Pharmacogenomics (Pharmacogenetics) – Noncancer Indications

Humana

Medical Coverage Policy

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Change Summary: Updated Description, Limitations and References

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Disclaimer

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.

Human leukocyte antigen-B (HLA-B) gene variations are associated with adverse reactions to some medications. Before taking carbamazepine, HLA-B*1502 testing may be used in individuals of Asian ancestry to identify an increased risk of developing severe skin disorders (eg, Stevens-Johnson syndrome (SJS) and toxic epidermal

necrolysis [TEN]). Additionally, individuals who have tested positive for HLA-B 1502 may be directed to a medication other than phenytoin.

HLA-B*5701 screening is indicated prior to initiation of an abacavir-containing regimen to reduce the risk of a hypersensitivity reaction in HIV individuals.

Before taking allopurinol, HLA-B*5801 testing may be done for individuals of Korean descent with stage 3 or greater chronic kidney disease or of Han-Chinese or Thai descent to avoid serious cutaneous reactions.

Human immunodeficiency virus (HIV) phenotypic tropism testing (ie,Trofile) is a molecular assay that identifies the tropism of an individual's HIV strain to determine if the virus has the ability to invade cells that have the CCR5 marker. This test helps to identify those who may benefit from treatment with maraviroc (Selzentry), a CCR5-receptor antagonist.

IFNL3 (interferon, lambda-3) gene, formerly known as IL28B (interleukin-28B),(5) encodes a cytokine related to type I interferons and interleukin-10. IFNL3 genotyping is proposed to assist with the evaluation and management of patients with hepatitis C. **(Refer to Coverage Limitations section)**

Kinesin family member 6 (KIF6) genotype testing has been proposed to be used to aid in the assessment of individuals being considered for statin medication therapy. **(Refer to Coverage Limitations section)**

LP(a) aspirin genotype testing (eg, Cardio IQ LPA Aspirin Genotype Test and LPA-Aspirin Genotype Test) has been proposed to identify individuals at risk of cardiovascular disease (CVD) which may respond to aspirin therapy. **(Refer to Coverage Limitations section)**

PHEX gene testing has been proposed to identify individuals at risk of X-linked hypophosphatemia (XLH) which may respond to Crysvita (BUROSUMAB-TWZA). **Refer to Coverage Limitations section)**

SLCO1B1 testing has been proposed to predict risk of statin-induced myopathy. **(Refer to Coverage Limitations section)**

Thiopurine s-methyltransferase (TPMT) is an enzyme that is involved in the metabolism of medications called thiopurines that are used in the treatment of inflammatory bowel disease (IBD). Genotyping tests (eg, PRO-PredictRx) and phenotyping tests (eg, PRO-Predict EnzAct) for TPMT enzyme activity can be used to help guide treatment options involving thiopurine medications such as azathioprine and 6-mercaptopurine in IBD.

Humana recognizes that the field of genetic testing is rapidly changing and that other tests may become available.

Coverage Determination

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

Any services for **pharmacogenomics/pharmacogenetic testing** that are considered primarily educational or training in nature are generally **NOT** covered under most Humana benefit plans.

General Criteria for Genetic Tests

The General Criteria for Genetic Tests may be applied if specific criteria for a genetic test are not available on any medical coverage policy

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

- Individual has not previously received genetic testing for the disorder. **Note:** In general, genetic testing for a particular disorder should be performed once per lifetime; however, there are rare instances in which testing may be performed more than once in a lifetime (eg, previous testing methodology is inaccurate, a new discovery has added significant relevant mutations for a disease, significant changes in technology or treatments indicate that test results or outcomes may change as a result of repeat testing); **AND**

- Laboratory or clinical tests to definitively diagnose the genetic disorder are unavailable or results are equivocal; **AND**

- Panels including, but may not be limited to, multiple genes or multiple conditions, and in cases where a tiered approach/method is clinically available, may be

covered **ONLY** for the number of genes or tests deemed medically necessary to establish a diagnosis; **AND**

- Results of genetic testing will directly impact and change clinical management of the individual being tested who is a covered member; **AND**

- Technical and clinical performance of the genetic test is supported by published peer-reviewed medical literature.

