration, 04/23.

45. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.104 Genetic Testing for  $\alpha$ -Thalassemia, 07/23.
46. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.106 Genetic Testing for CHARGE Syndrome, 03/23.
47. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.107 Carrier Screening for Genetic Diseases, 10/22.
48. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.108 Fetal RHD Genotyping Using Maternal Plasma, 09/23.
49. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.110 Genetic Testing for Diagnosis and Management of Mental Health Conditions, 08/23.
50. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.111 Gene Expression Profiling and Protein Biomarkers for Prostate Cancer Management, 12/22.
51. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.114 Genetic Testing for Idiopathic Dilated Cardiomyopathy, 03/23.
52. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.116 Invasive Prenatal (Fetal) Diagnostic Testing, 09/23.
53. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.121 Miscellaneous Genetic and Molecular Diagnostic Tests, 09/23.
54. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.122 Chromosomal Microarray Analysis for the Evaluation of Pregnancy Loss, 09/23.
55. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.124 Genetic Testing for FLT3, NPM1, and CEBPA Variants in Cytogenetically Normal Acute Myeloid Leukemia, 02/23.
56. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.126 Moderate Penetrance Variants Associated With Breast Cancer in Individuals at High Breast Cancer Risk, 09/23.
57. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.131 Pharmacogenetic Testing for Pain Management, 12/22.
58. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.137 Genetic Testing for Neurofibromatosis, 02/23.
59. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.147 Next-Generation Sequencing for the Assessment of Measurable Residual Disease, 01/23.
60. Blue Cross Blue Shield Association Evidence Positioning System® . 2.04.149 Molecular Testing for Variants Associated with Hereditary Ovarian Cancer, 09/23.
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### COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 12/08/23.

### GUIDELINE UPDATE INFORMATION:

11/15/03	Medical Coverage Guideline Annual review. Developed separate guideline for Genetic Testing For Miscellaneous Diagnoses. Developed separate genetic testing guidelines for the following: BRCA1 and BRCA2, colon cancer (FAP and HNPCC), and medullary carcinoma of the thyroid (RET proto-oncogene).
01/01/04	Annual HCPCS coding update: added S3853.
07/01/05	HCPCS update: added S0265.
12/15/05	Biennial review: coverage unchanged.
01/01/06	Annual HCPCS coding update: added 83900, 83907, 83908, 83909, 83914; revised 83898, 83901.
06/15/06	Revision to include new codes into limitation section.
01/01/07	Annual HCPCS coding update: added 96040; deleted 99401, 99402, 99403, and 99404.
07/15/07	Annual review, coverage statements maintained, guideline reformatted, references updated.
01/01/08	Annual HCPCS coding update: revised 83898, 83900, 83901, and 83908.
01/01/09	Annual HCPCS coding update: descriptor revised for codes 83890, 83891, 83892, 83893, 83894, 83897, 83900, 83903, 83907, 83909, and 83914.
10/15/09	Annual review: position statement, reimbursement section, guideline title and references updated.
12/15/10	Revision; description section, inheritable disease diagnosis table reimbursement and coding sections updated; prenatal test table and Other Genetic Tests section added.
07/15/10	Revision; Other Genetic Tests section updated.
10/01/11	Revision; formatting changes.
11/15/11	Revision; CPT code 88275 removed from the Reimbursement Information section.

