JOHNS HOPKINS HEALTH PLANS	Johns Hopkins Health Plans **Medical Policy Manual** **Medical Policy**	*Policy Number*	CMS07.03
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	Subject **Genetic Testing**	*Supersedes Date*	04/01/2024
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This document applies to the following Participating Organizations:

EHP US Family Health Plan

Keywords: Carrier, Genetic, Preimplantation , Prenatal

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I. ACTION

	New Policy	
X	Revising Policy Number	CMS07.03
	Superseding Policy Number	
	Retiring Policy Number	

II. POLICY DISCLAIMER

Johns Hopkins Health Plans (JHHP) provides a full spectrum of health care products and services for Advantage MD, Employer Health Programs, Johns Hopkins Health Plan of Virginia Inc., Priority Partners, and US Family Health Plan. Each line of business possesses its own unique contract, benefits, regulations, and regulators' clinical guidelines that supersede the information outlined in this policy.

III. POLICY

Cross Reference:

- CMS04.03 Pharmacogenomics

For Advantage MD, refer to: eviCore Guidelines

For Employer Health Programs (EHP) refer to:

- Plan specific Summary Plan Descriptions (SPDs)

For Johns Hopkins Health Plan of Virginia Inc. (JHHPVA) refer to: eviCore Guidelines

For Priority Partners (PPMCO) refer to: eviCore Guidelines

For US Family Health Plan refer to: Tricare Policy Manuals

- TRICARE Policy Manual 6010.63-M, April 1, 2021, Chapter 6, Section 3.1 Genetic Testing and Counseling
- TRICARE Policy Manual 6010.63-M, April 1, 2021, Chapter 4, Section 18.1 Maternity Care
- TRICARE Policy Manual 6010.63-M, April 1, 2021, Chapter 4, Section 18.2 Antepartum Services
- TRICARE Operations Manual 6010.62-M, April 1, 2021, Chapter 18, Section 2 Defense Health Agency (DHA) Evaluation Of Non-United States (U.S.) Food and Drug Administration (FDA) Approved Laboratory Developed Tests (LDTs) Demonstration Project

IV. POLICY CRITERIA

A. When benefits are provided under the member's contract, JHHP considers genetic and genomic testing to be medically necessary when the *Universal Requirements in section B* AND the *Specific Genetic Test Category Criteria in section C (if available)* are met:

B. Universal Requirements:

1. All genetic tests must be ordered by a treating specialist physician (e.g., neurologist, cardiologist, OB/GYN, clinical geneticist), a nurse practitioner or physician assistant working with a specialist physician, or genetic counselor practicing within the scope of their license, who will ensure that the medical necessity criteria below are met *(For USFHP, genetic counselors are not ordering providers),* AND;
2. The requested genetic test is as targeted as possible for the clinical situation and is performed for ONE of the following reasons:
   a. For the diagnosis of genetic disease in a symptomatic individual (diagnostic), OR;
   b. For the determination of future risk of suspected disease (presymptomatic/predictive), OR;
   c. For the detection of risks of specific diseases to future children (carrier status, prenatal, pre-implantation), AND;
3. Supporting documentation submitted for utilization review must include the following:
   a. Test specific information:
      i. Proprietary test name(s)/gene names(s), and applicable CPT codes, AND;
      ii. Name of laboratory performing the test and name of billing provider (if institutional/facility billing, indicate name of the performing laboratory), AND;
   b. Clinical documentation submitted to support medical necessity reflects the following:
      i. Clinical rationale for genetic testing, AND;
      ii. Result of the test will directly impact the management of the member (e.g., treatment, screening, or surveillance), or member's current pregnancy, AND;
      iii. The member or parent/guardian received genetic counseling regarding possible outcomes (positive or negative results) and a suggested plan of action by a healthcare professional with expertise in genetics, AND;
   c. Documentation indicating the requested test has adequate clinical validity and utility based on ONE of the following:
      i. Genetic testing for requested indication is supported by well-recognized professional societies or government organizations (e.g., American College of Obstetrician and Gynecologists (ACOG), American College of Medical Genetics and Genomics (ACMG), National Comprehensive Cancer Network (NCCN), American Heart Association (AHA), Heart Rhythm Society (HRS), National Institutes of Health OR;
      ii. Genetic testing is supported by credible scientific evidence-based peer-reviewed medical literature generally recognized by the relevant medical community.
      Note: Examples of publicly available resources hosted by the National Institute of Health (NIH) include:

- GeneReviews®: an international point-of-care resource that provides clinically relevant and medically actionable information for inherited conditions (clinical characteristics, diagnosis, testing, and management)
- Clinical Genome Resource (ClinGen): a central resource that defines the clinical relevance of genes and variants (search for gene-disease validity and actionability [clinical intervention]; search by gene[s] or disease)
- OMIM®: a comprehensive compendium of human genes and genetic phenotypes containing full-text information on all known Mendelian disorders (resource is updated daily)
- PDQ® Cancer Information Summaries, Genetics: a cancer database developed and maintained by the U.S. National Cancer Institute (NCI). The PDQ is a comprehensive source of cancer information, including cancer risk assessment and genes associated with hereditary cancers, OR;

iii. Genetic tests that have received a Hayes rating of A or B for specific indication(s) requested by the ordering provider, AND;

4. The member has not had the requested genetic test done previously (genetic testing is indicated once per lifetime per condition). Exceptions may be considered if:
   a. Technical advances in testing demonstrate significant advantages that would support a medical need to retest, OR;
   b. New pathologic familial variant is identified in an immediate blood relative and the member has not yet been tested, OR;
   c. There is a relapse of cancer or failure of cancer treatment and a new sample of primary tumor will be examined.
5. Unless specific benefits are provided under the member's contract, JHHP considers the following genetic tests experimental and investigational for all indications as they do not meet the Technology Evaluation Criteria (TEC) as defined in CMS01.00 Medical Policy Introduction: (*not all-inclusive*)
   a. Genetic tests that have received a Hayes Rating of D1 or D2, OR;
   b. Genetic testing for polymorphisms (e.g., C677T and A1298C) in the MTHFR gene, OR;
   c. Genetic testing for single nucleotide polymorphisms (SNPs), OR;
   d. Polygenic risk score testing, OR;
   e. Direct-to-consumer genetic tests (e.g., 23andMe PGS Genetic Health Risk Report, 23andMe Personal Genome Service (PGS), 23andMe MUTYH-Associated Polyposis (MAP), AncestryDNA Factor V Leiden Genetic Health Risk Test), OR;
   f. Optical genome mapping.

