Sentara Health Plans

Medicaid

# Pharmacogenetic Testing

**Table of Content**



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|---|---|
| Effective Date | 1/2012 |
| Next Review Date | 8/15/2024 |
| Coverage Policy | Medical 34E |
| Version | 1 |

**All requests for authorization for the services described by this medical policy will be reviewed per Early and Periodic Screening, Diagnostic and Treatment (EPSDT) guidelines. These services may be authorized under individual consideration for Medicaid members under the age of 21-years if the services are judged to by medically necessary to correct or ameliorate the member's condition. Department of Medical Assistance Services (DMAS), Supplement B - EPSDT (Early and Periodic Screening, Diagnosis and Treatment) Manual.*.**

## Purpose:

This policy addresses pharmacogenetic testing.

## Description & Definitions:

**Pharmacogenomics** is the study of the role of inherited and acquired genetic variation on drug response. It is distinguished from pharmacogenetics, which focuses on individual candidate genes (identified by approaches such as genome-wide association studies (GWAS), genome-wide expression profiling, or methylation studies) to identify markers across the genome that affect drug metabolism, distribution, receptor targets, and biologic effect.

**Autosomal recessive:** A genetic condition that appears only in individuals who have received two copies of an autosomal gene, one copy from each parent. The gene is on an autosome, a nonsex chromosome. The parents are carriers who have only one copy of the gene and do not exhibit the trait because the gene is recessive to its normal counterpart gene.

**X-linked recessive inheritance**: 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.

## Criteria:

Pharmacogenetic Testing is considered medically necessary for the prevention diagnosis and treatment of patients who meet **ALL** of the following:

- There must be **1 or more** of the following:
  - There is sufficient Published Scientific Evidence or 3rd party Consensus in the Medical Community that the results of the specific genetic Testing improves clinical outcomes
  - There is an approved mutation specific treatment available
- The genetic disorder is associated with a potentially significant disability or has a lethal natural history
- The results of the genetic test could impact the medical management of the individual

- After completion of a thorough history, physical examination, pedigree analysis, genetic counseling, relevant diagnostic and biochemical tests (if any), the patient meets criteria for **1 or more** of the following approved tests:
    - **HLA-B 1502** testing is medically necessary for persons of Asian ancestry before initiating treatment with carbamazepine (Tegretol)
    - **HLA-B 5701** Screening is approved for **ANY** HIV member who is being considered for treatment with the HIV medication or Abacavir Hypersensitivity
    - **HIV Drug Susceptibility and Resistance Tests** (Phenotypic or Genotypic ) approved with no criteria.
    - **CYP2C19 variant of Cytochrome P450** to determine the drug-metabolizer status for clopidogrel is medically necessary for **1 or more** of the following;
        - Member is currently undergoing treatment with clopidogrel and has not been tested;
        - Members whom the use of clopidogrel is being proposed.
    - **Cystic fibrosis transmembrane conductance regulator** (CFTR) potentiator for Kalydeco (ivacaftor) is medically necessary for individuals who are 6 years of age or older with a diagnosis of Cystic Fibrosis.
    - **G6PD testing** is medically necessary prior to starting therapy with rasburicase and **1 or more** of the following:
        - Female at high risk for G6PD deficiency, including **1 or more** of the following:
            - History of previous hemolytic episode;
            - Originating from geographic area with high prevalence of G6PD deficiency
        - Male at high risk for G6PD deficiency and inconclusive results of biochemical testing of enzyme activity
        - Neonate with history of jaundice
    - **CYP2D6 polymorphisms** (see exclusions below) (81226) is medically necessary for **1 or more** of the following:
        - For individuals with Huntington's Disease who have been or who are being considered to be prescribed doses of tetrabenazine (Xenazine) greater than 50 mg per day
        - For individuals with Gaucher's disease type 1 who are being considered for treatment with eliglustat (Cerdelga)
        - Amitriptyline or nortriptyline for treatment of depressive disorders
        - Tetrabenazine doses greater than 50 mg/day, or re-initiation of therapy with doses greater than 50 mg/day
    - **Methylguanine-DNA methyltransferase(PredictMDxTM)** (81287) is medically necessary for predicting response to temozolomide (Temodar) in persons with glioblastoma.
    - **Co-receptor tropism testing (i.e., Trofile™)** 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
    - **Congenital sucrase-isomaltase deficiency Testing (CSID)** is medically necessary for **ALL** of the following:
        - Stool PH <6
        - Increase in breath hydrogen of >10ppm when challenged with Sucrose after fasting
        - Negative Lactose breath test
        - Low sucrose activity on duodenal biopsy
        - Normal other disaccharidases on duodenal biopsy
    - **Retinoid isomerohydrolase (RPE65)** Gene Testing for Luxturna is medically necessary for **ALL** of the following:
        - Testing results will effect treatment the individual is getting
        - Individual's diagnosis is still unclear after documentation **ALL** of the following:
            - Physical examination
            - Individual's history reviewed
            - Pedigree analysis