Criteria for Specific Genetic Tests

The following genetic tests must meet the above General Criteria for Genetic Tests in addition to the individual criteria outlined below for each test.

HIV Phenotypic Tropism Testing

Humana members may be eligible under the Plan for **HIV phenotypic tropism testing** (ie, Trofile) when the following criteria are met:

- Testing is performed prior to initiation of maraviroc (Selzentry); **AND**
- Individual is HIV-1 positive; **AND**
- Have viral load of at least 1000 copies of HIV-1 RNA per mL of blood

HLA Allele Testing

Humana members may be eligible under the Plan for screening for **HLA-B*1502** when testing is performed prior to the initiation of carbamazepine (Tegretol) or phenytoin (Dilantin) for individuals of Asian ancestry.

Humana members may be eligible under the Plan for screening for **HLA-B*5701** when testing is performed prior to the initiation or reinitiation of an abacavir-containing regimen in the treatment of HIV infection.

Humana members may be eligible under the Plan for screening for **HLA-B*5801 prior to the initation of allopurinol for the treatment of gout** when the following criteria are met:

- Testing is performed prior to initiation of allopurinol;

AND either of the following:

- Individual of Korean descent with stage 3 or greater chronic kidney disease; **OR**
- Individual of Han-Chinese or Thai descent

Thiopurine s-methyltransferase (TPMT) Gene Mutation Assay/TPMT Phenotypic Assays

Humana members may be eligible under the Plan for **TPMT gene mutation assay** or **TPMT phenotypic assays** when the following criteria are met:

- Testing is performed prior to initiation of thiopurine medication therapy (eg, 6-mercaptopurine, azathioprine); **AND**

- Thiopurine therapy is for the treatment of inflammatory bowel disease (IBD)

For information regarding **CYP2D6 genotyping including, but may not be limited to, CYP2C9, CYP2C19, CYP2D6, CYP3A4, VKORC1 and Warfarin**, please refer to Pharmacogenomics - Cytochrome P450 Polymorphisms and VKORC1 Medical Coverage Policy.

Examination and selection of retrieved archival tissue(s) for molecular analysis is considered integral to the primary molecular pathology procedure/laboratory testing and not separately reimbursable.

Coverage Limitations

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

- General population screening

This is considered not medically necessary as defined in the member's individual certificate. Please refer to the member's individual certificate for the specific definition.

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

- An at-risk (unaffected) individual or affected individual when a family member has been tested for mutations and received a result of variant of unknown significance (VUS) (also known as unclassified variant or variant of uncertain significance); **OR**
- HLA-B testing other than noted above; **OR**
- IFNL3; **OR**
- KIF6 testing; **OR**
- LP(a) aspirin; **OR**
- Repeat HIV tropism testing during or after CCR5 antagonist therapy (eg, maraviroc); **OR**
- Other testing for CCR5; **OR**
- SLCO1B1 testing

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

Background

Additional information about **pharmacogenomics/pharmacogenetics** may be found from the following websites:

- AIDS*info*
- American Heart Association
- Centers for Disease Control National Office of Public Health Genomics
- National Library of Medicine
- US Food and Drug Administration

Medical Alternatives

Physician consultation is advised to make an informed decision based on an individual's health needs.

Humana may offer a disease management program for this condition. **The member may call the number on his/her identification card to ask about our programs to help manage his/her care.**

Provider Claims Codes

Any CPT, HCPCS or ICD codes listed on this medical coverage 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
81283	IFNL3 (interferon, lambda 3) (eg, drug response), gene analysis, rs12979860 variant	**Not Covered** **New Code Effective 01/01/2018**
81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (eg, adverse drug reaction), gene analysis, common variant(s) (eg, *5)	**Not Covered** **New Code Effective 01/01/2018**
81335	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)	**New Code Effective 01/01/2018**
81381	HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each	**Not Covered if used to report any test outlined in Coverage Limitations section**
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)	**Not Covered if used to report any test outlined in Coverage Limitations section**