C. Specific Genetic Test Category Criteria:
   1. *Diagnostic testing in a symptomatic individual:*
      a. Clinical presentation is consistent with a certain or highly probable genetic etiology, OR;
      b. Newborn screening results are positive, borderline, or inconclusive for a specific disorder for which confirmatory genetic testing is required.
   2. *Predictive testing in an asymptomatic individual:*
      a. Individual is at increased risk of developing cancer or multifactorial genetic disorder (e.g., cardiomyopathy, pulmonary hypertension) due to family history, AND;
      b. Presence of genetic variant(s) is highly predictive for the development of the genetic condition, AND;
      c. The results will be used for clinical management or recommendations for surveillance, AND;
      d. Development of symptoms is certain in the presence of a gene mutation (e.g., Huntington's disease, spinocerebellar ataxia, APC gene), OR;
      e. Development of symptoms is likely but not certain in the presence of a gene mutation (e.g., predisposition to breast cancer [BRCA gene] or colon cancer [e.g., MSH2 or MSH6 gene]).

3. *Carrier status testing:* Preconception or prenatal carrier testing for an individual who has the capacity and intention to reproduce is considered medically necessary when the following criteria are met:
    a. Routine screening when mandated by governmental organizations and/or recommended by well-recognized professional societies in the United States (e.g., routine screening for cystic fibrosis and spinal muscular atrophy as recommended by the American College of Obstetricians and Gynecologists ([ACOG]), OR;
    b. Carrier screening based on family history of a genetic condition:
        i. Genetic testing is for disease-causing (pathogenic or likely pathogenic) variant(s) with a well-defined phenotype that would have a detrimental effect on health and/or quality of life (e.g., cause cognitive or physical impairment, require surgical or medical intervention), AND;
        ii. The member is at risk of being a carrier of a genetic condition due to family history (e.g., Fragile-X Syndrome), ethnicity (e.g., Ashkenazi Jewish, African descent), or abnormal laboratory findings (e.g., hemoglobinopathies), OR;
        iii. The member's reproductive partner is affected or a known carrier of a genetic condition, OR;
        iv. There is a known disease-causing (pathogenic or likely pathogenic) variant(s) in a blood relative (known familial mutation), OR;
        v. Genetic diagnosis has been clinically confirmed in an affected blood relative, but genetic testing was not or could not be done, OR;
        vi. Family history and/or ethnicity of a member or reproductive partner is unknown, AND;
    c. Genetic testing should be tailored and limited to the number of genes or tests reasonably necessary to establish carrier status when the carrier frequency is one in 100 or greater (e.g., Ashkenazi Jewish multi-gene panel carrier screening is limited to conditions specified by the ACMG and/or ACOG), AND;
    d. Carrier testing is indicated only in adults. Carrier screening in minor children for adult-onset genetic conditions is not indicated, except in the case of a pregnancy of a minor child.
4. *Prenatal screening and diagnosis:*
    a. Noninvasive Prenatal Testing (NIPT) is considered medically necessary when it is ordered by a qualified specialist provider (e.g., OB/GYN, maternal fetal medicine) and is in accordance with the most current recommendations by ACOG.
    b. Prenatal diagnostic genetic testing of a fetus is medically necessary for any pregnant person undergoing amniocentesis or chorionic villus sampling (CVS) for the diagnosis of a genetic condition/suspected fetal aneuploidy in accordance with ACOG recommendations.
5. *Preimplantation Genetic Diagnostic (PGD) testing of an embryo*: When benefits for advanced reproductive technologies (ART), including but not limited to in-vitro fertilization (IVF), are available, JHHP considers pre-implantation diagnostic genetic testing medically necessary when ANY of the following criteria are met:
    a. PGT for Monogenic/single gene defects (PGT-M):
        1. Both partners (or member and donor) are known carriers of a single autosomal recessive disorder, OR;
        2. One partner (or donor) is a known carrier of a single gene autosomal recessive disorder and the partners (or member and donor) have one offspring that has been diagnosed with that recessive disorder, OR;
        3. One partner (or donor) is affected by a single gene autosomal dominant disorder, OR;
        4. One partner (or donor) is a known carrier of an X-linked disorder, OR;
        5. One partner (or donor) has a 50% risk of having a single gene autosomal dominant disorder based on having an affected parent, but has chosen to forego pre-symptomatic testing as no treatment is available.
    b. PGD for Structural Chromosome Rearrangements (PGT-SR):
        1. One partner (or donor) has a known balanced or unbalanced translocation or known deletion/duplication.
    c. Unless specific benefits are provided under the member's contract, JHHP considers preimplantation genetic testing for aneuploidy (PGT-A) not medically necessary for ALL indications.
6. *Hereditary cancer syndromes and cancer susceptibility:*
    a. An individual diagnosed with cancer suspected to be caused by an inherited pathogenic variant(s), OR;

b. An unaffected individual at risk of developing cancer due to family history, AND;
c. The corresponding NCCN Guidelines™ criteria must be met.

