



ADMINISTRATIVE POLICY STATEMENT

Marketplace

Policy Name & Number	Date Effective
Pharmacogenomics - CYP Gene Testing-MP-AD-1347	GA, IN, KY, WV, OH: 08/01/2023-01/31/2025
Policy Type	
ADMINISTRATIVE	

Administrative Policy Statement prepared by CareSource and its affiliates are derived from literature based on and supported by clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Administrative Policy Statements prepared by CareSource and its affiliates do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Administrative Policy Statement. If there is a conflict between the Administrative Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

According to the rules of Mental Health Parity Addiction Equity Act (MHPAEA), coverage for the diagnosis and treatment of a behavioral health disorder will not be subject to any limitations that are less favorable than the limitations that apply to medical conditions as covered under this policy.

<input checked="" type="checkbox"/> Georgia	<input checked="" type="checkbox"/> Indiana	<input checked="" type="checkbox"/> Kentucky	<input checked="" type="checkbox"/> Ohio	<input checked="" type="checkbox"/> West Virginia
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A. Subject

Pharmacogenomics – CYP Gene Testing

B. Background

Pharmacogenomics is an area of precision medicine that provides information about an individual’s genes, influencing therapeutic strategies and assessing the likelihood of benefit or toxicity to a given drug. This form of medication management has been evaluated in a variety of clinical scenarios. As pharmacogenomics expands and laboratories offering testing proliferate, the value of a given test in terms of patient benefit may be obscured by multiple contributing factors, including exaggerated public marketing claims, inconsistencies in test standardization, continued patient variation in response to prescribed medication, incomplete knowledge of drug metabolism, and limitations in regulatory oversight. To manage these challenges, the clinical validity and clinical utility of a specific gene or biomarker with a specific drug target should demonstrate improvement in patient outcomes.

C. Definitions

- **Clinical Utility** - The likelihood that a test will, by prompting an intervention, result in an improved health outcome.
- **Clinical Validity** - The predictive value of a test for a given clinical outcome.
- **Unbundling** - HCPCS/CPT codes should be reported only if all services described by the code are performed. Multiple codes should not be reported if a single code exists that describes the services performed. The codes include all services usually performed as part of the procedure as a standard of medical/ surgical practice and should not be separately reported simply because codes exist for the services

D. Policy

I. General Guidelines

- A. Biomarker testing with uncertain clinical significance in MCG will be considered experimental and investigational.
- B. Unbundling of codes in a panel is an incorrect billing practice and may result in payment recovery.
- C. Any drug, biologic, device, diagnostic, product, equipment, procedure, treatment, service, or supply used in or directly related to the diagnosis, evaluation, or treatment of a disease, injury, illness, or other health condition which CareSource determines in its sole discretion to be experimental or investigational is not covered by CareSource.

- II. Based on review of existing evidence, there are currently no clinical indications for the high-volume tests below, and the current role remains uncertain. Therefore, CareSource considers these requests experimental and investigational. This is not an all-inclusive list.

CPT® Codes	Testing Examples
81225 - CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *8, *17)	Genecept Assay, GeneSight,

The ADMINISTRATIVE Policy Statement detailed above has received due consideration as defined in the ADMINISTRATIVE Policy Statement Policy and is approved.

81226 - CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)	OneOme RightMed, PGxOnePlus, CQuentia, IDGenetix, PROOVE, GARSPREDX, SureGene, PharmacoDx
81227 - CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *5, *6)	
81230 - CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (e.g., drug metabolism), gene analysis, common variant(s) (e.g., *2, *22)	
81291 - MTHFR (5, 10-methylenetetrahydrofolate reductase) (e.g., hereditary hypercoagulability) gene analysis, common variants (e.g., 677T, 1298C)	
0345U – Psychiatry (e.g., depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6	

III. CareSource applies coding edits to medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards. Proper billing and submission guidelines must be followed, including the following:

- A. Use of industry standard, compliant codes on all claims submissions, including CPT codes and/or HCPCS codes.
- B. Services considered to be mutually exclusive, incidental to or integral to the primary service rendered are not allowed additional payment.
- C. Proprietary panel testing requires evidence-based documentation of medical necessity.
- D. Submission of the most accurate and appropriate CPT/HCPCS code(s) for the product or service being provided, including coding to the highest level of specificity.

IV. CareSource considers the following not medically necessary (not an all-inclusive list):

- A. Pharmacogenomic testing or screening in the general population.
- B. A non-covered test billed by using unlisted procedure codes.
- C. The use of multi-gene panels for genetic polymorphisms, including, but not limited to, pain management, cardiovascular drugs, anthracyclines, or polypharmacy for evaluating drug-metabolizer status (i.e., GeneSight ADHD, SureGene Test, PharmacoDx).
- D. Tests considered screening in the absence of clinical signs/symptoms of disease.
- E. Tests that do not confirm new data for decision making but confirm a known diagnosis or information.
- F. Tests to determine risk for developing a disease or condition.
- G. Tests without diagnosis-specific indications.
- H. Tests performed to ensure a tissue specimen matches an individual.

E. Conditions of Coverage

Codes referenced in this policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage.

F. Related Policies/Rules

Overpayment Recovery
Experimental and Investigational Items and Services

The ADMINISTRATIVE Policy Statement detailed above has received due consideration as defined in the ADMINISTRATIVE Policy Statement Policy and is approved.

G. Review/Revision History

	DATE	ACTION
Date Issued	04/26/2023	Approved at Committee.
Date Revised		
Date Effective	08/01/2023	
Date Archived	01/31/2025	This Policy is no longer active and has been archived. Please note that there could be other Policies that may have some of the same rules incorporated and CareSource reserves the right to follow CMS/State/NCCI guidelines without a formal documented Policy.