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)	
81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)	**Not Covered if used to report any test outlined in Coverage Limitations section**
81479	Unlisted molecular pathology procedure	**Not Covered if used to report any test outlined in Coverage Limitations section**
87999	Unlisted microbiology procedure	
88363	Examination and selection of retrieved archival (ie, previously diagnosed) tissue(s) for molecular analysis (eg, KRAS mutational analysis)	**Examination and selection of retrieved archival tissue(s) for molecular analysis is considered integral to the primary molecular pathology procedure/laboratory testing and not separately reimbursable**
88364	In situ hybridization (eg, FISH), per specimen; each additional single probe stain procedure (List separately in addition to code for primary procedure)	
88366	In situ hybridization (eg, FISH), per specimen; each multiplex probe stain procedure	
0015U	Drug metabolism (adverse drug reactions), DNA, 22 drug metabolism and transporter genes, real-time PCR, blood or buccal swab, genotype and metabolizer status for therapeutic decision support	**Not Covered** **Deleted Code Effective 12/31/2017**

0034U	TPMT (thiopurine S-methyltransferase), NUDT15 (nudix hydroxylase 15)(eg, thiopurine metabolism), gene analysis, common variants (ie, TPMT *2, *3A, *3B, *3C, *4, *5, *6, *8, *12; NUDT15 *3, *4, *5)	**New Code Effective 01/01/2018**
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

No ICD-10-CM code(s) have been applied to this policy. No code(s) identified and/or policy criteria too broad.

Medical Terms

Abacavir (Ziagen) – Drug therapy indicated for the treatment of human immunodeficiency virus 1 (HIV-1) in adults and children and is taken in combination with other anti-HIV medications to lower the amount of HIV in the blood. Abacavir is also available in combination with lamivudine (Epzicom) and lamivudine/zidovudine (Trizivir).

Allopurinol – Drug used to treat recurrent kidney stones and gout.

Carbamazepine – Drug used to treat seizure activity.

Chromosome – Cell-replicating genetic structures of the cells containing the cellular DNA that bears in its nucleotide sequence the linear array of genes.

Deoxyribonucleic Acid (DNA) – Molecule that encodes genetic information in the nucleus of cells. It determines the structure, function and behavior of the cell.

Gene – Formed from DNA, carried on the chromosomes and are responsible for the inherited characteristics that distinguish one individual from another. Each human individual has an estimated 100,000 separate genes.

Genome – Complete set of DNA, including all of its genes. Each genome contains all of the information needed to build and maintain that organism. In humans, a copy of the entire genome is contained in all cells that have a nucleus.

Genomics – The study of all the genes in a cell or organism.

Genotype – Genetic makeup of a cell or individual. Genotyping measures the features of an individual's genotype (eg, genetic testing for mutations).

Mutation – Change of the DNA sequence within a gene or chromosome of an organism resulting in the creation of a new character or trait not found in the parental type.

Myopathy – A skeletal muscle disease that causes muscular pain, stiffness, and weakness.

Phenotype – Visible expressions that are produced by the interaction of the genotype and the environment.

Phenytoin – Drug used to treat seizure activity.

Ribonucleic Acid (RNA) – Nucleic acid found in all living cells. It plays a role in transferring information from DNA to the protein forming system of the cell.

Selzentry – Drug used to treat adults infected with CCR5-tropic HIV-1.

Statin Induced Myopathy – Muscle fatigue, pain, tenderness, weakness and/or cramping caused by reaction to statin therapy.

Stevens Johnson Syndrome (SJS) – An inflammatory disorder of the skin triggered by an allergic reaction to certain drugs that can lead to TEN and become life threatening.

Toxic Epidermal Necrolysis (TEN) – A life-threatening skin condition, in which cell death causes the epidermis to separate from the dermis.

Thiopurine s-methyltransferase (TPMT) – An enzyme that is involved in the metabolism of thiopurine medications, such as azathioprine and 6-mercaptopurine.

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