Sentara Health Plans

Commercial

Genetic and Molecular Testing, Medical 34

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Effective Date	8/1/2025
Next Review Date	5/2026
Coverage Policy	Medical 34
Version	5

Member-specific benefits take precedence over medical policy and benefits may vary across plans. Refer to the individual's benefit plan for details *.

Description of Item or Service:

Genetic and Molecular Testing (also known as a biomarker or molecular profile) is a laboratory process that examines an individual's DNA or RNA for genetic changes or abnormalities that may indicate a disease or condition.

Hereditary cancer is a cancer that developed because a gene mutation was passed from a parent to a child. Inheriting a gene mutation does not necessarily mean that person will develop cancer, but increase their risk of cancer. Research and studies have found that certain gene mutations increase the chances of a person to develop certain kinds of cancers, depending on family history, or to respond to certain therapies for cancer, based on the genetic components of the tumor.

- **Autosomal recessive inheritance** is a genetic condition that appears only in individuals who have received two copies of an autosomal gene, one copy from each parent. The gene is on an autosome, a non-sex chromosome. The parents are carriers who have only one copy of the gene and do not exhibit the trait because the gene is recessive to its normal counterpart gene.
- **First-degree relative** is defined as a relative which includes the individual's parents, full siblings, or children
- **Second-degree relative** is defined as a blood relative which includes the individual's grandparents, grandchildren, aunts, uncles, nephews, nieces or half-siblings
- **Third-degree relative** is defined as a blood relative which includes the individual's first-cousins, great-grandparents or great grandchildren
- **X-linked recessive inheritance** is a hereditary pattern in which a recessive gene on the X chromosome results in the manifestation of characteristics in male offspring and a carrier state in female offspring.

Clinical Indications and Criteria:

Genetic and/or Molecular testing is considered medically necessary for **1 or more** of the following:

- **Acute Myeloid Leukemia** with **1 or more** of the following:
  - CMFB/MHY11 (*81401, 81403, 81479*) to confirm diagnosis in individuals with abnormal eosinophils
- **CD40 ligand deficiency** (*81479*), also known as **Hyper IgM (HIGM) syndrome** testing may be confirmed by genetic testing when **1 or more** the following criteria are met:
  - The individual has an absent or decreased expression of the CD40 ligand (CD40L) protein on flow cytometry
  - The individual has at least one first- or second- degree relative with X-Linked Hyper IgM syndrome

- The individual has clinical characteristics indicative of X-linked hyper IgM syndrome (examples include, but are not limited to low serum concentrations of IgG and IgA and normal or elevated serum concentrations of IgM, neutropenia, thrombocytopenia, anemia, autoimmune and/or inflammatory disorders, or recurrent upper and lower respiratory tract bacterial infections, opportunistic infections, and recurrent or protracted diarrhea associated with failure to thrive)

- **Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)** *(81479, 81406)* **DNA** testing for **1 or more** of the following:
  - Pre-symptomatic individuals younger than 60 years of age with a family history consistent with an autosomal dominant pattern of inheritance and a known mutation in an affected member of the family
  - Symptomatic individual younger than 60 years of age with a family history consistent with an autosomal dominant pattern of inheritance of this condition
- **Congenital adrenal hyperplasia** (CYP21A (*81404, 81405*)) testing is considered medically necessary for **1 or more** of the following:
  - Completed baseline serum 17-hydroxyprogesterone (17OHP) level as borderline or elevated
  - Cosyntropin stimulation test completed (ACTH stimulation test)
- **Congenital sucrase-isomaltase deficiency** testing (CSID (*81479*)) is medically necessary for **ALL** of the following:
  - Increase in breath hydrogen of >10ppm when challenged with Sucrose after fasting
  - Low sucrose activity on duodenal biopsy
  - Negative Lactose breath test
  - Normal other disaccharidases on duodenal biopsy
  - Stool PH <6
- **Co-receptor tropism** testing (*87999*) is medically necessary for **1 or more** of the following:
  - To determine virus tropism prior to initiating a CCR5 antagonist (e.g., Miraviroc [Selzentry])
  - For an individual demonstrating virologic failure while receiving therapy that contains a CCR5 antagonist
- **CSF3R gene** (*81479*) testing in an individual with **1 or more** of the following:
  - Asymptomatic individual with persistent, moderately elevated neutrophil counts
  - History of severe congenital neutropenia
  - Molecular testing of peripheral blood to detect chromosomal abnormality for diagnosis of **1 or more** of the following:
    - Atypical chronic myeloid leukemia (aCML)
    - Acute myeloid leukemia (AML)
    - Chronic neutrophilic leukemia (CNL)
    - Evidence needed for the use of Ruxolitinib
    - Myelodysplastic Syndromes as evidence by 1 or more of the following:
      - MDS
      - Myelodysplasia
      - Pre-leukemia
      - Refractory anemia
- **Familial Mediterranean Fever (FMF), (MEFV) gene** (*81404*)) testing may be indicated when clinical findings or diagnostic testing are suggestive of familial Mediterranean fever, as indicated by **1 or more** of the following:
    - Amyloidosis (senile systemic type)
    - Carrier testing for MEFV gene may be indicated when one of the following are present: Member is from an ethnic group at increased risk (eg, Armenian, Turkish, Arab, North African Jewish) and of reproductive age.
    - Favorable response to colchicine therapy
    - First-degree relative of individual with confirmed diagnosis of familial Mediterranean fever
    - Prior to gamete donation if gamete recipient is known carrier
    - Recurrent episodes of fever associated with **2 or more** of the following:
      - Acute abdominal pain with possible peritoneal signs
      - Acute arthritis of ankle, knee, or hip
      - Elevated erythrocyte sedimentation rate or C-reactive protein

