

Legacy Policy for all Full Insured and some ASO Group effective 12.14.2024

Pharmacogenetic Testing, Medical 34E

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Member-specific benefits take precedence over medical policy and benefits may vary across plans. Refer to the individual’s benefit plan for details [*](#).

Purpose:

This policy addresses pharmacogenetic testing.

For other types of liquid biopsy testing refer to Medical 34A – Genetic Testing-Cancer Prevention, Diagnosis and Treatment

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:
 - **ARSA** (81405) testing is medically necessary in individuals being considered for treatment with Lenmeldy (atidarsagene autotemcel).
 - **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.
 - **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
 - **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.
 - **Dystrophic epidermolysis bullosa (DEB)** molecular testing containing **1 or more** of the following is medically necessary for individuals being considered for Filsuvez® (birch triterpenes):
 - COL17A1 (81479)
 - LAMA3 (81479)
 - LAMB3 (81479)
 - LAMC3 (81479)
 - **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
 - **Methylguanine-DNA methyltransferase(PredictMDx™)** (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
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
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)
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)
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)
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:

- 2024: May
- 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
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- 2015: April
- 2015: March
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References:

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

(2022, Aug 31). Retrieved Aug 10, 2023, from MCG: <https://careweb.careguidelines.com/ed26/index.html>

(2023). Retrieved Aug 10, 2023, from Department of Medical Assistance Services: <https://vamedicaid.dmas.virginia.gov/manuals/provider-manuals-library#gsc.tab=0&gsc.q=PLA%20&gsc.sort=>

Clinical Use of Pharmacogenetic Tests in Prescribing Psychotropic Medications for Children and Adolescents. (2020, Mar). Retrieved Aug 11, 2023, from American Academy of Child and Adolescent Psychiatry: https://www.aacap.org/AACAP/Policy_Statements/2020/Clinical-Use-Pharmacogenetic-Tests-Prescribing-Psychotropic-Medications-for-Children-Adolescents.aspx

For Clinicians. (2023). Retrieved Aug 07, 2023, from GeneSight: <https://genesight.com/for-clinicians/>

GeneSight Psychotropic (Assurex Health Inc./Myriad Neuroscience). (2022, Oct 20). Retrieved Aug 07, 2023, from Hayes, Inc: <https://evidence.hayesinc.com/report/gte.genesight3945>

Genetic Testing Collateral Document. (2023, Feb 15). Retrieved Aug 10, 2023, from Cigna: https://static.cigna.com/assets/chcp/pdf/coveragePolicies/medical/Genetic_Testing_Collateral_Document.pdf

LCA: Billing and Coding: MolDX: Pharmacogenomics Testing (A58318). (2023, Apr 20). Retrieved Aug 07, 2023, from Centers for Medicare and Medicaid Services: <https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=58318&ver=43>

LCD: MolDX: Pharmacogenomics Testing (L38294). (2020, Jul 26). Retrieved Aug 07, 2023, from Centers for Medicare and Medicaid Services: <https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lclid=38294&ver=16&keyword=GeneSight&keywordType=starts&areaId=s53&docType=NCA,CA L,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1>

Panel and other Multi-Gene Testing for Polymorphisms to Determine Drug-Metabolizer Status. (2023, Jun 28). Retrieved Aug 09, 2023, from Anthem: https://www.anthem.com/dam/medpolicies/abcbs_va/active/policies/mp_pw_a050309.html

Pharmacogenetic and Pharmacodynamic Testing. (2023, Jul 01). Retrieved Aug 09, 2023, from Aetna: https://www.aetna.com/cpb/medical/data/700_799/0715.html

Pharmacogenetic Panel Testing. (2023, Jul 01). Retrieved Aug 10, 2023, from United Healthcare: <https://www.uhcprovider.com/content/dam/provider/docs/public/policies/comm-medical-drug/pharmacogenetic-testing.pdf>

Pharmacogenomic Testing. (2023, Feb 12). Retrieved Aug 07, 2023, from Carelon Medical Benefits Management: <https://guidelines.carelonmedicalbenefitsmanagement.com/pharmacogenomic-testing-2023-02-12/?highlight=GeneSight&hilite=GeneSight>