7. *Germline testing, after a somatic variant is identified through the evaluation of solid or hematologic malignancy:*
   a. The gene/variant detected through tumor profiling is pathogenic or likely pathogenic and the test is to identify a potential hereditary etiology for the person's tumor, AND;
   b. The variant identified has a high rate of germline incidence based on gene and tumor type and/or family history (e.g., BRCA1/2, TP53, APC, CDH1 genes), AND;
   c. The corresponding NCCN Guidelines™ or other published evidence-based clinical criteria for management (e.g., early cancer screening, lifestyle changes, prophylactic medications) must be met.
8. *Genetic testing for heritable disorders of non-covered relatives:*
   a. The information is needed to adequately assess risk in the JHHP member, AND;
   b. The information will directly impact the current specific medical treatment being delivered to the JHHP member, AND;
   c. The non-JHHP member's benefit plan, if any, will not cover the test (a copy of the denial letter from the non-JHHP member's benefit plan must be provided or, in the case of individuals without a health insurance policy, a written statement documenting a lack of coverage).
9. *Multi-gene panel:*
   a. Multiple genes are known to cause the same condition and a limited subset of genes does not account for the majority of disease-causing mutations (e.g., Noonan syndrome, Stickler syndrome), OR;
   b. The clinical presentation is highly suspicious of a genetic disorder, but the constellation of findings in the personal or family history does not suggest a specific diagnosis or limited set of conditions (e.g., epilepsy, intellectual disability, hearing loss, retinal disorders), AND;
   c. Only one multi-gene panel should be requested at one time. Multi-gene panel testing should be performed in a tiered fashion with independent justification for each panel requested.
10. *Whole Exome Sequencing (WES):*
    a. The member is suspected to have a genetic disorder that demonstrates a high degree of genetic heterogeneity or with a phenotype or phenotypes, (e.g., intellectual disability, seizures, multiple congenital anomalies), AND;
    b. The clinical presentation does not fit a well-defined genetic syndrome that can be diagnosed by a single gene or multi-gene panel, AND;
    c. Documentation of pretest genetic counseling by a board-certified genetic counselor or geneticist, AND
    d. WES is more efficient and cost-effective than a single-gene or multi-gene panel based on the diagnosis.
11. *Whole Genome Sequencing (WGS): (Requires Medical Director review)*
    a. The member has been evaluated by a board-certified genetic provider, AND;
    b. The test is intended for diagnostic use and the results are expected to affect clinical decision making (guiding treatment, surveillance, initiation or withdrawal of palliative care), AND;
    c. The member presents with a complex genetic phenotype suggestive of a rare genetic condition, which may include unexplained developmental disabilities, intellectual disability or multiple congenital anomalies, AND;
    d. The clinical presentation does not fit a well-defined genetic condition that can be diagnosed by standard clinical workup, including single-gene or multi-gene panel testing, AND;
    e. WGS test is more practical than a sequential genetic testing approach (e.g., eliminating lower-yield or potentially unnecessary testing, reducing the financial and psychological impact of diagnostic uncertainty), which may allow identification of a molecularly confirmed diagnosis in a more timely manner, AND;
    f. The clinical presentation is consistent with a condition in which non-coding variants in multiple genes are known to contribute to the etiology of the presentation (e.g., refractory or very-early onset inflammatory bowel disease, autoinflammatory disorders, multiple congenital anomalies), making WES not an appropriate option.
12. *Whole mitochondrial genome sequencing*:

a. When benefits are available, JHHP considers whole mitochondrial genome sequencing medically necessary when performed in cases of suspected mitochondrial disease.

13. *Chromosome analysis (karyotype):*
    a. A woman with a history of previous unexplained stillbirth or repeated (3 or more; 2 or more among infertile couples) first trimester miscarriages, OR;
    b. A man whose partner has a history of previous unexplained stillbirth or repeated (3 or more; 2 or more among infertile couples) first trimester miscarriages, OR;
    c. A man or woman with a first, second, or third-degree relative with an abnormal chromosome arrangement (translocation or inversion), OR;
    d. One of the following diagnoses is suspected: Turner Syndrome, Down Syndrome (trisomy 21), Klinefelter Syndrome, Trisomy X Syndrome, Edwards Syndrome (trisomy 18), Patau Syndrome (trisomy 13), OR;
    e. One of the following diagnoses was identified by chromosome microarray (CMA): Turner Syndrome, Down Syndrome (trisomy 21), Klinefelter Syndrome, Trisomy X Syndrome, Edwards Syndrome (Trisomy 18), Patau Syndrome (trisomy 13), copy number variant suggestive of a structural chromosome abnormality (i.e., unbalanced translocation, supernumerary chromosome, or inversion), OR;
    f. The parent of a child with a chromosomal abnormality, OR;
    g. A fetus with an increased risk for aneuploidy based on prenatal screening result or ultrasound findings, OR;
    h. Males with azoospermia or severe oligospermia, OR;
    i. Females with ovarian failure.
14. *Chromosome Microarray (CMA)*:
    a. A member with unexplained developmental delay/intellectual disability, OR;
    b. A member with Autism Spectrum Disorder, OR;
    c. A member or fetus with major congenital anomalies not specific to a well-delineated genetic syndrome, OR;
    d. A member or fetus with an apparently isolated cardiac anomaly that is highly suggestive of a specific chromosomal condition (e.g., Tetralogy of Fallot and 22q11.2 deletion syndrome; supravalvular aortic stenosis and Williams Syndrome), OR;
    e. A member or fetus with a first-degree family member with a chromosomal deletion/duplication detectable only in microarray not karyotype (chromosome abnormality).
15. *Genetic testing for Early-Onset Alzheimer's Disease (EOAD)*:
    a. When benefits for Alzheimer's disease genetic testing are available, JHHP considers genetic testing for PSEN1, PSEN2, and APP (genes associated with EOAD) medically necessary in the following situations:
        i. A symptomatic individual with EOAD in the setting of a family history of dementia or in the setting of an unknown family history (e.g., adoption), OR;
        ii. Autosomal dominant family history of dementia with one or more cases of EOAD, OR;
        iii. A relative with a mutation consistent with EOAD (currently PSEN1/2 or APP).
    b. When benefits for Alzheimer's disease genetic testing are available, JHHP considers symptomatic APOE genotyping for the purposes of determining amyloid-related imaging abnormalities (ARIA) risk for patients being considered for lecanemab therapy medically necessary.
        i. Predictive genetic testing for susceptibility genes, including APOE, is considered experimental and investigational due to limited clinical utility and poor predictive value.
    c. Pediatric testing for AD should not occur.
    d. Prenatal testing for AD is not advised if the patient intends to continue a pregnancy with a mutation.