                - Elevated serum fibrinogen
                - Erysipelas-like erythema of skin[C]
                - Leukocytosis
                - Pleuritis
            - Reproductive partner of MEFV gene mutation carrier
- **Hemophilia A** (Factor VIII (*85240*)) or **Hemophilia B** (Factor IX (*81238*)) testing when **1 or more** of the following:
    - Individual displays clinical features, is at direct risk of inheritance with **ALL** of the following:
        - The result of the testing will directly impact the treatment being delivered to individual
        - After history, physical examination, and completion of conventional diagnostic studies, a definitive diagnosis remains uncertain.
    - Individual pregnancy planning for members of reproductive age or prenatal genetic testing to determine carrier status of a fetus
- **Hereditary Fructose Intolerance Testing** (ALDOB Gene (*81479*)) testing for specific mutation if known in a family or panel specific mutation is unknown, based on family history and clinical features requiring a specific diagnosis
- **HLA-A29 Uveitis** (HLA I Typing Allele HR (*81381*)) screening is considered medically necessary to rule out or confirm **Birdshot Chorioretinopathy (BSCR)**, a rate form of autoimmune posterior uveitis that affects visual function if left untreated.
- **Liquid (ctDNA) based panel tests (**multiple codes**)** are considered medically necessary for individuals with invasive malignancy for whom the liquid biopsy test is a companion diagnostic test described by the U.S. Food and Drug Administration (FDA) as necessary for patient selection, and **ALL** of the following criteria are met:
    - Specific cancer treatment is being considered to correspond with the FDA companion diagnostic indication
    - Other somatic tumor testing results do not already provide support for the specific cancer therapy being considered that corresponds to the FDA companion diagnostic indication
- **Methylguanine-DNA methyltransferase** (81287) is medically necessary for predicting response to temozolomide (Temodar) in persons with glioblastoma
- **Mucopolysaccharidosis** (GALNS (*81479*), IDUA (*81406*), ARSB (*81479*)) testing is medically necessary for **1 or more** of the following criteria:
    - Confirm diagnosis of Mucopolysaccharidosis
    - Treatment management
    - Documented reduced fibroblast or leukocyte GALNS enzyme activity
    - Pregnancy planning for members of reproductive age or prenatal genetic testing to determine carrier status of a fetus
- **Muscular Dystrophy genetic testing** may be indicated when the appropriate clinical situation is present, as indicated by **1 or more** of the following:
    - Prenatal testing for **1 or more** of the following
        - Prenatal diagnosis when CNBP expansion has been identified in affected parent
        - Preimplantation, prenatal, or preconceptional genetic testing when a CNBP mutation has been identified in an affected first-degree relative
        - Congenital Muscular Dystrophy type 1C (MDC1C (*81404*))
        - Ullrich Muscular Dystrophy (COL6A2 (*81407*))
    - Non-prenatal testing for **ALL** of the following:
        - The individual has unexplained progressive muscle weakness, abnormal gait, or other clinical findings consistent with muscular dystrophy or spinal muscular atrophy. These findings may also include abnormal laboratory findings (e.g., elevated creatine kinase serum (CK)), or a positive family history
        - The individual has a confirmed diagnosis of muscular dystrophy and genetic testing is required to establish the disease-causing mutation
        - Test is for **1 or more** of the following:
            - Congenital Muscular Dystrophy (MDC1C (*81404*))
            - Emery-Dreifuss Muscular Dystrophy (EDMD1, 2, and 3 (*81406*))(FGFR2 (*81404*))