Pharmacogenomic Testing for Attention-Deficit/Hyperactivity Disorder Treatment. (2023, Mar 31). Retrieved Aug 07, 2023, from Hayes, Inc: <https://evidence.hayesinc.com/report/pmu.pharmoadhd5242>

Pharmacogenomic Testing of Selected Mental Health Conditions. (2021, Dec 06). Retrieved Aug 07, 2023, from Hayes, Inc.: <https://evidence.hayesinc.com/report/gti.pharmacogenetics3715>

Regulation of Genetic Tests. (2023). Retrieved Aug 11, 2023, from Code of Federal Regulations (National Archives): <https://www.genome.gov/about-genomics/policy-issues/Regulation-of-Genetic-Tests>

Table of Pharmacogenetic Associations. (2022, Oct 26). Retrieved Aug 14, 2023, from U.S. Food and Drug Administration: <https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations>

(2020). Retrieved May 11, 2020, from Centers for Medicare and Medicaid Services: <https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=53&KeyWord=pharmacogenetic&KeyWordLookU>

(2020). Retrieved May 12, 2020, from National Comprehensive Cancer Network:
<https://cse.google.com/cse?cx=007894372670309631110:voocdaeamxuy&ie=UTF-8&q=allopurinol&safe=high>

(2020, Feb 05). Retrieved May 12, 2020, from MCG: <https://careweb.careguidelines.com/ed23/index.html>

(2020). Retrieved May 12, 2020, from Department of Medical Assistance Services:
<https://www.viriniamedicaid.dmas.virginia.gov/wps/portal/ProviderManual>

Allopurinol: Drug information (Lexicomp). (2020). Retrieved May 11, 2020, from UpToDate:
https://www.uptodate.com/contents/allopurinol-drug-information?search=HLA%20b5801&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3#F131725

Genetic Testing to Predict Allopurinol Toxicity. (2019, Aug 29). Retrieved May 11, 2020, from Hayes, Inc.:
<https://evidence.hayesinc.com/report/gti.predictallopurinol3969>

Gout. (2020). Retrieved May 11, 2020, from American College of Rheumatology: <https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines/Gout>

Hyperuricemia and Gout in Chronic Kidney Disease. (2019, Jul 25). Retrieved May 12, 2020, from DynaMed:
<https://www.dynamed.com/condition/hyperuricemia-and-gout-in-chronic-kidney-disease>

Pharmacogenomic Testing and Genetic Testing for Thrombotic Disorders. (2020, Mar 03). Retrieved May 12, 2020, from AIM Specialty Health: https://aimproviders.com/genetic-testing/wp-content/uploads/sites/15/2019/12/PharmacogeneticandThrombophilia_Mar_2020.pdf

Redwood, A. J., Pavlos, R. K., White, K. D., & Phillips, E. J. (2018, Jan). HLAs: Key Regulators of T-cell-mediated Drug Hypersensitivity. Retrieved May 12, 2020, from PubMed: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5743596/>

(2019, Sep 10). Retrieved Sep 18, 2019, from Genetics Home Reference: <https://ghr.nlm.nih.gov/gene/RPE65#synonyms>

(2019). Retrieved Sep 19, 2019, from Hayes, Inc.:
<https://evidence.hayesinc.com/search?q=%257B%2522phrase%2522:%2522Invitae%2520Singel%2520gene%2522,%2522style%2522:%2522PHRASE%2522,%2522size%2522:10,%2522page%2522:1,%2522bundle%2522:%257B%2522pat h%2522:%2522%2522,%2522title%2522:%2522%2522%257D,%2522tot>

(2019). Retrieved Sep 19, 2019, from AIM Specialty Health: <https://aimspecialtyhealth.com/resources/clinical-guidelines/genetic-testing/>

(2019). Retrieved Sep 19, 2019, from National Comprehensive Cancer Network:
<https://cse.google.com/cse?cx=007894372670309631110:voocdaeamxuy&ie=UTF-8&q=RPE65&safe=high>