V. DEFINITIONS

Analytical Validity: Refers to the laboratory assay's ability to accurately detect the presence or absence of the genetic variant of interest (McCarthy, 2019; NIH).

Autoinflammatory diseases: A family of disorders characterized by atypical activation of inflammatory pathways in the absence of antigen-directed autoimmunity. Classically, periodic fevers are the common presenting manifestation in cases of familial Mediterranean fever (FMF), TNF receptor-1 associated periodic syndrome (TRAPS), and neonatal-onset multisystem inflammatory disorder (NOMID). However, the spectrum of autoinflammatory disorders continues to expand and now includes disorders in which recurrent fevers may be absent (e.g., deficiency of the interleukin (IL) 1 receptor antagonist (DIRA), syndrome of pyogenic sterile arthritis, pyoderma gangrenosum, and acne (PAPA), Blau syndrome (juvenile systemic granulomatosis) (Nigrovic, 2024).

Clinical Utility: Refers to whether the genetic testing result can provide information about diagnosis, treatment, management, or prevention of disease and improve health outcomes (NIH).

Clinical Validity: Refers to how well a positive genetic test result correlates with the risk of disease, drug response, or other outcomes. A clinically valid test conclusively shows the specific genetic variant increases the risk of having or developing a disease (NIH). There are two components of clinical validity: 1) scientific validity, referring to the scientifically valid association between the genetic variant and trait and predictive ability, and 2) clinical validity, which encompasses specificity, sensitivity, prevalence, penetrance, positive predictive value (PPV), and negative predictive value (NPV) of the test. (McCarthy, 2019; NIH).

Exome: The part of the genome that includes all coding nuclear DNA sequences. The human exome comprises approximately 180,000 exomes that are transcribed into mature RNA (GeneReviews).

Exome Sequencing: (Whole Exome Sequencing) Sequence analysis of the exons of protein-coding genes in the genome is typically performed by target enrichment or capture of exons followed by next-generation sequencing (NGS). Exome sequencing techniques have non-standardized, highly variable coverage; of particular note are regions of the exome refractory to accurate sequencing by this method (including genes with a pseudogene, highly repetitive coding regions, and large deletions and duplications). Laboratories may also include sequence analysis of some noncoding regions of the genome (e.g., promoters, highly conserved regulatory sequences) (GeneReviews).

First-Degree Relative: A parent, full sibling, or child of an individual.

Genome Sequencing: (Whole Genome Sequencing) Sequence analysis of the genome including coding and noncoding regions typically performed by next-generation sequencing (NGS) of sheared genomic DNA; genome sequencing techniques have non-standardized, highly variable coverage (GeneReviews).

Hayes Ratings: Developed to reflect the strength of evidence, safety and efficacy of healthcare procedures, devices and interventions and their impact on health outcomes (Hayes Inc., 2021).

- *A:* Established benefit. Published evidence shows conclusively that safety and impact on health outcomes are comparable to or better than standard treatment/testing. Long-term safety and impact on health outcomes have been established, and other important questions concerning application of the technology have been answered.
- *B:* Some proven benefit. Published evidence indicates that safety and impact on health outcomes are at least comparable to standard treatment/testing. However, there are outstanding questions regarding long-term safety and impact on health outcomes, clinical indications, contraindications, optimal treatment/testing parameters, and/or effects in different patient subpopulations.
- *C:* Potential but unproven benefit. Some published evidence suggests that safety and impact on health outcomes are at least comparable to standard treatment/testing. However, substantial uncertainty remains about safety and/or impact on health outcomes because of poor-quality studies, sparse data, conflicting study results, and/or other concerns.

- *D1:* No proven benefit and/or not safe. Published evidence shows that the technology does not improve health outcomes or patient management for the reviewed application(s) or is unsafe.
- *D2*: Insufficient evidence. There is insufficient published evidence to assess the safety and/or impact on health outcomes or patient management.

Immunohistochemistry (IHT): A laboratory method that uses monoclonal and polyclonal antibodies for the detection of specific antigens in tissue sections. The antibodies are usually linked to an enzyme or a fluorescent dye. After the antibodies bind to the antigen in the tissue sample, the enzyme or dye is activated, and the antigen can then be visualized under a microscope. Immunohistochemistry is used to help diagnose diseases, such as cancer. It may also be used to help tell the difference between different types of cancer (NIH).

Karyotype: A photographic representation of the chromosomes of a single cell, cut and arranged in pairs based on their size and banding pattern according to a standard classification (GeneReviews).

Molecular Genetic Testing: A term widely used in clinical genetics encompassing the diverse techniques used to identify the molecular basis of genetic disease. Examples of molecular genetic tests include: genotyping to detect specific pathogenic variants; sequencing of a gene to detect pathogenic variants; amplification or hybridization methods to detect copy number variants involving one or more genes; methylation-specific techniques to detect epigenetic changes that influence gene expression; and exome and genomic sequencing (GeneReviews).

Multi-Gene Panel: Simultaneous molecular testing of multiple genes associated with the same or similar clinical phenotypes. The genes included in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and over time. Methods used may include sequence analysis, deletion/duplication analysis, or other non-sequencing-based tests (GeneReviews).

Polygenic Risk Score (PRG; PRS): An estimate of an individual's genetic risk for a specific polygenic phenotype that is derived from contributions of alleles at multiple loci, up to thousands. Allele-specific contributions are estimated using specialized linear regression methods. The scores are typically generated in a model-building population, then validated in additional independent test populations. PGR is synonymous with polygenic score and contrasts with genetic risk score, which calculates the contribution of the known risk alleles carried by an individual (Raby & Blank, 2024).