        - Familial Myotonic Dystrophy, (DMPK (81234, 81239), DM2 (*81479*), ZNF9 (*81479*), or CNBP (*81479*))
        - Fascioscapulohumeral Muscular Dystrophy (FSHD, FSHMD1A *(81404)*, FGFR3 (81400, 81401)
        - Limb girdle Muscular Dystrophy (LGMD1/LGMD2/FKRP (*81405*))
        - Ullrich Muscular Dystrophy (COL6A2 (*81407*))
- **nAbCyte™ Anti-AAVRh74var HB-FE Assay** (*81479*) is medically necessary as a companion diagnostic to determine patient eligibility for treatment with Beqvez™ (fidanacogene elaparvovec-dzkt)
- **NTRK NGS Fusion Profile** (*81194*) is medically necessary for an individual who has a solid tumor who is being considered for Vitrakvi (larotrectinib) therapy
- **Pathfinder TG** *(81479*) (aka PancraGEN) is medically necessary for 1 or more of the following:
    - To be used adjunctively in cases in which a definitive pathologic diagnosis cannot be rendered on a tissue or cytology specimen, either due to inadequate specimen or equivocal histologic or cytologic findings.
- **Phenylalanine hydroxylase** (PAH gene (*81403, 81479*)) Testing is medically necessary to confirm phenylketonuria (PKU) diagnosis.
- **Preconceptional carrier status genetic testing** for pregnancy planning for members of reproductive age or prenatal genetic testing to determine carrier status of a fetus for other inherited disorders when **ALL** of the following criteria are met:
    - Family history genetic testing are considered medically necessary when **1 or more** of the following criteria is met:
        - An affected child is identified with either an autosomal recessive disorder, an x-linked disorder, or an inherited disorder with variable penetrance;
        - One or both parents or prospective parent(s) have another first or a second degree relative who is affected, or the first degree relative has an affected child, with either an autosomal recessive disorder, an x-linked disorder, or an inherited disorder with variable penetrance;
        - The parent or prospective parent is at high risk for a genetic disorder with a late onset presentation;
        - The parents or prospective parents are members of an ethnic group with a high risk of a specific genetic disorder with an autosomal recessive pattern of inheritance and testing is performed to determine carrier status and to guide subsequent reproductive decisions.
    - Specific genetic testing is considered medically necessary when **ALL** of the following criteria are met:
        - Testing is accompanied by genetic counseling.
        - Testing is for **1 or more** of the following:
            - A biochemical or other test is identified and the results are indeterminate
            - The genetic disorder cannot be identified through biochemical or other testing
    - Approved Disorders for targeted disease processes testing is for **1 or more** of the following:
        - 22q11.2 deletion syndromes (ie Velocardiofacial / DiGeorge syndrome, Catch22, Familial third and fourth pharyngeal pouch syndrome, Hypoplasia of thymus and parathyroid, Pharyngeal pouch syndrome, Sedlackova syndrome, Third and fourth pharyngeal pouch syndrome, Thymic aplasia syndrome, and Velofacial hypoplasia (*88271, 88273, 88291, and 88230*))
        - Adrenoleukodystrophy DNA Sequencing (ABCD1 gene (*81403, 81405, 81479*))
        - Autosomal recessive or autosomal dominant centronuclear myopathy (DNM2 (*81403, 81405, 81406*) and/or BIN1 (*81479*))
        - Disease-causing mutation in RYR1 ((*81406, 81408*) Malignant Hyperthermia) gene has been identified in one parent
        - Ellis-van Creveld syndrome (EVC (*81479*), EVC2 (*81479*))
        - Hemophagocytic Lymphohistiocytosis (HLH Gene (*81479*))
        - Hereditary sensory and autonomic neuropathies (81173, 81185, 81404, 81405, 81479)
        - Leopard syndrome (PTP11 gene (*81406*))
        - Lissencephaly (LIS1 (*81405*), RELN (*81479*), TUBA1A (*81479*), NDE1 (*81479*), KATNB1 (*81479*), CDK5 (81479), ARX (*81404*), AND/OR DCX (81405))
        - Pontocerebellar Hypoplasia (TSEN54 (*81479*), EXOSC8 (*81479*))

