Pharmacogenomics — Cytochrome P450 Polymorphisms and VKORC1

Humana®

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Medical Coverage Policy

Table of Contents

Related Medical/Pharmacy Coverage Policies

Genetic Testing
Pharmacogenomics - Noncancer Indications
Cerdelga (eliglustat) Pharmacy Coverage Policy
Preferred Multiple Sclerosis Products Pharmacy Coverage Policy
Xenazine (tetrabenazine) Pharmacy Coverage Policy

Description

Pharmacogenomics testing is laboratory testing which has the potential to determine how an individual's genetic factors may affect the safety and effectiveness of that individual's response to a specific medication. The goal of pharmacogenomics testing is to reduce the incidence of adverse medication reactions while improving an individual's positive response to the medication. Additionally, some tests may help provide information on how well a specific treatment may work for an individual.

Cytochrome P450 enzymes are a group of enzymes that account for approximately 75 percent of drug metabolism in the human body. Enzymes encoded by the *P450* genes (eg, *CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5*) are found primarily in the liver. The action of the P450 enzymes affects the blood levels of

many drugs. Genotyping for cytochrome P450 has been proposed for possible use in medical management of drug therapies including, but may not be limited to, anticoagulants, antiplatelet, barbiturates, opioid analgesics, proton pump inhibitors, psychotropic medications and selective estrogen receptor modulator (SERM). Examples of pharmacogenomic tests include, but may not be limited to, GeneSight Psychotropic, IDGenetix, Neuropsychiatric Panel EffectiveRX, PersonalisedRX, Roche Amplichip CYP450 Test, STA2R SureGene, VerifyNow and Warfarin Response Genotype. **(Refer to Coverage Limitations)**

Coverage Determination

Services provided by a psychiatrist, psychologist or other behavioral health professionals are subject to the provisions of the applicable behavioral health benefit.

Any state mandates for pharmacogenomic/pharmacogenetic testing take precedence over this medical coverage policy.

Apply General Criteria for Genetic and Pharmacogenomics Tests when disease- or gene-specific criteria are not available on a medical coverage policy. For information regarding **general criteria for genetic and pharmacogenomics tests**, please refer to Genetic Testing Medical Coverage Policy.

***CYP2C9* Genotyping**

Humana members may be eligible under the Plan for ***CYP2C9* genotyping** when the following criteria are met:

- Individual has been diagnosed with multiple sclerosis; **AND**
- Testing performed prior to initiation of treatment with siponimod (Mayzent)

***CYP2D6* Genotyping**

Humana members may be eligible under the Plan for ***CYP2D6* genotyping** (eg, Roche Amplichip CYP450 Test) when the following criteria are met:

- Individual has been diagnosed with Gaucher type I disease; **AND**
    - Testing performed using a US Food & Drug Administration (FDA)-approved test prior to initiation of treatment with eliglustat (Cerdelga); **OR**
- Individual has been diagnosed with chorea associated with Huntington's disease; **AND**
    - Prior to initiation of treatment with a daily dose of tetrabenazine (Xenazine) over 50 mg to determine dosing regimen

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **pharmacogenomics/pharmacogenetic testing** for any indications other than those listed above including, but may not be limited to, the following:

- Assessment of multiple conditions including, but not limited to:
  - Single gene analysis for any of the following:
    - *COMT* (eg, Mayo Clinic Catechol-O-Methyltransferase [*COMT*] Genotype [0032U])
    - Mayo Clinic *CYP2D6* Common Variants and Copy Number (0070U)
    - Mayo Clinic *CYP2D6* Full Gene Sequencing (0071U)
    - Mayo Clinic *CYP2D6-2D7* Hybrid Gene Targeted Sequence Analysis (0072U)
    - Mayo Clinic *CYP2D7-2D6* Hybrid Gene Targeted Sequence Analysis (0073U)
    - Mayo Clinic *CYP2D7-2D6* trans-duplication/multiplication non-duplicated gene targeted sequence analysis (0074U)
    - Mayo Clinic *CYP2D6 5'* gene duplication/multiplication targeted sequence analysis (0075U)
    - Mayo Clinic *CYP2D6 3*' gene duplication/multiplication targeted sequence analysis (0076U)
  - Multigene panel analysis including, but may not be limited to:
    - Drug metabolism (eg, pharmacogenomic testing of at least 6 genes, including *CYP2C19, CYP2D6*, and *CYP2D6* duplication/deletion analysis [81418])
    - EffectiveRX Comprehensive Panel (0438U)
    - Focused Pharmacogenomics Panel (0029U)
    - MyGenVar Pharmacogenomics Test (0516U)
    - PersonalisedRX (0380U)
    - RightMed Comprehensive Test (0349U)
    - RightMed Comprehensive Test exclude F2 and F5 (0348U)
    - RightMed Gene Report (0350U)
    - RightMed Gene Test Exclude F2 and F5 (0434U)
    - RightMed Oncology Gene Report (0460U)