Second-Degree Relative: A relative who shares one quarter of an individual's genes (grandparent, grandchild, uncle, aunt, nephew, niece, half-sibling) (GeneReviews).

Single Nucleotide Polymorphism (SNP): A polymorphism (difference in base sequence) that affects a single base pair. This terminology was previously used to refer to variation that had a population frequency of at least 1 percent. The term SNP is commonly used in research such as in genome-wide association studies (GWAS) (Raby & Blank, 2024).

Technology Evaluation Criteria (TEC): A service, device or supply must meet all of the following criteria:

1. The technology must have final approval from the appropriate government regulatory bodies for intended use
2. There must be sufficient scientific evidence-based studies to permit conclusions concerning the effect of the technology on health outcomes
3. The technology must improve the member's net health outcome
4. The technology must be as beneficial as any established alternatives
5. The improvement must be attainable outside the investigational setting

Whole Mitochondrial Genome Sequencing: Mitochondrial DNA (mtDNA) whole genome sequencing detects pathogenic point mutations and single large-scale deletions with heteroplasmy levels in the mtDNA, which contribute to mitochondrial

dysfunction. Nuclear gene variants that may cause mitochondrial dysfunction are not detected by this analysis (Columbia University, 2024).

VI. BACKGROUND

The purpose of genetic testing is to determine the likelihood that an individual has or will develop a certain condition or disease phenotype, and in some cases to characterize the likely response to treatment. The factors influencing genetic testing and diagnosis are technical considerations (accuracy of testing), the existing knowledge base (certainty regarding pathogenicity of the variants identified), and biologic factors (inheritance pattern, penetrance, and expressivity) (Kohlmann & Slavotinek, 2024).

Testing can involve a single gene, a panel of genes, or the entire exome or genome. For each gene, it is possible to analyze a single variant (e.g., factor V Leiden), a panel of commonly observed variants, or the entire coding nucleotide sequence. The methods used to identify specific variants include Sanger sequencing, microarray technologies, and next-generation sequencing (NGS). Other methods include cytogenetic analysis and fluorescence in situ hybridization, which can be used to assess alterations in chromosome number or structure (Kohlmann & Slavotinek, 2024).

Carrier screening is performed on prospective parents to identify genetic risks that can be passed to offspring. Carriers themselves are unaffected but at risk of producing affected children. Increasing population intermixing confounds what people believe to be their ethnicity, thus carrier screening panels should be inclusive of diverse populations. Commercial laboratories offer test panels that screen for only a few, or up to several hundred, disorders. The majority are autosomal recessive, but some may be X-linked or autosomal dominant single gene disorders. Selection of the disorders in the panel is generally based on gene frequency and inclusion of pathogenic variants within a disorder that contribute to the highest detection of carriers (Rink, 2024).

Guidelines from professional organizations usually recommend that the condition being screened for should be a health problem associated with one or more of the following:

- Cognitive or physical impairment
- Need for surgical or medical intervention
- Decreased life expectancy
- Poor quality of life
- Prenatal diagnosis that could lead to prenatal intervention to improve perinatal outcome, delivery interventions to optimize newborn and infant outcome, parental education regarding special medical needs and intervention after birth (Rink, 2024).

The American College of Medical Genetics (ACMG) recommends routinely offering carrier screening to people with Ashkenazi Jewish descent for the following nine disorders: Tay-Sachs disease, Canavan disease, cystic fibrosis, familial dysautonomia, mucolipidosis IV, Niemann Pick disease type A, Fanconi anemia group C, Bloom Syndrome, and Gaucher disease, because of carrier detection rates ≥90% and population carrier frequency of ≥1%. The American College of Obstetricians and Gynecologists (ACOG) recommendations are to offer an expanded panel with the addition of the following five disorders: familial hyperinsulinism, glycogen storage disease type I, Joubert syndrome, maple syrup urine disease, and Usher syndrome. In addition, both the ACMG and ACOG recommend offering spinal muscular atrophy carrier screening to all pregnant people or people planning pregnancy, regardless of race or ethnicity (Roman, 2024).

Whole exome sequencing (WES) and whole genome sequencing (WGS) have built upon the advances introduced by NGS (Lapin, 2016). These techniques are reflective of the advancement in molecular biology technology – sequencing the entire

human genome was a 12-year process in the 1990's, but it is now completed in a little more than one day (International Human Geome Sequencing Consortium, 2004). Whole mitochondrial genome sequencing is another emerging technique in which the 16,569 base pair mitochondrial genome is sequenced. Sequencing mitochondrial DNA can be a useful diagnostic tool for identifying various mitochondrial diseases, almost all of which result in neurological or neuromuscular disorders (Columbia University, 2024; Parikh et al., 2015). A current concern about performing WES and WGS on individuals is the detection of variants of unknown significance (VUS) in genes that are unrelated to the phenotype. These are gene variants about which there is currently no clear guidance regarding their clinical consequences (McDermott, 2015; Schulz, 2015). However, there is expanding evidence of advantages of exome and genome sequencing, including the ability to detect clinically significant variants in genes that were not initially considered by the clinician and the ability to effectively evaluate genetic etiology for multiple disease states with a single test (Chinn, 2024).

The ACMG 2021 Evidence-Based Clinical Guidelines recommend exome and genome sequencing to be considered as a first-or second-tier test for pediatric patients with one or more congenital anomalies with onset prior to age one year, or developmental delay or intellectual disability with onset prior to age 18 years (Manickam et al., 2021). A Position Paper from the Paediatric IBD Porto Group of the European Society of Pediatric Gastroenterology, Hepatology and Nutrition, published in 2021, has summarized their recommendations stating that genomic technologies should be considered an integral part of multidisciplinary care to investigate patients at risk for monogenic forms of inflammatory bowel disease (Uhlig et al., 2021). Acknowledging the current lack of published evidence of clinical utility for the adult population and across various ancestral groups, Shickh et al. published a systematic review suggesting that there is evidence for a higher range of diagnostic yield of exome/genome sequencing compared to standard genetic tests, particularly in neurological and acute indications (2021). The Medical Genome Initiative, a consortium of leading healthcare research organizations in the US and Canada, formed in 2020, sought to address the lack of standards and best practice recommendations for the interpretation and reporting of clinical diagnostic WGS. Their current publication, "Best practices for the interpretation and reporting of clinical whole genome sequencing" includes recommendations for analysis and reporting of VUS, emphasizing the need for open communication between ordering providers and the laboratory regarding reporting decisions, particularly for more challenging cases when there is uncertainty as to whether a finding aligns with patient phenotype (Austin-Tse et al., 2022).