        - Primary Ciliary Dyskinesia (PCD) (*81479*)
        - Walker-Warburg Syndrome (POMGNT1 (*81406*))
- **ProMark® Risk Score** (81479) may be covered by **ALL** of the following:
    - Individuals have not had previous tumor-based assay to guide management of prostate cancer in an individual's lifetime
    - Individuals are candidates for definitive therapy or active surveillance
    - Life expectancy of greater than 10 years
    - Individuals must fall into either **1 or more of the following** stages:
        - Low Risk
        - Favorable Intermediate Risk
- **Severe Combined Immunodeficiency (SCID) Genetic Testing** (*81479*) for individuals with inconclusive screening results from an immune function test or T cell and B cell counts who are considered eligible for transplant to confirm diagnosis.
- **Susceptibility to malignant disease** which is not addressed by MCG, or another vender is covered when **ALL** of the following are met:
    - The genetic disorder is associated with a potentially significant cancer or has a lethal natural history;
    - The risk of the type of cancer from the genetic disorder cannot be identified through biochemical or other testing
    - Specific mutation(s) have been established in the scientific literature to be reliably associated with the disease;
    - The results of the genetic test impact the medical management of the individual;
    - Testing is accompanied by genetic counseling
- **Tumor testing and/or liquid biopsy** (IE: FoundationOne Liquid CDx, Caris, Tempus, Myriad: Precise Tumor (*multiple codes*) testing may be indicated when **1 or more** of the following are present:
    - For tissue-based testing with **ALL** of the following:
        - For Patient diagnosed with solid tumor malignancy (eg, breast, cervical, colorectal, non-small cell, pancreatic, prostate, sarcoma, thyroid)
        - Systemic targeted therapy being considered (eg, crizotinib, erlotinib, olaparib, pembrolizumab, vemurafenib), and FDA-approved prescribing drug label requires use of biomarker from this assay to effectively use the therapy in specific cancer or tumor type
    - For when tissue-based testing is infeasible (i.e., quantity not sufficient for tissue- based test, invasive biopsy is medically contraindicated, or inconclusive information for tissue based testing) with **ALL** of the following:
        - An individual being considered for ICI targeted therapy, liquid biopsy based TMB and/or MSI testing for the solid tumors
        - Systemic targeted therapy being considered (eg, crizotinib, erlotinib, olaparib, pembrolizumab,
        - vemurafenib), and FDA-approved prescribing drug label requires use of biomarker from this assay to effectively use the therapy in specific cancer or tumor type
    - Repeat testing for Tumor progression or relapse of disease
    - For Non-small cell lung cancer consider sending both tissue and liquid biopsy to increase yield of treatment information for treatment purposes.
- **Wiskott-Aldrich syndrome** (WAS gene (*81406, 81479*)) testing **1 or more** of the following:
    - Individual born male with **ALL** of the following:
        - Initial testing points to a WAS related disorder (Wiskott Aldrich Syndrome, X linked thrombytopenia, X-linked congenital neutropenia)
    - Individual born female with **ALL** of the following:
        - There is a known family history of WAS gene mutation (testing is to identify female carriers)
    - Testing is prenatal with **ALL** of the following indications:
        - Fetus is male. Testing is being done with chorionic villi sampling or cultured amniocytes.
        - There is known risk of WAS gene mutation (positive family history of WAS gene mutation and/or of known positive carrier females)
- **Various additional tests** may be indicated for **ALL** of the following:
    - Criteria must be met for appropriateness with **1 or more** of the following:
        - Equivocal or indeterminate diagnostic testing of a symptomatic individual
        - Individual with positive family history or known mutation of the disease in the family

        - Need to establish disease-causing mutation in individual with confirmed diagnosis
        - Reproductive partner of known gene mutation carrier
    - Disorder must be met for appropriateness with **1 or more** of the following:
        - Familial Hemophagocytic Lymphohistiocytosis (81403, 81479)
        - Familial hyperinsulinism Deficiency (FHI) include genes ABCC8 (*81407*) and/or KCN11 (*81403*)
        - Glycogen storage disease type 1 (G6PC (*81250*) and SLC37A4 (*81406*) Genes)
        - Hypophosphatasia (ALPL gene – 81479)
        - McKusick-Kaufman Syndrome (MKKS – *81403*) single gene only

The following molecular and/or genetic tests are considered to be **not medically necessary** do to lack of proven clinical utility:

- 13C-Spirulina Gastric Emptying Breath Test (GEBT) by Cairn Diagnostics d/b/a Advanced Breath Diagnostics, LLC (0106U)
- AlloSure CareDX for lung transplant rejection testing (81479)
- AlloSure® Donor-Derived Cell-Free DNA Test Renal Transplant Rejection Testing (81479)
- AlloSure Heart Testing (81479)
- Direct to consumer genetic testing
- EsoGuard Genetic Lab Test (*0114U*)
- Genetic Ancestry Testing
- Heartsbreath Testing (84999)
- Heart Molecular Microscope Diagnostic System (MMDx-Heart) (0087U)
- KidneyIntelX™ by RenalytixAI *(0105U)*
- Molecular Microscope Diagnostic System for Kidney (MMDx Kidney) (0088U)
- myTAIHEART (0055U)
- QSant (NephroSant) (81599)
- Repeat/Duplicative testing not addressed in above criteria.
- Scoliosis DNA testing *(0004M)*
- Skeletal Disorders Panel
- Syn-One test (cutaneous alpha-synuclein) *(81479)*
- Transcutaneous multispectral measurement of tissue oxygenation and hemoglobin using spatial frequency domain imaging (SFDI) BY Modulated Imaging, Inc *(0061U)*
- TruGraf (*81479*)
- Twins Zygosity PLA by Natera *(0060U)*

Document History:

Revised Dates:

- 2025: May – Implementation date of August 1, 2025. Criteria updated references updated.
- 2025: April – Implementation date of July 1, 2025. added items to not medically necessary. Criteria updated references updated.
- 2025: March – add not medically necessary items from Medical 99 – Transplantation rejection testing. Implementation date June 01, 2025
- 2025: January – Implementation date of 3/1/2025, criteria updated references updated

Reviewed Dates:

Origination Date: December 2024

Coding:

Medically necessary with criteria:

Coding	Description
0179U	Oncology (non-small cell lung cancer), cell-free DNA, targeted sequence analysis of 23 genes (single nucleotide variations, insertions and deletions, fusions without prior knowledge of partner/breakpoint, copy number variations), with report of significant mutation(s) (Resolution ctDx Lung™)