H. References

1. American Academy of Child & Adolescent Psychiatry. Pharmacogenetic Testing. (2019, December). Retrieved February 14, 2023 from www.aacap.org.
2. American Health Information Management Association. Documenting Pharmacogenomic Testing with CPT Codes. Retrieved February 23, 2023 from www.ahima.org.
3. CareSource 2023 Evidence of Coverage. Retrieved March 1, 2023 from www.caresource.com.
4. Centers for Disease Control and Prevention (CDC). Clinical Laboratory Improvement Amendments (CLIA). (2022, November 14). Retrieved February 27, 2023 from www.cdc.gov.
5. Centers for Medicaid and Medicare Services. National Correct Coding Initiative Policy Manual For Medicaid Services. (2021, January 1). Retrieved February 23, 2023 from www.medicaid.gov.
6. Code of Federal Regulations, Part 493, Laboratory Requirements. (2023, February 27). Retrieved March 1, 2023 from www.ecfr.gov.
7. Food and Drug Administration (FDA). List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools). (2023, February 14). Retrieved February 23, 2023 from www.fda.gov.
8. Hayes Clinical Utility Evaluation: APOE Genetic Testing for Alzheimer Disease. (2022, March 18). Retrieved March 16, 2023 from www.hayesinc.com.
9. Hayes Clinical Utility Evaluation: MTHFR Genetic Testing for Severe MTHFR Enzyme Deficiency. (2021, May 23). Retrieved March 16, 2023 from www.hayesinc.com.
10. Hayes Clinical Utility Evaluation: MTHFR Genetic Testing in Common Clinical Conditions. (2021, May 23). Retrieved March 16, 2023 from www.hayesinc.com.
11. Hayes Clinical Utility Evaluation: MTHFR Pharmacogenetic Genotyping for Altering Drug Treatment. (2021, May 23). Retrieved March 16, 2023 from www.hayesinc.com.
12. Hayes Clinical Utility Evaluation: Pharmacogenetic and Pharmacogenomic Testing for Opioid Treatment for Pain in Adults. (2022, October 26). Retrieved March 16, 2023 from www.hayesinc.com.
13. Hayes Clinical Utility Evaluation: Pharmacogenetic and Pharmacogenomic Testing to Improve Outcomes Related to Opioid Use Disorder. (2022, January 27). Retrieved March 16, 2023 from www.hayesinc.com.

The ADMINISTRATIVE Policy Statement detailed above has received due consideration as defined in the ADMINISTRATIVE Policy Statement Policy and is approved.

14. Hayes Clinical Utility Evaluation: Pharmacogenomic Testing for Attention-Deficit/Hyperactivity Disorder. (2022, January 12). Retrieved March 16, 2023 from www.hayesinc.com.
15. Hayes Clinical Utility Evaluation: Pharmacogenomic Testing of Selected Mental Health Conditions. (2021, December 6). Retrieved March 16, 2023 from www.hayesinc.com.
16. Hayes Molecular Test Assessment: GeneSight Psychotropic (Assurex Health Inc./Myriad Neuroscience). (2021, September 10). Retrieved March 16, 2023 from www.hayesinc.com.
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21. Kohlmann W, Slavotinek A. Genetic Testing. (2023, February). Retrieved March 16, 2023 from www.uptodate.com.
22. MCG. 27th Edition. Pharmacogenetics. Retrieved March 16, 2023 from www.careweb.careguidelines.com.
23. National Human Genome Research Institute. Deoxyribonucleic Acid (DNA) Fact Sheet. (2020, August 24). Retrieved February 14, 2023 from www.genome.gov.
24. National Institutes of Health, Library of Medicine. Pharmacogenetic Tests. (2021, July 7). Retrieved February 14, 2023 from www.medlineplus.gov.
25. National Institute of Health. National Cancer Institute (NCI). NCI Dictionary of Genetics Terms. Retrieved February 20, 2023 from www.cancer.gov.
26. Raby B. Personalized Medicine. (2023, February). Retrieved March 16, 2023 from www.uptodate.com.
27. Tantisira K, Weiss S. Overview of Pharmacogenomics. (2023, February). Retrieved March 16, 2023 from www.uptodate.com.

I. State-Specific Information

A. Georgia

1. Effective: 08/01/2023
2. Additional References:
 - a. Official Code of Georgia Annotated. O.C.G.A. Title 33, Chapter 54 Genetic testing. (2023). Retrieved March 1, 2023 from www.advance.lexis.com.
 - b. Official Code of Georgia Annotated. O.C.G.A. Title 31, Chapter 22 Clinical laboratories. (2023). Retrieved March 1, 2023 from www.advance.lexis.com.

B. Indiana, effective: 08/01/2023

C. Kentucky

1. Effective: 08/01/2023
2. Kentucky General Assembly. 907 KAR 1:028. Independent Laboratory and Radiological Service Coverage and Reimbursement. (2019, December 6). Retrieved March 1, 2023 from www.legislature.ky.gov.

3. Kentucky General Assembly. Subtitle 17A. Chapter 304. HB 180. (2023, February). Retrieved April 13, 2023 from www.legislature.ky.gov.
- D. Ohio
1. Effective: 08/01/2023
 2. Additional References:
 - a. Ohio Administrative Code. Rule 5160-11-11. Laboratory services. Retrieved February 23, 2023 from www.codes.ohio.gov.
 - b. Ohio Administrative Code. Rule 5160-26-05. Managed care: Provider network and contracting requirements. Retrieved February 23, 2023 from www.codes.ohio.gov.
- E. West Virginia, effective: 08/01/2023