- Genetic counselin
- Standard diagnostic studies have been completed

- Individual has indications of **1 or more** of the following:
  - Individual exhibits clinical features
  - Individual is pre-symptomatic (specific risk of inheriting the mutation)
- Individual has sufficiently viable retinal cells as determined by optical coherence tomography (OCT) and/or ophthalmoscopy with **ALL** of the following:
  - Individual has **1 or more** of the following:
    - Area of retina within the posterior pole of greater than 100μm thickness per optical coherence tomography (OCT)
    - At least 3 disc areas of retina without atrophy or pigmentary degeneration within the posterior pole
  - Individual has **1 or more** of the following:
    - Visual field within 20 degrees in any meridian as measured by III4e isopter OR equivalent in both eyes
    - Visual acuity worse than 20/60 in both eyes

- **HLA-B 58:01** Allopurinol Hypersensitivity Testing is medically necessary for an individual who is being considered for treatment with the medication Allopurinol and is of Asian descent
- **Genetic testing to detect somatic/tumor BRCA mutations and or large genomic rearrangements** (e.g. myChoice CDx) is medically necessary for **1 or more** of the following:
  - Advanced epithelial Ovarian, fallopian tube or primary peritoneal cancer who have been treated with three or more prior lines of chemotherapy and being considered for niraparib (Zejula).
  - Advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in a complete or partial response to two or more lines of platinum-based chemotherapy and are being considered for maintenance treatment with niraparib.
- **PD-L1** is medically necessary for triple negative breast cancer (Estrogen, progesterone and HER 2 negative)
- **NTRK NGS Fusion Profile** is medically necessary for an individual who has a solid tumor who is being considered for Vitrakvi (larotrectinib) therapy.
- **Liquid (ctDNA) based panel tests (e.g., Resolution ctDx Lung)** 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
  - The test selected has no more than 50 genes

Pharmacogenetic Testing is considered **not medically necessary** for any use other than those indicated in clinical criteria, to include but not limited to:

- ADRA2A
- ADRB1
- AGTR1
- ANKK1
- Apolipoprotein E (Apo E) for determining therapeutic response to lipid-lowering medications
- BDKRB1
- CACNA1C
- CYP3A4
- CYP1A2
- CYP2B6
- CYP2C19 except for covered indications below.
- CYP2C8
- CYP2C9
- CYP2D6 except for covered indications above
- CYP3A5 genes, including common variants *2, *3, *4, *5, *6
- CYP3A65
- DRD2
- DPYD, MTHFR, and TYMS Genes for 5-Fluorouracil Pharmacogenetics
- Exome Sequence Analysis (**81415, 81416, 81417**)
- EYA1 genetic testing

- Genome Sequence Analysis **(81425, 81426, 81427)**
- HTR2A
- HTR2C
- MTHFR
- OPRM1
- Repeat/Duplicative genetic testing
- SLCO1B1
- SLC6A4
- SULT4A1
- VKORC1
- UGT1A1 Gene
- UGT1A4
- UGT2B15 gene
- Whole Exome Sequencing (WES);
- Whole-genome sequencing in which a member's entire DNA is sequenced

**Pharmacogenetic screening panels** in the general population are considered **not medically necessary.** Examples include but are not limited of the following:

- AmpliChip Cytochrome P450 (CYP450) Genotyping Test
- EliteLabs panels
- Genecept™ Assay
- GeneSight® Analgesic
- GeneSight® Psychotropic
- GeneSight® ADHD
- GeneSight MTHFR
- Millennium PGT psychotropic testing
- Pathway Genomics Panels
  - Mental Health DNA Insight
  - Healthy Woman DNA Insight
  - Pain Medication DNA Insight
  - Cardiac DNA Insight
  - Healthy Weight DNA Insight
- PGX Profile Panels offered by G6 Genomics
  - Cardiology
  - Urology
  - Pain Management
  - Psychiatry
  - Comprehensive
- PrismRA
- rxSEEK Epilepsy Drug Metabolism Test (81225, 81227, 81401)
- SureGene Test for Antipsychotic and Antidepressant Response (STA2R)