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
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
81194	NTRK (neurotrophic receptor tyrosine kinase 1, 2, and 3) (eg, solid tumors) translocation analysis
81234	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles
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)
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)
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (eg, Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (eg, R83C, Q347X)
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (eg, glioblastoma multiforme) promoter methylation analysis
81381	HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each
81400	Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg, SNP] by techniques such as restriction enzyme digestion or melt curve analysis)
81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using 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)
81407	Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)
81408	Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis)
81455	Solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes, genomic sequence analysis panel, interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis
81456	Solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes, genomic sequence analysis panel, interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis
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
81479	Unlisted molecular pathology procedure
85240	Clotting; factor VIII (AHG), 1-stage
87999	Unlisted microbiology procedure
88230	Tissue culture for non-neoplastic disorders; lymphocyte
88271	Molecular cytogenetics; DNA probe, each (eg, FISH)
88273	Molecular cytogenetics; chromosomal in situ hybridization, analyze 10-30 cells (eg, for microdeletions)
88291	Cytogenetics and molecular cytogenetics, interpretation and report

Considered Not Medically Necessary:

Coding	Description
0004M	Scoliosis, DNA analysis of 53 single nucleotide polymorphisms (SNPs), using saliva, prognostic algorithm reported as a risk score

0055U	Cardiology (heart transplant), cell-free DNA, PCR assay of 96 DNA target sequences (94 single nucleotide polymorphism targets and two control targets), plasma (myTAIHEART by TAI Diagnostics, Inc)
0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood (Twins Zygosity PLA by Natera)
0061U	Transcutaneous measurement of five biomarkers (tissue oxygenation [StO2], oxyhemoglobin [ctHbO2], deoxyhemoglobin [ctHbR], papillary and reticular dermal hemoglobin concentrations [ctHb1 and ctHb2]), using spatial frequency domain imaging (SFDI) and multi-spectral analysis (Transcutaneous multispectral measurement of tissue oxygenation and hemoglobin using spatial frequency domain imaging (SFDI) by Modulated Imaging, Inc)
0063U	Neurology (autism), 32 amines by LC-MS/MS, using plasma, algorithm reported as metabolic signature associated with autism spectrum disorder (NPDX ASD ADM Panel I by Stemina Biomarker Discovery, Inc)
0087U	Cardiology (heart transplant), mRNA gene expression profiling by microarray of 1283 genes, transplant biopsy tissue, allograft rejection and injury algorithm reported as a probability score (Molecular Microscope® MMDx—Heart by Kashi Clinical Laboratories)
0088U	Transplantation medicine (kidney allograft rejection), microarray gene expression profiling of 1494 genes, utilizing transplant biopsy tissue, algorithm reported as a probability score for rejection (Molecular Microscope® MMDx—Kidney by Kashi Clinical Laboratories)
0105U	Nephrology (chronic kidney disease), multiplex electrochemiluminescent immunoassay (ECLIA) of tumor necrosis factor receptor 1A, receptor superfamily 2 (TNFR1, TNFR2), and kidney injury molecule-1 (KIM-1) combined with longitudinal clinical data, including APOL1 genotype if available, and plasma (isolated fresh or frozen), algorithm reported as probability score for rapid kidney function decline (RKFD) (KidneyIntelX™ by RenalytixAI)
0106U	Gastric emptying, serial collection of 7 timed breath specimens, non-radioisotope carbon-13 (13C) spirulina substrate, analysis of each specimen by gas isotope ratio mass spectrometry, reported as rate of 13CO2 excretion (13C-Spirulina Gastric Emptying Breath Test (GEBT) by Cairn Diagnostics d/b/a Advanced Breath Diagnostics, LLC)
0107U	Clostridium difficile toxin(s) antigen detection by immunoassay technique, stool, qualitative, multiple-step method (Singulex Clarity C. diff toxins A/B assay by Singulex)
0114U	Gastroenterology (Barrett's esophagus), VIM and CCNA1 methylation analysis, esophageal cells, algorithm reported as likelihood for Barrett's esophagus (EsoGuard™ by Lucid Diagnostics)
0116U	Prescription drug monitoring, enzyme immunoassay of 35 or more drugs confirmed with LC-MS/MS, oral fluid, algorithm results reported as a patient-compliance measurement with risk of drug to drug interactions for prescribed medications (Snapshot Oral Fluid Compliance by Ethos Laboratories)
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 (Foundation PISM by Ethos)
0122U	Sickle cell disease, microfluidic flow adhesion (P-Selectin), whole blood (Flow Adhesion of Whole Blood to P-SELECTIN (WB-PSEL) by Functional Fluidics)