01/01/12	Annual HCPCS update. Added codes 81200-81408.
02/15/12	Revision; Postnatal and Other Genetic Tests section, Billing/Coding Information section and references updated.
04/01/12	Quarterly HCPCS update. Deleted codes S3835, S3837, S3843, S3847, S3848, S3851, S3860, S3862.
08/15/12	Revision; Postnatal and Other Genetic Tests section updated.
10/15/12	Revision; Postnatal and Other Genetic Tests, Coding, and references updated.
01/01/13	Annual HCPCS update: added codes 81161, 81252-81254, 81321-81326; revised codes 81400-81408; deleted codes 83890-83914; updated reimbursement section. Prenatal & Postnatal Genetic Tests sections and references updated.
05/15/13	Revision; Genetic Testing to Establish a Diagnosis of Inheritable Disease and Postnatal and Other Genetic Tests sections updated; coding and references updated.
07/01/13	Quarterly HCPCS update. Added code 0004M; revised codes 81400-81408; Program Exceptions section updated.
08/15/13	Revision; Postnatal and Other Genetic Tests, Program Exceptions, and references updated.
09/15/13	Revision; experimental test list and references updated.
11/15/13	Revision; Postnatal and Other Genetic Tests section and references updated.
01/01/14	Annual HCPCS update. Added code 81287; revised codes 81371, 81376, & S3870.
02/15/14	Revision; position statement section updated.
07/01/14	Quarterly HCPCS update. Revised codes 81402 & 81404.
08/15/14	Revision; position statement section and references updated.
10/15/14	Revision; Position statement section and references updated.
01/01/15	Annual HCPCS/CPT update. Added codes 81246, 81313, 81410-81471; deleted code S3855.
03/15/15	Revision; position statement section, coding, and references updated.
07/01/15	Quarterly CPT/HCPCS update. Revised codes 81401 and 81406.
10/15/15	Revision; position statement section and references updated.
10/26/15	Revision; investigational test list updated.
11/15/15	Revision; coding section updated.
12/15/15	Revision; position statement section, coding, program exception, and references updated.
01/01/16	Annual HCPCS/CPT update; codes 81170, 81218, 81219, 81272, 81273, 81311, 81314, 81412, 81432-81434, 81437, 81438, 81442, 81493 added; codes 81355, 81401-81404, 81435, 81436, 81445-81455 revised; code S3721 deleted.
02/15/16	Revision; position statement section updated.
04/01/16	Quarterly HCPCS/CPT update; code 0010M revised.
05/15/16	Revision; Position statement section, coding, and references updated.
08/08/16	Revision; experimental test list updated.
08/31/16	Revision; Position Statement section; experimental test list updated.
11/08/16	Revision; deleted code 81311.
12/15/16	Revision; Position statement section and references updated.
01/01/17	Annual CPT/HCPCS update. Added 81413, 81414, 81439, 81539; revised 81400-81408; deleted 81280-81282, 0010M.

02/15/17	Revision; position statement section and references updated.
04/15/17	Revision; FMR1 Mutations, Acute Myeloid Leukemia, CHARGE Syndrome, Neurofibromatosis, PTEN Hamartoma Tumor Syndrome, and Cytogenetic Studies position statements added; Hereditary Pancreatitis and Inherited Peripheral Neuropathy position statements updated; description, coding, and references updated.
05/01/17	CPT Code update: code 0005U added.
06/15/17	Revision; Position statement section updated including CADASIL Syndrome position statements added and genetic testing for Alzheimer Disease position statement revised; references updated.
08/01/17	Coding Updates: Added codes 0007U, 0008U, 0010U, 0012U-0017U.
10/15/17	Revision; CMA investigational position statement added for the evaluation of all other conditions of delayed development; Diagnosis Table, coding, and references updated.
11/15/17	Revision to AML position statement section.
12/15/17	Revision; position statement section updated including testing for one or more single nucleotide polymorphisms (SNPs) and references updated.
01/01/18	Annual CPT/HCPCS update. Added codes 81230-81232, 81238, 81258-81269, 81328, 81334, 81335, 81346, 81448, 81541, 81551, 0011M, 0027U-0034U; revised codes 81257, 81432, 81439; deleted code 0015U. Investigational test list updated and code 0020U added.
02/15/18	Revision; position statements, test names, and references updated.
04/01/18	Quarterly HCPCS/CPT update. Added codes 0036U, 0037U, 0040U.
05/15/18	Revision; position statements, coding, program exception, and references updated.
05/16/18	Revision; RPE65 genetic testing position statement added and investigational test list updated.
07/01/18	Quarterly HCPCS/CPT update. Added codes 0046U-0050U, 0053U.
09/15/18	Revision; investigational status maintained but statements updated for genotype-guided warfarin dosing and testing for diagnosis/management of mental health conditions; position statements added for CYP450 genotype-guided treatment strategy; NCCN breast cancer risk criteria for PALB2 testing updated.
10/01/18	Quarterly HCPCS/CPT update. Added codes 0063U, 0069U-0076U, 0078U, 0079U; deleted 0028U.
10/15/18	Coding updated.
12/15/18	Revision; Next generation sequencing for measurable residual disease investigational statement added; genetic and protein biomarkers for the diagnosis of prostate cancer test list updated; coding and references updated.
01/01/19	Annual CPT/HCPCS coding update. Added codes 81171-81174, 81204, 81443, 0081U; revised codes 81244, 81287, 0008U; deleted code 0020U.
02/15/19	Revision; code 0081U deleted (refer to MCG 05-86000-22).
03/15/19	Revision; Position statements for FMR1 variants testing and FLT3, NPM1, and CEBPA variants testing updated; coding and references updated.
05/15/19	Revision; Position statements, including testing for dilated cardiomyopathy, and references updated.
07/01/19	Quarterly CPT/HCPCS update. Added codes 0094U, 0101U-0104U.