## Coding:

Medically necessary with criteria:

| Coding | Description |
|---|---|
| 81194 | NTRK (neurotrophic receptor tyrosine kinase 1, 2, and 3) (eg, solid tumors) translocation analysis |
| 81220 | CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines) |
| 81226 | CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN) |
| 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 |
| 81287 | MGMT (O-6-methylguanine-DNA methyltransferase) (eg, glioblastoma multiforme) promoter methylation analysis |

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| 81380 | HLA Class I typing, high resolution (ie, alleles or allele groups); one locus (eg, HLA-A, -B, or -C), each |
| 81381 | HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each |
| 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) |
| 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 |
| 81479 | Unlisted molecular pathology procedure |
| 81599 | Unlisted multianalyte assay with algorithmic analysis |
| 88360 | Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; manual |
| 0172U | Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score |
| 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) |
| 87999 | Unlisted microbiology procedure |

Considered Not Medically Necessary:

| Coding | Description |
|---|---|
| 81225 | CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17) |
| 81227 | CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6) |
| 81230 | CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22) |
| 81231 | CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7) |
| 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 |
| 81291 | MTHFR (5,10-methylenetetrahydrofolate reductase) (eg, hereditary hypercoagulability) gene analysis, common variants (eg, 677T, 1298C) |
| 81350 | UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (eg, drug metabolism, hereditary unconjugated hyperbilirubinemia [Gilbert syndrome]) gene analysis, common variants (eg, *28, *36, *37) |
| 81355 | VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G>A, c.173+1000C>T) |

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| 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) |
| 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) |
| 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) |
| 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) |
| 0173U | Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes |
| 0345U | Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6 |

## Document History:

Revised Dates:

- 2023: September
- 2023: January
- 2021: October
- 2020: September
- 2020: June
- 2019: November
- 2019: August
- 2016: June
- 2016: May
- 2016: April
- 2016: February
- 2015: December
- 2015: October
- 2015: June
- 2015: May
- 2015: April
- 2015: March
- 2014: December
- 2014: November
- 2014: June
- 2014: March
- 2014: January
- 2013: November

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- 2016: April
- 2015: December
- 2013: October

Effective Date:

- January 2012

## References:

Including but not limited to: Specialty Association Guidelines; Government Regulations; Winifred S. Hayes, Inc; UpToDate; Literature Review; Specialty Advisors; National Coverage Determination (NCD); Local Coverage Determination (LCD).


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## Special Notes: *

This medical policy express Sentara Health Plan's determination of medically necessity of services, and they are based upon a review of currently available clinical information. These policies are used when no specific guidelines for coverage are provided by the Department of Medical Assistance Services of Virginia (DMAS). Medical Policies may be superseded by state Medicaid Plan guidelines. Medical policies are not a substitute for clinical judgment or for any prior authorization requirements of the health plan. These policies are not an explanation of benefits.

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.

The Early and Periodic Screening, Diagnostic and Treatment (EPSDT) covers services, products, or procedures for children, if those items are determined to be medically necessary to "correct or ameliorate" (make better) a defect, physical or mental illness, or condition (health problem) identified through routine medical screening or examination, regardless of whether coverage for the same service or support is an optional or limited service under the state plan. Children enrolled in the FAMIS Program are not eligible for all EPSDT treatment services. All requests for authorization for the services described by this medical policy will be reviewed per EPSDT guidelines. These services may be authorized under individual consideration for Medicaid members under the age of 21-years if the services are judged to by medically necessary to correct or ameliorate the member's condition. *Department of Medical Assistance Services (DMAS), Supplement B - EPSDT (Early and Periodic Screening, Diagnosis and Treatment) Manual.*

## Keywords:

Pharmacogenetics, Medical 34E, genetic, drug metabolism, CYP, Pathway Genomics, PGX, Cardiology, Urology, Pain Management, Psychiatry, PharmaRisk, PrismRA, rxSeek, whole exome, exosome sequencing, sequence analysis, GeneSight, HLA-B 1502, carbamazepine, HLA-B 5701, HIV phenotype, HIV genotype, CYPC19, CFTR, G6PD, Rasburicase, Methylguanine-DNA methyltransferase, PredictMDx™, Co-receptor tropism testing, Trofile™, Congenital sucrose-isomaltase deficiency Testing, CSID, Retinoid isomerohydrolase, RPE65, Luxturna, HLA-B 58:01, Allopurinol, myChoice CDx, PD-L1, ctDx-lung biopsy