Understanding and identifying changes in a patient's genome through genetic testing can aid in clinical decision-making and prove to be cost-effective. The administration of drugs to a patient as a result of genetic testing can also reduce risk/side effects while maximizing benefits. Interpretation of genetic testing results transcends many disciplines within medicine. Laboratory scientists, pathologists, genetic counselors, physicians, and nurses all collaborate to ensure accurate interpretation of results and to discuss treatment options for patients.

Alzheimer's disease is a progressive, irreversible neurodegenerative disease and the most common cause of dementia. Early-onset Alzheimer's disease (EOAD) is classified by the onset of symptoms before 65 years of age and affects approximately 250,000 Americans. EOAD genetic testing may allow patients to receive a definitive diagnosis and at-risk relatives to receive predictive testing. Currently, there are three known deterministic genes in which mutations are associated with autosomal dominant EOAD with a high penetrance: PSEN1, PSEN2, and APP. The American College of Medical Genetics (ACMG) and the National Society of Genetics Counselors (NSGC) published joint practice guidelines which provide a framework for assessing patients' genetic risk for Alzheimer disease and identifying which individuals may benefit from genetic testing. These recommendations include criteria for family history of dementia that warrant genetic testing and contexts in which testing is inappropriate, including in the pediatric population and for susceptibility genes like APOE (Goldman et al., 2011; reaffirmed 2018; Cummings et al., 2023).

VII. CODING DISCLAIMER

Note: The following CPT/HCPCS codes are included below for informational purposes and may not be all inclusive. Inclusion or exclusion of a CPT/HCPCS code(s) below does not signify or imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member's specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee of payment. Other policies and coverage determination guidelines may apply.

Note: All inpatient admissions require preauthorization.

Adherence to the provisions in this policy may be monitored and addressed through post payment data analysis and/or medical review audits
Employer Health Programs (EHP): Specific Summary Plan Descriptions (SPDs) supersedes JHHP Medical Policy. If there are no criteria in the SPD, apply the Medical Policy criteria.
US Family Health Plan (USFHP): Regulatory guidance supersedes JHHP Medical Policy. If there are no TRICARE policies, or other regulatory guidelines, apply the Medical Policy criteria.

VIII. CODING INFORMATION

CPT® CODES ARE FOR INFORMATIONAL PURPOSES ONLY	
CPT® CODES	**DESCRIPTION**
0016U	Oncology (hematolymphoid neoplasia), RNA, BCR/ABL1 major and minor breakpoint fusion transcripts, quantitative PCR amplification, blood or bone marrow, report of fusion not detected or detected with quantitation
0017U	Oncology (hematolymphoid neoplasia), JAK2 mutation, DNA, PCR amplification of exons 12-14 and sequence analysis, blood or bone marrow, report of JAK2 mutation not detected or detected
0027U	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, targeted sequence analysis exons 12-15
0040U	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis, major breakpoint, quantitative
0046U	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia) internal tandem duplication (ITD) variants, quantitative
0049U	NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, quantitative
0050U	Targeted genomic sequence analysis panel, acute myelogenous leukemia, DNA analysis, 194 genes, interrogation for sequence variants, copy number variants or rearrangements
0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood
0260U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping
0264U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping

0267U	Rare constitutional and other heritable disorders, identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping and whole genome sequencing
0299U	Oncology (pan tumor), whole genome optical genome mapping of paired malignant and normal DNA specimens, fresh frozen tissue, blood, or bone marrow, comparative structural variant identification
0300U	Oncology (pan tumor), whole genome sequencing and optical genome mapping of paired malignant and normal DNA specimens, fresh tissue, blood, or bone marrow, comparative sequence analyses and variant identification
0331U	Oncology (hematolymphoid neoplasia), optical genome mapping for copy number alterations and gene rearrangements utilizing DNA from blood or bone marrow, report of clinically significant alterations
0413U	Oncology (hematolymphoid neoplasm), optical genome mapping for copy number alterations, aneuploidy, and balanced/complex structural rearrangements, DNA from blood or bone marrow, report of clinically significant alterations
0454U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping
81105	Human Platelet Antigen 1 genotyping (HPA-1), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-1a/b (L33P)
81106	Human Platelet Antigen 2 genotyping (HPA-2), GP1BA (glycoprotein Ib [platelet], alpha polypeptide [GPIba]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-2a/b (T145M)
81107	Human Platelet Antigen 3 genotyping (HPA-3), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex], antigen CD41 [GPIIb]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-3a/b (I843S)
81108	Human Platelet Antigen 4 genotyping (HPA-4), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-4a/b (R143Q)
81109	Human Platelet Antigen 5 genotyping (HPA-5), ITGA2 (integrin, alpha 2 [CD49B, alpha 2 subunit of VLA-2 receptor] [GPIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant (eg, HPA-5a/b (K505E))
81110	Human Platelet Antigen 6 genotyping (HPA-6w), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa, antigen CD61] [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-6a/b (R489Q)
81111	Human Platelet Antigen 9 genotyping (HPA-9w), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex, antigen CD41] [GPIIb]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-9a/b (V837M)
81112	Human Platelet Antigen 15 genotyping (HPA-15), CD109 (CD109 molecule) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-15a/b (S682Y)
81120	IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma), common variants (eg, R132H, R132C)