08/15/19	Revision; Genetic testing panels for mental health disorders & genetic testing for diagnosis and management of mental health disorders position statements maintained; testing for Rett syndrome position statements and references updated.
10/01/19	Quarterly CPT/HCPCS update. Added codes 0113U, 0117U, 0129U-0138U; deleted code 0104U. Deleted codes 81206-81208, 0016U.
10/24/19	Revision; PALB2 testing section updated.
01/01/20	Review; Assessment of MRD statements updated; statements for assays & gene expression profiling for diagnosis, cancer risk assessment, or management of prostate cancer maintained; coding & references updated. Annual CPT/HCPCS coding update. Added codes 81277, 81307, 81308, 81542, 0156U-0162U; revised code 81350.
04/01/20	Quarterly CPT/HCPCS update. Added codes 0170U & 0171U.
05/15/20	Revision; Whole exome and whole genome position statements updated; coding, and references updated.
07/01/20	Revision: CADASIL syndrome position statements updated; gene expression analysis and protein biomarkers to guide management of prostate cancer reviewed and position statement maintained; references updated. Quarterly CPT/HCPCS update. Added codes 0173U and 0175U.
09/15/20	Revision; References updated; code 0069U removed (refer to policy 05-86000-28).
10/01/20	Quarterly CPT/HCPCS update. Added codes 0203U-0222U.
11/15/20	Revision; PALB2 position statements updated; Testing for BRIP1, RAD51C, and RAD51D variants position statements added; coding and references updated.
01/01/21	Annual CPT/HCPCS update. Codes 0228U, 0234U, 0235U, 0237U added; codes 81400-81400-81408 revised.
02/15/21	Review; Measurable residual disease (MRD) statements updated; gene expression analysis and protein biomarkers to guide management of prostate cancer maintained; prenatal whole exome/whole genome sequencing statement added; investigational test list, coding, and references updated. Codes 0007U & 0079U removed (refer to policy 05-86000-32).
06/15/21	Revision; Carrier screening position statements added; coding and references updated.
09/01/21	Revision: Breast cancer risk statements updated; coding and references updated
10/01/21	Quarterly CPT/HCPCS update. Code 0265U added.
11/15/21	Review: ExoDX Prostate IntelliScore test position statement maintained.
01/01/22	Annual CPT/HCPCS coding update. Codes 81349, 0290U- 0293U, 0297U added; 81228, 81229 revised.
02/15/22	Revision: Genetic testing to guide initiation or management FDA-approved amyloid-beta targeting therapy (aducanumab) investigational statement added; gene expression profiling and protein biomarkers for prostate cancer management position statement maintained; references updated.
05/15/22	Review: Gene expression analysis and protein biomarkers to guide management of prostate cancer position statement maintained; references updated.
07/15/22	Revision: Genetic testing for Rett syndrome associated genes position statement updated; references updated.
10/01/22	Quarterly CPT/HCPCS update. Codes 0339U and 0345U added.

11/15/22	Review: Cytochrome P450, carrier screening, gene variants associated with breast cancer risk and ovarian cancer position statements updated; coding and references updated.
01/01/23	Annual CPT/HCPCS coding update. Code 81418 added.
02/15/23	Revision: coding and references updated.
04/01/23	Quarterly CPT/HCPCS update. Code 0364U added.
06/15/23	IsoPSA test added to prostate cancer section; genetic cancer susceptibility panel testing statement removed, investigational test list and references updated.
07/01/23	Quarterly CPT/HCPCS update. Codes 0392U & 0400U added; code 0053U deleted. Coding section updated and note in position statement section updated.
10/01/23	Quarterly CPT/HCPCS update. Codes 0403U & 0411U added. References updated.
01/01/24	Position statements maintained. Annual CPT/HCPCS coding update. Codes 0425U, 0426U, 0434U, 0437U, 0438U added. Program exception and references updated.
04/01/24	Quarterly CPT/HCPCS coding update. Code 0449U added.