About Luxturna. (2019). Retrieved Sep 18, 2018, from Spark Therapeutics: <https://luxturna.com/about-luxturna/>
LCD: Voretigene Neparvovec-rzyl (Luxturna) (L37863). (2019, Sep 05). Retrieved Sep 19, 2019, from Centers for Medicare and Medicaid Services: <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=37863&ver=11&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=53&KeyWord=RPE65&KeyWo>

Recommendations on Clinical Assessment of Patients with Inherited Retinal Degenerations - 2016. (2016, Jun). Retrieved Sep 19, 2019, from American Academy of Ophthalmology: <https://www.aao.org/clinical-statement/recommendations-on-clinical-assessment-of-patients>

Retinal Disorders - Gene Panels, A-0912. (2019, Feb 11). Retrieved Sep 19, 2019, from MCG:
<https://careweb.careguidelines.com/ed23/index.html>

Retinitis pigmentosa: Treatment. (2018, Apr 11). Retrieved Sep 19, 2019, from UpToDate:
https://www.uptodate.com/contents/retinitis-pigmentosa-treatment?search=RPE65&source=search_result&selectedTitle=1~4&usage_type=default&display_rank=1

Retinitis Pigmentosa. (2019, Nov 18). Retrieved Sep 19, 2019, from DynaMed:
<https://www.dynamed.com/condition/retinitis-pigmentosa#GUID-E50FA4AE-CEB8-4AB3-B3D8-F1F06CB66D7C>

RPE65. (2019). Retrieved Sep 18, 2019, from Invitae: <https://www.invitae.com/en/physician/genes/21284/16>. RPE65 single gene test. (2019). Retrieved Sep 19, 2019, from Blueprint Genetics: <https://blueprintgenetics.com/tests/single-gene-tests/rpe65-single-gene-test-2/>

Pao W, Miller V, Zakowski M, et al. EGF receptor gene mutations are common in lung cancers from "never smokers" and are associated with sensitivity of tumors to gefitinib and erlotinib. *Proc Natl Acad Sci U S A* 2004; 101:13306.

Lynch TJ, Bell DW, Sordella R, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib. *N Engl J Med* 2004; 350:2129.

Paez JG, Jänne PA, Lee JC, et al. EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy. *Science* 2004; 304:1497.

Keedy VL, Temin S, Somerfield MR, et al. American Society of Clinical Oncology provisional clinical opinion: epidermal growth factor receptor (EGFR) Mutation testing for patients with advanced non-small-cell lung cancer considering first-line EGFR tyrosine kinase inhibitor therapy. *J Clin Oncol* 2011; 29:2121.

Mok TS, Wu YL, Thongprasert S, et al. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. *N Engl J Med* 2009; 361:947.

Fukuoka M, Wu YL, Thongprasert S, et al. Biomarker analyses and final overall survival results from a phase III, randomized, open-label, first-line study of gefitinib versus carboplatin/paclitaxel in clinically selected patients with advanced non-small-cell lung cancer in Asia (IPASS). *J Clin Oncol* 2011; 29:2866.

Leufkens HG. The interface between pharmacoepidemiology and pharmacogenetics. *Eur J Pharmacol* 2000; 410:121.

Ingelman-Sundberg M. Pharmacogenetics: an opportunity for a safer and more efficient pharmacotherapy. *J Intern Med* 2001; 250:186.

Drazen JM, Silverman EK, Lee TH. Heterogeneity of therapeutic responses in asthma. *Br Med Bull* 2000; 56:1054.

Evans WE, McLeod HL. Pharmacogenomics--drug disposition, drug targets, and side effects. *N Engl J Med* 2003; 348:538.

Wang L, McLeod HL, Weinshilboum RM. Genomics and drug response. *N Engl J Med* 2011; 364:1144.

Vesell ES. Therapeutic lessons from pharmacogenetics. *Ann Intern Med* 1997; 126:653.

Evans WE, Relling MV. Pharmacogenomics: translating functional genomics into rational therapeutics. *Science* 1999; 286:487.

Mancinelli L, Cronin M, Sadée W. Pharmacogenomics: the promise of personalized medicine. *AAPS PharmSci* 2000; 2:E4.

Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA* 1998; 279:1200.

Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. *Ann Pharmacother* 2008; 42:1017.

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.

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