81121	IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (eg, glioma), common variants (eg, R140W, R172M)
81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis and duplication analysis, if performed
81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene rearrangements)
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81164	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81165	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81166	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81167	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81170	ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (eg, acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain
81171	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81172	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; characterization of alleles (eg, expanded size and methylation status)
81173	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence
81174	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; known familial variant
81175	ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence
81176	ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; targeted sequence analysis (eg, exon 12)
81177	ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; targeted sequence analysis (eg, exon 12)
81178	ATXN1 (ataxin 1) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81179	ATXN2 (ataxin 2) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles

81180	ATXN3 (ataxin 3) (eg, spinocerebellar ataxia, Machado-Joseph disease) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81181	ATXN7 (ataxin 7) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81182	ATXN8OS (ATXN8 opposite strand [non-protein coding]) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81183	ATXN10 (ataxin 10) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81184	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81185	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; full gene sequence
81186	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; known familial variant
81187	CNBP (CCHC-type zinc finger nucleic acid binding protein) (eg, myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81188	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81189	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; full gene sequence
81190	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; known familial variant(s)
81200	ASPA (aspartoacylase) (eg,Canavan disease) gene analysis, common variants
81201	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence
81202	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; known familial variants
81203	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants
81204	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; characterization of alleles (eg, expanded size or methylation status)
81205	BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (eg, Maple syrup urine disease) gene analysis, common variants (eg, R183P, G2785, E422X)
81206	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative
81207	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative
81208	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; other breakpoint, qualitative or quantitative
81209	BLM (Bloom syndrome, RecQ helicase-like) (eg, Bloom syndrome) gene analysis, 2281del6ins7 variant

81212	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
81215	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81218	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (eg, acute myeloid leukemia), gene analysis, full gene sequence
81219	CALR (calreticulin) (eg, myeloproliferative disorders), gene analysis, common variants in exon 9
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/ deletion variants
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)
81228	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (eg, bacterial artificial chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)
81229	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities
81233	BTK (Bruton's tyrosine kinase) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F)
81234	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles
81236	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence
81237	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, diffuse large B-cell lymphoma) gene analysis, common variant(s) (eg, codon 646)
81238	F9 (coagulation factor IX) (eg, hemophilia B), full gene sequence
81239	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)
81240	F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant
81241	F5 (coagulation Factor V) (eg, hereditary hypercoagulability gene analysis, Leiden variant

81242	FANCC (Fanconi anemia, complementation group C) (eg, Fanconi anemia type C) gene analysis, common variant (eg, IVS4+4A>T)
81243	FMR1 (Fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81244	FMR1 (Fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; characterization of alleles (eg, expanded size and methylation status)
81245	FLT3 (fms-related tyrosine kinase 3) (eg, 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)
81247	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, A, A-)
81248	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; known familial variant(s)
81249	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; full gene sequence
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (eg, Glycogen storage disease, Type 1a, von Gierke disease) gene analysis, common variants (eg, R83C, Q347X)
81251	GBA (glucosidase, beta, acid) (eg, Gaucher disease) gene analysis, common variants (eg, N370S, 84GG, L444P, IVS2+1G>A)
81252	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; full gene sequence
81253	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; known familial variants
81254	GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (eg, nonsyndromic hearing loss) gene analysis, common variants (eg, 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6- D13S1854)])
81255	HEXA (hexosaminidase A [alpha polypeptide]) (eg, Tay-Sachs disease) gene analysis, common variants (eg, 1278insTATC, 1421+1G>C, G269S)
81256	HFE (hemochromatosis) (eg, hereditary hemochromatosis) gene analysis, common variants (eg, C282Y, H63D)
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (eg, Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and 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 complexassociated protein) (eg, familial dysautonomia) gene analysis, common variants (eg, 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
81270	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant
81271	HTT (huntingtin) (eg, Huntington disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81272	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (eg, exons 8, 11, 13, 17, 18)
81273	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, mastocytosis), gene analysis, D816 variant(s)
81274	HTT (huntingtin) (eg, Huntington disease) gene analysis; characterization of alleles (eg, expanded size)
81284	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; evaluation to detect abnormal (expanded) alleles
81285	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; characterization of alleles (eg, expanded size)
81286	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; full gene sequence
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis
81289	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; known familial variant(s)
81290	MCOLN1 (mucolipin 1) (eg, Mucolipidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb)
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (eg, hereditary hypercoagulability) gene analysis, common variants (eg, 677T, 1298C)
81292	MLH1 (mutL homomlog 1, colon cancer, nonpolyposis type 2) (eg, hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81293	MLH1 (mutL homomlog 1, colon cancer, nonpolyposis type 2) (eg, hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81294	MLH1 (mutL homomlog 1, colon cancer, nonpolyposis type 2) (eg, hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81296	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81297	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81298	MSH6 (mutS homolog 6 [E. coli] (eg, hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81299	MSH6 (mutS homolog 6 [E. coli] (eg, hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants

81300	MSH6 (mutS homolog 6 [E. coli] (eg, hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81301	Microsatellite instability analysis (eg, hereditary nonpolyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (eg, BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed
81302	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; full sequence analysis
81303	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; known familial variant
81304	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; duplication/deletion variants
81305	MYD88 (myeloid differentiation primary response 88) (eg, Waldenstrom's macroglobulinemia, lymphoplasmacytic leukemia) gene analysis, p.Leu265Pro (L265P) variant
81307	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) gene analysis; full gene sequence
81308	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) gene analysis; known familial variant
81310	NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, exon 12 variants
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (eg, colorectal carcinoma), gene analysis, variants in exon 2 (eg, codons 12 and 13) and exon 3 (eg, codon 61)
81312	PABPN1 (poly[A] binding protein nuclear 1) (eg, oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81313	PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer)
81314	PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (eg, gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (eg, exons 12, 18)
81315	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative
81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; single breakpoint (eg, intron 3, intron 6 or exon 6), qualitative or quantitative
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyoisus colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81320	PLCG2 (phospholipase C gamma 2) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F)
81321	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis

81322	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant
81323	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant
81324	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis
81325	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence analysis
81326	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; known familial variant
81327	SEPT9 (Septin9) (eg, colorectal cancer) promoter methylation analysis
81329	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/ deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed
81330	SMPD1 (sphingomyelin phosphodiesterase 1, acid lysosomal) (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330)
81331	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (eg, Prader-Willi syndrome and/or Angelman syndrome), methylation analysis
81332	SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, member 1) (eg, alpha-1-antitrypsis deficiency), gene analysis, common variants (eg, *S and *Z)
81333	TGFBI (transforming growth factor beta-induced) (eg, corneal dystrophy) gene analysis, common variants (eg, R124H, R124C, R124L, R555W, R555Q)
81336	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence
81337	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)
81343	PPP2R2B (protein phosphatase 2 regulatory subunit Bbeta) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81344	TBP (TATA box binding protein) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81345	TERT (telomerase reverse transcriptase) (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region)
81351	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; full gene sequence
81352	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; targeted sequence analysis (eg, 4 oncology)
81353	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; known familial variant
81361	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (eg, HbS, HbC, HbE)

81362	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); known familial variant(s)
81363	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)
81364	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); full gene sequence
81400	Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg,SNP] by techniques such as restriction enzyme digestion or melt curve analysis)
81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNP's, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
81402	Molecular pathology procedure, Level 3 (eg, >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon loss of heterozygosity [LOH], uniparental disomy [UPD])
81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
81404	Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
81405	Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis
81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)
81407	Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scannion or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)
81408	Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis)
81410	Aortic dysfunction or dilation (eg, Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); genomic sequence analysis panel, must include sequencing of at least 9 genes, including FBN1, TGFBR1, TGFBR2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, and MYLK
81411	Aortic dysfunction or dilation (eg, Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); duplication/deletion analysis panel, must include analyses for TGFBR1, TGFBR2, MYH11, and COL3A1
81412	Ashkenazi Jewish associated disorders (eg, Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GA, 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)
81420	Fetal chromosomal aneuploidy (eg, trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood
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)
81430	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); genomic sequence analysis panel, must include sequencing of at least 60 genes, including CDH23, CLRN1, GJB2, GPR98, MTRNR1, MYO7A, MYO15A, PCDH15, OTOF, SLC26A4, TMC1, TMPRSS3, USH1C, USH1G, USH2A, and WFS1
81431	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); duplication/deletion analysis panel, must include copy number analyses for STRC and DFNB1 deletions in GJB2 and GJB6 genes
81432	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53
81433	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11
81434	Hereditary retinal disorders (eg, retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy), genomic sequence analysis panel, must include sequencing of at least 15 genes, including ABCA4, CNGA1, CRB1, EYS, PDE6A, PDE6B, PRPF31, PRPH2, RDH12, RHO, RP1, RP2, RPE65, RPGR, and USH2A
81435	Hereditary colon cancer syndromes (eg, Lynch syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include analysis of at least 7 genes, including APC, CHEK2, MLH1, MSH2, MSH6, MUTYH, and PMS2

81436	Hereditary colon cancer syndromes (eg, Lynch syndrome, familial adenomatosis polyposis); duplication/ deletion gene analysis panel, must include analysis of at least 8 genes, including APC, MLH1, MSH2, MSH6, PMS2, EPCAM, CHEK2, and MUTYH
81437	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL
81438	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL
81439	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
81442	Noonan spectrum disorders (eg, Noonan syndrome, cardio-facio-cutaneous syndrome, Costello syndrome, LEOPARD syndrome, Noonan-like syndrome), genomic sequence analysis panel, must include sequencing of at least 12 genes, including BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NRAS, PTPN11, RAF1, RIT1, SHOC2, and SOS1
81443	Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (eg, ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH)
81448	Hereditary peripheral neuropathies (eg, Charcot-Marie-Tooth, spastic paraplegia), genomic sequence analysis panel, must include sequencing of at least 5 peripheral neuropathy-related genes (eg, BSCL2, GJB1, MFN2, MPZ, REEP1, SPAST, SPG11, SPTLC1)
81450	Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA and RNA analysis when performed, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
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

81465	Whole mitochondrial genome large deletion analysis panel (eg, Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed
81470	X-linked intellectual disability (XLID) (eg, syndromic and non-syndromic XLID); genomic sequence analysis panel, must include sequencing of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2
81471	X-linked intellectual disability (XLID) (eg, syndromic and non-syndromic XLID); duplication/deletion gene analysis, must include analysis of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2
81507	Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy
81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score
83006	Growth stimulation expressed gene 2 (ST2, Interleukin 1 receptor like-1)
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 (eg, FISH)
88272	Molecular cytogenetics; chromosomal in situ hybridization, analyze 3-5 cells (eg, for derivatives and markers)
88273	Molecular cytogenetics; chromosomal in situ hybridization, analyze 10-30 cells (eg, for microdeletions)
88274	Molecular cytogenetics; interphase in situ hybridization, analyze 25-99 cells
88275	Molecular cytogenetics; 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

IX. REFERENCE STATEMENT

Analyses of the scientific and clinical references cited below were conducted and utilized by the Johns Hopkins Health Plans (JHHP) Medical Policy Team during the development and implementation of this medical policy. The Medical Policy Team will continue to monitor and review any newly published clinical evidence and revise the policy and adjust the references below accordingly if deemed necessary.

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XI. APPROVALS

Historical Effective Dates: 08/26/2003, 03/15/2004, 10/22/2004, 10/21/2005, 10/19/2006, 01/07/2008, 01/05/2009, 01/07/2011, 06/07/2013, 06/05/2015, 09/02/2016, 12/02/2016, 09/01/2017, 10/01/2019, 05/03/2021, 08/01/2022, 11/01/2023, 04/01/2024, 10/01/2024