0123U	Mechanical fragility, RBC, shear stress and spectral analysis profiling (Mechanical Fragility, RBC by shear stress profiling and spectral analysis by Functional Fluidics)
0156U	Copy number (eg, intellectual disability, dysmorphology), sequence analysis (SMASH™, New York Genome Center by Marvel Genomics™)
0170U	Neurology (autism spectrum disorder [ASD]), RNA, next-generation sequencing, saliva, algorithmic analysis, and results reported as predictive probability of ASD diagnosis (Clarifi™ by Quadrant Biosciences)
0173U	Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes
0243U	Obstetrics (preeclampsia), biochemical assay of placental-growth factor, time-resolved fluorescence immunoassay, maternal serum, predictive algorithm reported as a risk score for preeclampsia (PlGF Preeclampsia Screen by PerkinElmer Genetics)
0247U	Obstetrics (preterm birth), insulin-like growth factor-binding protein 4 (IBP4), sex hormone-binding globulin (SHBG), quantitative measurement by LC-MS/MS, utilizing maternal serum, combined with clinical data, reported as predictive-risk stratification for spontaneous preterm birth (PreTRM® by Sera Prognostics)
0253U	Reproductive medicine (endometrial receptivity analysis), RNA gene expression profile, 238 genes by next-generation sequencing, endometrial tissue, predictive algorithm reported as endometrial window of implantation (eg, pre-receptive, receptive, post-receptive) (ERA® (Endometrial Receptivity Analysis) by Igenomix®)
0255U	Andrology (infertility), sperm-capacitation assessment of ganglioside GM1 distribution patterns, fluorescence microscopy, fresh or frozen specimen, reported as percentage of capacitated sperm and probability of generating a pregnancy score (Cap-Score™ Test, Androvia LifeSciences, Avantor Clinical Services (previously known as Therapak))
0256U	Trimethylamine/trimethylamine N-oxide (TMA/TMAO) profile, tandem mass spectrometry (MS/MS), urine, with algorithmic analysis and interpretive report (Trimethylamine (TMA) and TMA N-Oxide, Children's Hospital Colorado Laboratory)
0258U	Autoimmune (psoriasis), mRNA, next-generation sequencing, gene expression profiling of 50-100 genes, skin-surface collection using adhesive patch, algorithm reported as likelihood of response to psoriasis biologics (Mind.Px by Mindera)
0259U	Nephrology (chronic kidney disease), nuclear magnetic resonance spectroscopy measurement of myo-inositol, valine, and creatinine, algorithmically combined with cystatin C (by immunoassay) and demographic data to determine estimated glomerular filtration rate (GFR), serum, quantitative (GFR by NMR, Labtech™ Diagnostics)
0263U	Neurology (autism spectrum disorder [ASD]), quantitative measurements of 16 central carbon metabolites (ie, a-ketoglutarate, alanine, lactate, phenylalanine, pyruvate, succinate, carnitine, citrate, fumarate, hypoxanthine, inosine, malate, S-sulfocysteine, taurine, urate, and xanthine), liquid chromatography tandem mass spectrometry (LC-MS/MS), plasma, algorithmic analysis with result reported as negative or positive (with metabolic subtypes of

	ASD) (NPDX ASD and Central Carbon Energy Metabolism by Stemina Biomarker Discovery, Inc) (Authorization required – effective 1/1/2025)
0275U	Hematology (heparin-induced thrombocytopenia), platelet antibody reactivity by flow cytometry, serum (Versiti™ Heparin-Induced Thrombocytopenia Evaluation – PEA by Versiti™ Diagnostic Laboratories)
0279U	Hematology (von Willebrand disease [VWD]), von Willebrand factor (VWF) and collagen III binding by enzyme-linked immunosorbent assays (ELISA), plasma, report of collagen III binding (Versiti™ VWF Collagen III Binding by Versiti™ Diagnostic Laboratories)
0280U	Hematology (von Willebrand disease [VWD]), von Willebrand factor (VWF) and collagen IV binding by enzyme-linked immunosorbent assays (ELISA), plasma, report of collagen IV binding (Versiti™ VWF Collagen IV Binding by Versiti™ Diagnostic Laboratories)
0281U	Hematology (von Willebrand disease [VWD]), von Willebrand propeptide, enzyme-linked immunosorbent assays (ELISA), plasma, diagnostic report of von Willebrand factor (VWF) propeptide antigen level (Versiti™ VWF Propeptide Antigen by Versiti™ Diagnostic Laboratories)
0283U	von Willebrand factor (VWF), type 2B, platelet-binding evaluation, radioimmunoassay, plasma (Versiti™ VWD Type 2B Evaluation by Versiti™ Diagnostic Laboratories)
0284U	von Willebrand factor (VWF), type 2N, factor VIII and VWF binding evaluation, enzyme-linked immunosorbent assays (ELISA), plasma (Versiti™ VWD Type 2N Binding by Versiti™ Diagnostic Laboratories)
0290U	Pain management, mRNA, gene expression profiling by RNA sequencing of 36 genes, whole blood, algorithm reported as predictive risk score (MindX Blood Test™ - Pain by MindX Sciences™ Laboratory)
0291U	Psychiatry (mood disorders), mRNA, gene expression profiling by RNA sequencing of 144 genes, whole blood, algorithm reported as predictive risk score (MindX Blood Test™ - Mood by MindX Sciences™ Laboratory)
0292U	Psychiatry (stress disorders), mRNA, gene expression profiling by RNA sequencing of 72 genes, whole blood, algorithm reported as predictive risk score (MindX Blood Test™ - Stress by MindX Sciences™ Laboratory)
0293U	Psychiatry (suicidal ideation), mRNA, gene expression profiling by RNA sequencing of 54 genes, whole blood, algorithm reported as predictive risk score (MindX Blood Test™ - Suicidality by MindX Sciences™ Laboratory)
0294U	Longevity and mortality risk, mRNA, gene expression profiling by RNA sequencing of 18 genes, whole blood, algorithm reported as predictive risk score (MindX Blood Test™ - Longevity by MindX Sciences™ Laboratory)
0301U	Infectious agent detection by nucleic acid (DNA or RNA), Bartonella henselae and Bartonella quintana, droplet digital PCR (ddPCR); (Bartonella ddPCR by Galaxy Diagnostics Inc)