- RightMed Oncology Medication Report (0461U)
- RightMed PGx16 (0347U)
- SyncView Pain (0518U)
- SyncView PainPlus (0519U)
- SyncView Rx (0520U)

- Cardiovascular conditions including, but not limited to:
  - Single gene analysis for any of the following:
    - *CYP2C19*
    - *CYP2C9*
    - *CYP4F2*
    - *P2Y12* (eg, VerifyNow)
    - *SLCO1B1*
    - *VKORC1* (81355)
  - Multigene panel analysis including, but may not be limited to, Warfarin Drug Response (0030U)
- Psychiatric conditions including, but not limited to:
  - Single gene analysis for any of the following:
    - *CYP1A2* (eg, Cytochrome P450 1A2 Genotype [0031U])
    - *CYP2C19*
    - *CYP2C9*
    - *CYP2D6*
    - *CYP2D7*
    - *CYP3A4*
    - *CYP3A5*
    - *CYP4F2*
    - *HTR2A*
    - *HTR2C*
  - Multigene panel analysis including, but may not be limited to:
    - EffectiveRX Neuropsychiatric Panel (0392U)
    - GeneSight Psychotropic (0345U)
    - Genomind Pharmacogenetics Report – Full (0423U)
    - Genomind Professional PGx Express CORE (0175U)
    - IDGenetix (0411U)
    - PrecisView CNS (0517U)

- Psych HealthPGx Panel (0173U)
- RightMed Mental Health Gene Report (0476U)
- RightMed Mental Health Medication Report (0477U)
- Serotonin Receptor Genotype (0033U)
- SureGene STA2R
- Tempus nP (0419U)

These are considered experimental/investigational as they are not identified as widely used and generally accepted for the proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17)	**Not Covered**
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)	**Not Covered if used to report any test outlined in Coverage Limitations section**
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6)	**Not Covered if used to report any test outlined in Coverage Limitations section**
81230	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22)	**Not Covered**
81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7)	**Not Covered**
81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (eg, adverse drug reaction), gene analysis, common variant(s) (eg, *5)	**Not Covered**
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G>A, c.173+1000C>T)	**Not Covered**

81418	Drug metabolism (eg, pharmacogenomics) genomic sequence analysis panel, must include testing of at least 6 genes, including CYP2C19, CYP2D6, and CYP2D6 duplication/deletion analysis	**Not Covered**
81479	Unlisted molecular pathology procedure	**Not Covered if used to report any test outlined in Coverage Limitations section**
85576	Platelet, aggregation (in vitro), each agent	**Not Covered if used to report any test outlined in Coverage Limitations section**
0029U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis (ie, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 and rs12777823)	**Not Covered**
0030U	Drug metabolism (warfarin drug response), targeted sequence analysis (ie, CYP2C9, CYP4F2, VKORC1, rs12777823)	**Not Covered**
0031U	CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7)	**Not Covered**
0032U	COMT (catechol-O-methyltransferase)(drug metabolism) gene analysis, c.472G>A (rs4680) variant	**Not Covered**
0033U	HTR2A (5-hydroxytryptamine receptor 2A), HTR2C (5-hydroxytryptamine receptor 2C) (eg, citalopram metabolism) gene analysis, common variants (ie, HTR2A rs7997012 [c.614-2211T>C], HTR2C rs3813929 [c.-759C>T] and rs1414334 [c.551-3008C>G])	**Not Covered**
0070U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, common and select rare variants (ie, *2, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14A, *14B, *15, *17, *29, *35, *36, *41, *57, *61, *63, *68, *83, *xN)	**Not Covered**
0071U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, full gene sequence (List separately in addition to code for primary procedure)	**Not Covered**
0072U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D6-2D7 hybrid gene) (List separately in addition to code for primary procedure)	**Not Covered**

0073U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D7-2D6 hybrid gene) (List separately in addition to code for primary procedure)	**Not Covered**
0074U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, non-duplicated gene when duplication/multiplication is trans) (List separately in addition to code for primary procedure)	**Not Covered**
0075U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 5' gene duplication/multiplication) (List separately in addition to code for primary procedure)	**Not Covered**
0076U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 3' gene duplication/multiplication) (List separately in addition to code for primary procedure)	**Not Covered**
0173U	Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes	**Not Covered**
0175U	Psychiatry (eg, depression, anxiety), genomic analysis panel, variant analysis of 15 genes	**Not Covered**
0345U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6	**Not Covered**
0347U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 16 gene report, with variant analysis and reported phenotypes	**Not Covered**
0348U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 25 gene report, with variant analysis and reported phenotypes	**Not Covered**
0349U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 27 gene report, with variant analysis, including reported phenotypes and impacted gene-drug interactions	**Not Covered**
0350U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 27 gene report, with variant analysis and reported phenotypes	**Not Covered**
0380U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis, 20 gene variants and CYP2D6 deletion or duplication analysis with reported genotype and phenotype	**Not Covered** **New Code Effective 04/01/2023**

0392U	Drug metabolism (depression, anxiety, attention deficit hyperactivity disorder [ADHD]), gene-drug interactions, variant analysis of 16 genes, including deletion/duplication analysis of CYP2D6, reported as impact of gene-drug interaction for each drug	**Not Covered** **New Code Effective 07/01/2023**
0411U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6 (For additional PLA code with identical clinical descriptor, see 0345U. See Appendix O to determine appropriate code assignment)	**Not Covered** **New Code Effective 10/01/2023**
0419U	Neuropsychiatry (eg, depression, anxiety), genomic sequence analysis panel, variant analysis of 13 genes, saliva or buccal swab, report of each gene phenotype	**Not Covered** **New Code Effective 10/01/2023**
0423U	Psychiatry (eg, depression, anxiety), genomic analysis panel, including variant analysis of 26 genes, buccal swab, report including metabolizer status and risk of drug toxicity by condition	**Not Covered** **New Code Effective 01/01/2024**
0434U	Drug metabolism (adverse drug reactions and drug response), genomic analysis panel, variant analysis of 25 genes with reported phenotypes	**Not Covered** **New Code Effective 01/01/2024**
0438U	Drug metabolism (adverse drug reactions and drug response), buccal specimen, gene-drug interactions, variant analysis of 33 genes, including deletion/duplication analysis of CYP2D6, including reported phenotypes and impacted gene-drug interactions	**Not Covered** **New Code Effective 01/01/2024**
0460U	Oncology, whole blood or buccal, DNA single-nucleotide polymorphism (SNP) genotyping by real-time PCR of 24 genes, with variant analysis and reported phenotypes	**Not covered** **New Code 07/01/2024**
0461U	Oncology, pharmacogenomic analysis of single-nucleotide polymorphism (SNP) genotyping by real-time PCR of 24 genes, whole blood or buccal swab, with variant analysis, including impacted gene-drug interactions and reported phenotypes	**Not covered** **New Code 07/01/2024**
0476U	Drug metabolism, psychiatry (eg, major depressive disorder, general anxiety disorder, attention deficit hyperactivity disorder [ADHD], schizophrenia), whole blood, buccal swab, and pharmacogenomic genotyping of 14 genes and CYP2D6 copy number variant analysis and reported phenotypes	**Not covered** **New Code 10/01/2024**

0477U	Drug metabolism, psychiatry (eg, major depressive disorder, general anxiety disorder, attention deficit hyperactivity disorder [ADHD], schizophrenia), whole blood, buccal swab, and pharmacogenomic genotyping of 14 genes and CYP2D6 copy number variant analysis, including impacted gene-drug interactions and reported phenotypes	**Not covered** **New Code 10/01/2024**
0516U	Drug metabolism, whole blood, pharmacogenomic genotyping of 40 genes and CYP2D6 copy number variant analysis, reported as metabolizer status	**Not covered** **New Code 10/01/2024**
0517U	Therapeutic drug monitoring, 80 or more psychoactive drugs or substances, LC-MS/MS, plasma, qualitative and quantitative therapeutic minimally and maximally effective dose of prescribed and non-prescribed medications	**Not covered** **New Code 10/01/2024**
0518U	Therapeutic drug monitoring, 90 or more pain and mental health drugs or substances, LC-MS/MS, plasma, qualitative and quantitative therapeutic minimally effective range of prescribed and non-prescribed medications	**Not covered** **New Code 10/01/2024**
0519U	Therapeutic drug monitoring, medications specific to pain, depression, and anxiety, LC-MS/MS, plasma, 110 or more drugs or substances, qualitative and quantitative therapeutic minimally effective range of prescribed, non-prescribed, and illicit medications in circulation	**Not covered** **New Code 10/01/2024**
0520U	Therapeutic drug monitoring, 200 or more drugs or substances, LC-MS/MS, plasma, qualitative and quantitative therapeutic minimally effective range of prescribed and non-prescribed medications	**Not covered** **New Code 10/01/2024**
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
G9143	Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)	**Not Covered**

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Change Summary

01/25/2024 Update, Coverage Change, Updated Coding Information.
07/01/2024 Updated Coding Information
08/29/2024 Annual Review, Coverage Change