0302U	Infectious agent detection by nucleic acid (DNA or RNA), Bartonella henselae and Bartonella quintana, droplet digital PCR (ddPCR); following liquid enhancement (Bartonella Digital ePCR™ by Galaxy Diagnostics Inc)
0303U	Hematology, red blood cell (RBC) adhesion to endothelial/subendothelial adhesion molecules, functional assessment, whole blood, with algorithmic analysis and result reported as an RBC adhesion index; hypoxic (Hypoxic BioChip Adhesion by BioChip Labs™)
0304U	Hematology, red blood cell (RBC) adhesion to endothelial/subendothelial adhesion molecules, functional assessment, whole blood, with algorithmic analysis and result reported as an RBC adhesion index; normoxic (Normoxic BioChip Adhesion by BioChip Labs™)
0305U	Hematology, red blood cell (RBC) functionality and deformity as a function of shear stress, whole blood, reported as a maximum elongation index (Ektacytometry by BioChip Labs™)
0310U	Pediatrics (vasculitis, Kawasaki disease [KD]), analysis of 3 biomarkers (NT-proBNP, C-reactive protein, and T-uptake), plasma, algorithm reported as a risk score for KD (HART KD® by Atlas Genomics)
0311U	Infectious disease (bacterial), quantitative antimicrobial susceptibility reported as phenotypic minimum inhibitory concentration (MIC)-based antimicrobial susceptibility for each organism identified (Accelerate PhenoTest® BC kit, AST configuration by Accelerate Diagnostics, Inc)
0322U	Neurology (autism spectrum disorder [ASD]), quantitative measurements of 14 acyl carnitines and microbiome-derived metabolites, liquid chromatography with tandem mass spectrometry (LC-MS/MS), plasma, results reported as negative or positive for risk of metabolic subtypes associated with ASD (NPDX ASD Test Panel III by Stemina Biomarker Discovery d/b/a NeuroPointDX)
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 (Augusta Hematology Optical Genome Mapping, Georgia Esoteric and Molecular Labs)
0351U	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, or venous whole blood, algorithm reported as likelihood of bacterial infection (MeMed BV® by MeMed Diagnostics, Ltd)
0355U	APOL1 (apolipoprotein L1) (eg, chronic kidney disease), risk variants (G1, G2) (Apolipoprotein L1 (APOL1) Renal Risk Variant Genotyping by Quest Diagnostics®)
81599	Unlisted multianalyte assay with algorithmic analysis
84999	Unlisted chemistry procedure

The preceding codes for treatments and procedures applicable to this policy are included above for informational purposes only. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Policy Approach and Special Notes: *

- Coverage: See the appropriate benefit document for specific coverage determination. Member specific benefits take precedence over medical policy.
- Application to Products: Policy is applicable to Sentara Health Plan Commercial products.
- Authorization Requirements: Pre-certification by the Plan is required.
- Special Notes:
    - Medical policies can be highly technical and complex and are provided here for informational purposes. These medical policies are intended for use by health care professionals. The medical policies do not constitute medical advice or medical care. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Sentara Health Plan members should discuss the information in the medical policies with their treating health care professionals. Medical technology is constantly evolving, and these medical policies are subject to change without notice, although Sentara Health Plan will notify providers as required in advance of changes that could have a negative impact on benefits.
    - Services mean both medical and behavioral health (mental health) services and supplies unless We specifically tell You otherwise. We do not cover any services that are not listed in the Covered Services section unless required to be covered under state or federal laws and regulations. We do not cover any services that are not Medically Necessary. We sometimes give examples of specific services that are not covered but that does not mean that other similar services are covered. Some services are covered only if We authorize them. When We say You or Your We mean You and any of Your family members covered under the Plan. Call Member Services if You have questions.

References:

Specialty Association Guidelines; Government Regulations; Winifred S. Hayes, Inc; UpToDate; Literature Review; Specialty Advisors; National Coverage Determination (NCD); Local Coverage Determination (LCD).

(2024, Mar 14). Retrieved Mar 18, 2025, from MCG 28th Edition: https://careweb.careguidelines.com/ed28/index.html

(2025). Retrieved Mar 18, 2025, from Palmetto GBA - DEX: Diagnostics Exchange Registry: https://app.dexzcodes.com/login

AHS –M2175 – Minimal Residual Disease (MRD). (2025, Apr 01). Retrieved Mar 18, 2025, from Avalon Healthcare Solutions: https://www.avalonhcs.com/wp-content/uploads/sentarahealth/M2175%20Minimal%20Residual%20Disease%20(MRD).pdf

Cell-free DNA Testing (Liquid Biopsy) for the Management of Cancer 2024-11-17 updated 2025-04-01. (2025, Apr 01). Retrieved Mar 18, 2025, from Carelon Medical Benefits Management: https://guidelines.carelonmedicalbenefitsmanagement.com/cell-free-dna-testing-liquid-biopsy-for-the-management-of-cancer-2024-11-17-updated-2025-04-01/?highlight=NavDx&hilite=NavDx

Cervical Cancer. (2025, Feb 10). Retrieved Mar 18, 2025, from National Comprehensive Cancer Network: https://www.nccn.org/professionals/physician_gls/pdf/cervical_blocks.pdf

Clinical validity of TTMV-HPV DNA liquid biopsies for the diagnosis and surveillance of HPV-associated oropharyngeal carcinoma. (2023). Retrieved Mar 18, 2025, from American Society of Clinical Oncology: https://www.asco.org/abstracts-presentations/ABSTRACT418458

Lab Management Program - Clinical Guidelines. (2025, Feb 10). Retrieved Mar 18, 2025, from Cigna Healthcare: https://www.evicore.com/sites/default/files/clinical-guidelines/2025-03/Cigna_LabMgmt_V1.1.2025_Eff02.10.2025_pub02.07.2025_upd03.14.2025_0.pdf

LCD: Billing and Coding: MolDX: Minimal Residual Disease Testing for Solid Tumor Cancers (A58376). (2025, Feb 06). Retrieved Mar 18, 2025, from Centers for Medicare and Medicaid Services: https://www.cms.gov/medicare-coverage-

database/view/article.aspx?articleid=58376&ver=43&keyword=NavDx&keywordType=starts&areaId=s53&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1

Miles, B., Yom, S., Burtness, B., & Bhatia, A. (2024, Mar 06). Treatment of human papillomavirus associated oropharyngeal cancer. Retrieved Mar 19, 2025, from UpToDate: https://www.uptodate.com/contents/treatment-of-human-papillomavirus-associated-oropharyngeal-cancer?search=NavDx%20TTMV-HPV%20DNA&source=search_result&selectedTitle=7%7E150&usage_type=default&display_rank=7#H2451511189

NavDx (Naveris). (2024, Sep 10). Retrieved Mar 18, 2025, from Hayes: https://evidence.hayesinc.com/report/mta.naveris5582

NavDx. (2025). Retrieved Mar 19, 2025, from NavDx: https://navdx.com/

Procedure Fee Files & CPT Codes. (2025). Retrieved Mar 18, 2025, from Virginia Department of Medical Assistance Services: https://www.dmas.virginia.gov/for-providers/rates-and-rate-setting/procedure-fee-files-cpt-codes/#searchCPT

Regulation of Genetic Tests. (2024, Feb 19). Retrieved Mar 19, 2025, from National Human Genome Research Institute: https://www.genome.gov/about-genomics/policy-issues/Regulation-of-Genetic-Tests

LCD: MolDX: Molecular Diagnostic Tests (MDT) (L35025). (2023, May 04). Retrieved Dec 30, 2024, from Centers for Medicare and Medicaid Services: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=35025&ver=98&bc=0

Michigami, T., Ohata, Y., & Fujiwara, M. (2020, Jan 09). Clinical Practice Guidelines for Hypophosphatasia*. Retrieved Dec 31, 2024, from PubMed: https://pmc.ncbi.nlm.nih.gov/articles/PMC6958520/

Scheinman, S., & Carpenter, T. (2024, Dec 18). Hereditary hypophosphatemic rickets and tumor-induced osteomalacia. Retrieved Dec 30, 2024, from UpToDate: https://www.uptodate.com/contents/hereditary-hypophosphatemic-rickets-and-tumor-induced-osteomalacia?search=Hypophosphatemic%20Rickets&source=search_result&selectedTitle=1%7E105&usage_type=default&display_rank=1#H18

US Department of Health and Human Services has published guidance on Heartsbreath Test for Heart Transplant Rejection – JA6366. Retrieved 1.8.2024. https://www.hhs.gov/guidance/document/heartsbreath-test-heart-transplant-rejection

Centers for Medicare and Medicaid Services. NCD Heartsbreath Test for Heart Transplant Rejection (260.10). Effective date 12.8.2008. Retrieved 1.8.2024.https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=325&ncdver=1&keyword=heartsbreath&keywordType=starts&areaId=all&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1

Michael Phillips, John P. Boehmer, Renee N. Cataneo, Taseer Cheema, Howard J. Eisen, John T. Fallon, Peter E. Fisher, Alan Gass, Joel Greenberg, Jon Kobashigawa, Donna Mancini, Barry Rayburn, Mark J. Zucker, Prediction of heart transplant rejection with a breath test for markers of oxidative stress, The American Journal of Cardiology, Volume 94, Issue 12, 2004, Pages 1593-1594, ISSN 0002-9149, https://doi.org/10.1016/j.amjcard.2004.08.052.

Keywords: