MEDICAL POLICY STATEMENT
TrueCare

Policy Name & Number	Date Effective
Pharmacogenomics-Gene Testing for Behavioral Health Indications-TrueCare-MM-1724	07/01/2025
Policy Type	
MEDICAL	

Medical Policy Statements 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 or Certificate of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other plan policies and procedures.

Medical Policy Statements do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage or Certificate of Coverage) for the service(s) referenced in the Medical Policy Statement. Except as otherwise required by law, if there is a conflict between the Medical Policy Statement and the plan contract, then the plan contract 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.

Table of Contents

A. Subject

Pharmacogenomics- Gene Testing for Behavioral Health Indications

B. Background

Pharmacogenomics is the study of how genetic variation affects drug response. Pharmacokinetics analyzes how drugs move through the body, including absorption, distribution, metabolism, and excretion. In behavioral health medicine, cytochrome P450s (CYPs) are a common avenue for oxidative metabolism of therapeutic substances, which can be influenced by genetic and environmental factors. CYP genes are polymorphic and affect a significant portion of the population's ability to metabolize chemicals. Those with functional changes in CYP genes may have absent, diminished, or excessive metabolism of a drug compound. Individuals are therefore classified as poor metabolizers, extensive (normal) metabolizers, and ultra-rapid metabolizers.

The role of pharmacogenetics is promising as studies continue to show potential benefits of gene testing. Clinical research, however, is unable to adequately replicate studies and findings, and there is limited available research for a drug class or specific drugs. Most studies are based on small sample sizes and do not perform power calculations or correct for multiple testing scenarios. It is difficult to substantiate conclusions when not accounting for false positives or false negatives. Additionally, there is a lack of consensus regarding preemptive genotyping efficacy. Two societies publishing guidelines acknowledge that comprehensive guidelines regarding when testing should occur, who should receive testing, and which genes should be tested cannot be offered.

The Clinical Pharmacogenetics Implementation Consortium (CPIC®) is an international organization whose goal is to reduce the barrier of translating genetic laboratory test results into guided clinical decision support. CPIC guidelines are peer-reviewed, evidence-based and updated as new evidence emerges. The guidelines are indexed in PubMed and endorsed by the American Society of Health-System Pharmacists (ASHP) and the American Society for Clinical Pharmacology and Therapeutics (ASCPT). Published CPIC guidelines are available for certain drug classes and specific drugs which can lead to customized drug dosing, which is presumed to improve time to effective treatment and reduce undertreatment, medication-related adverse events, and costs. The guidelines consist of grading levels of evidence for prescription recommendations, which guide physicians on how results can optimize treatment.

The strength of recommendations is divided into 4 categories: strong, moderate, optional, and no recommendation. A strong recommendation is backed by high-quality evidence with desirable effects clearly outweighing undesirable effects. A moderate recommendation recognizes a close or uncertain balance as to whether the evidence is high quality and desirable effects clearly outweigh the undesirable. In an optional recommendation, the desirable effects are closely balanced with undesirable effects or the evidence is weak or based on extrapolations, and opinions differ as to the need for the recommended course of action. With no recommendation, there is insufficient evidence, confidence, or agreement to provide a recommendation to guide practice.
In 2018, the American Psychiatric Association (APA) Council of Research Workgroup on Biomarkers and Novel Treatments printed a position statement on pharmacogenomic

(PGx) tools for the treatment of depression indicating “at present there are insufficient data to support the widespread use of combinatorial pharmacogenetics testing in clinical practice.” The Food and Drug Administration (FDA) released a consumer warning, “The relationship between DNA variations and the effectiveness of antidepressant medications has never been established.” and also cautioned that changes in patient medications based on test results “could potentially lead to patient harm.” In 2024, Baum, et al., updated the APA’s statement upon review of new clinical trials and meta-analyses published from 2017 to 2022 using PGx tools for treatment selection in depression and found “addition of these new data do not alter the recommendations of the 2018 report, or the advice of the FDA, that the evidence does not support the use of currently available combinatorial PGx tools for treatment.” Additionally in 2019, the International Society of Psychiatric Genetics published the following statement: “Pharmacogenetic testing should be viewed as a decision-support tool… Evidence to support widespread use of other pharmacogenetic tests at this time is still inconclusive… Genetic information for CYP2C19 and CYP2D6 would likely be most beneficial for individuals who have experienced an inadequate response or adverse reaction to a previous antidepressant or antipsychotic trial.”

TrueCare covers items and services with sufficient medical and scientific evidence for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of disease(s) or condition(s) but does not cover experimental or investigational testing or products or services with insufficient data to determine net health impact. Insufficient data includes support that the test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), performs better than an existing standard of care medical management option, and/or is not generally accepted as standard of care in the evaluation or management of a particular condition. TrueCare provides appeal rights to any member or provider acting on behalf of a member who may disagree with denial decisions. Tests should be chosen to maximize the likelihood of identifying mutations in genes of interest for a specific medical reason, contribute to positive alterations in patient management, and minimize the chance of finding variants of uncertain significance.

C. Definitions

- **Actionable Use** – Genotype information may lead to selection of, avoidance of a specific therapy or modification of dosage of a therapy. Change must be based on the FDA label for the drug, an FDA warning or safety concern, or a CPIC level A or B gene-drug interaction. Intended changes in therapy based on the result of a genotyping test not supported by 1 of these sources is not an actionable use.
- **Adherence** – Consumption of a drug at or near the maximum FDA approved dosage and duration for the medication or documentation that higher doses are not tolerated when less than the FDA-approved maximum.
- **Biomarker** – A characteristic objectively measured and evaluated as an indicator of biological or pathogenic processes or pharmacologic responses to a specific therapeutic intervention (eg, gene mutations, protein expression, known gene-drug interactions for medications, characteristics of genes).
- **Biomarker Testing** – The analysis of tissue, blood, or other biospecimen for the presence of a biomarker.

- **Clinical Utility** – The likelihood that a test will, by prompting an intervention, result in an improved health outcome.
- **Clinical Validity** – The accuracy of a test for a given clinical outcome.
- **Consensus Statements** – Developed by an independent, multidisciplinary panel of experts utilizing a transparent methodology and reporting structure with a conflict-of-interest policy aimed at specific clinical circumstances and based on best available evidence for optimizing outcomes of clinical care.
- **Nationally Recognized Clinical Practice Guidelines** – Developed by independent organizations or medical professional societies utilizing a transparent methodology and reporting structure with a conflict-of-interest policy establishing standards of care informed by a systematic review of evidence and assessment of benefits and risks of alternative care options, including recommendations to optimize patient care.
- **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. Biomarker testing that is not addressed by the Mississippi Administrative Code or the Mississippi Division of Medicaid (DOM) in a recently published or updated provider document will follow MCG guidelines. Biomarker testing with uncertain clinical significance in MCG may be considered not covered as there is insufficient medical and scientific evidence for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of disease(s) or condition(s). If there are no MCG guidelines available, authorization for biomarker testing must be supported by the following scientific and medical evidence (as appropriate):
   A. labeled indications for a test approved or cleared by the FDA
   B. indicated tests for a drug approved by the FDA
   C. Centers for Medicare and Medicaid Services (CMS) national coverage determinations and/or local coverage determinations by Medicare Administrative Contractors
   D. nationally recognized clinical practice guidelines and/or consensus statements
   E. warnings and precautions on FDA-approved drugs

II. Any biomarker testing with clinical significance and evidence supported by scientific and medical evidence may be subject to medical necessity review. TrueCare uses CPIC guidelines level A or B to determine the appropriateness of testing requests. Guidelines may be located at www.cpicpgx.org/guidelines.
   A. General guidelines for all testing requests
      The use of pharmacogenomic tests for multi-gene panels to guide therapy decisions may be medically necessary for psychotropic medications when **ALL** of the following criteria are met:
      1. The member is currently or considering taking a drug potentially affected by a known mutation that can be detected by a corresponding test.
      2. The drug is to be prescribed for the condition and population consistent with FDA labeling.

3. The test demonstrates actionability in clinical decision making by CPIC guidelines level A or B and has demonstrated technical and clinical validity.
4. Providers can use results to guide changes in treatment that will improve patient outcomes or directly impact medical care (ie, clinical utility).
5. The ordering provider possesses the licensure, qualifications, and necessary experience/training to both diagnose the condition being treated and to prescribe medications for the condition either independently or in an arrangement as required by all applicable state laws.
6. The usefulness of the test is not significantly offset by negative factors, such as expense, clinical risk, or social, or ethical challenges (ie, reasonable use).
7. Requested testing is performed in a CLIA-certified laboratory and has not been previously performed.
8. **At least 1** of the following criteria is met:
   a. Documentation is provided that the requested testing is required to obtain health plan coverage for the medication being considered for treatment.
   b. An FDA label requires results from a genetic test to effectively or safely use the therapy in question or is listed in the FDA table of known gene-drug interactions.
   c. Documentation of member adherence and failure to see expected results from at least 2 prior medications to treat the diagnosed condition.

B. Specific testing requests
Testing in the following situations may be considered medically necessary and is subject to medical necessity review. To aid in therapy selection and/or dosing for members considered for therapy or in a course of therapy with any of the medications below, testing for following genotype(s) once per lifetime may be considered:
1. CYP2C19 and CYP2D6 testing for tricyclic antidepressants:
   a. Amitriptyline
   b. Imipramine
   c. Doxepin
2. CYP2C19 and CYP2B6 testing for sertraline, serotonin reuptake inhibitor
3. HLA-A and HLA-B testing for carbamazepine

III. Exceptions to this policy or an adverse utilization review determination might be explored via appeal rights, which are provided to any member or provider who requests testing on behalf of the member for any denial of authorization via the provider portal on www.caresource.com, fax, or mail by the US Postal Service.

IV. TrueCare considers the following not medically necessary (not all-inclusive):
A. Testing or screening
   1. in the general population
   2. considered non-covered but billed using unlisted procedure codes
   3. in the absence of clinical signs or symptoms or for determining a risk for developing a disease or condition
   4. not confirming new data for decision making but a known diagnosis
   5. without diagnosis-specific indications or ensuring matching tissue specimens

B. 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.
C. Broad symptom-based panels (eg, comprehensive ataxia panel) when a narrower panel is available and more appropriate based on clinical findings (eg, autosomal dominant ataxia panel).
D. More than 1 multigene panel at the same time (should be performed in a tiered fashion with independent justification for each panel requested).
E. Genes not identified as having actionable use.

E. Conditions of Coverage

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

I. Unbundling of codes in a panel may result in payment recovery. Procedures not meeting correct coding standards are not reimbursable, even if medical necessity criteria for the associated test(s) are met.
II. Providers must use industry standard, compliant codes on all claims submissions, including CPT codes and/or HCPCS codes to the highest level of specificity.
III. Services considered to be mutually exclusive, incidental to, or integral to the primary service rendered are not allowed additional payment.
IV. Proprietary panel testing requires documentation of medical necessity.
V. If a panel was previously performed and an updated, larger panel is being requested, only testing for the medically necessary, previously untested genes will be reimbursable. Therefore, only the most appropriate procedure codes for those additional genes will be considered for reimbursement.

F. Related Policies/Rules

Experimental or Investigational Items or Services
Medical Necessity Determinations

G. Review/Revision History

	DATE	ACTION
Date Issued	02/26/2025	New policy. Approved at Committee.
Date Revised		
Date Effective	07/01/2025	
Date Archived		

H. References

1. American College of Medical Genetics Board of Directors. Points to consider in the clinical application of genomic sequencing. *Genet Med*. 2012 Aug;14(8):759-61. doi:10.1038/gim.2012.74
2. Baum M, Widge A, Carpenter L, et al. Pharmacogenomic clinical support tool for the treatment of depression. *Am J Psychiatry*. 2024;181(7):591-607. doi:10.1176/appi.ajp.20230657

3. Bean LJH, Funke B, Carlston CM, et al. Diagnostic gene sequencing panels: from design to report—a technical standard of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2020;22(3):453-461. doi:10.1038/s41436-019-0666-z
4. Behavioral Health Medication Pharmacogenetics – Gene Panels: A-0861. MCG Health. 28th ed. Updated March 14, 2024. Accessed January 15, 2025. www.careweb.careguidelines.com
5. Beunk L, Nijenhuis M, Soree B, et al. Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction between CYP2D6, CYP3A4 and CYP1A2 and antipsychotics. *Eur J Hum Genet*. 2024;32(3):278-285. doi:10.1038/s41431-023-01347-3
6. Bousman CA, Stevenson JM, Ramsey LB, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A genotypes and serotonin reuptake inhibitor antidepressants. *Clin Pharmacol Ther*. 2023;114(1):51-68. doi:10.1002/cpt.2903
7. Brouwer JMJL, Wardenaar KJ, Nolte IM, et al. Association of CYP2D6 and CYP2C19 metabolizer status with switching and discontinuing antidepressant drugs: an exploratory study. *BMC Psych*. 2024;24:394-408. doi:10.1186/s12888-024-0576
8. Brown JT, Bishop JR, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for Cytochrome P450 (CYP)2D6 Genotype and Atomoxetine Therapy. *Clin Pharmacol Ther*. 2019;106(1):94-102. doi:10.1002/cpt.1409
9. Caudle K, Sangkuhl K, Whirl-Carrillo M, et al. Standardizing *CYP2D6* genotype to phenotype translation: consensus recommendations from the Clinical Pharmacogenetics Implementation Consortium and Dutch Pharmacogenetics Working Group. *Clin Transl Sci*, 2020;13:116-124. doi:10.1111/cts.12692
10. Chang M, Tybring G, Dahl ML, et al. Impact of cytochrome P450 2C19 polymorphisms on citalopram/escitalopram exposure: a systematic review and meta-analysis. *Clin Pharmacokinet*. 2014;53(9):801-811. doi:10.1007/s40262-014-0162-1
11. Cicali EJ, Smith DM, Duong BQ, et al. A scoping review of the evidence behind cytochrome p450 2d6 isoenzyme inhibitor classifications. *Clin Pharmacol Ther*. 2020;108(1):116-125. doi:10.1002/cpt.1768
12. Clinical laboratory improvement amendments (CLIA). Centers for Disease Control and Prevention. Reviewed January 16, 2024. Accessed January 15, 2025. www.cdc.gov
13. Clinical Pharmacogenetics Implementation Consortium. Accessed January 15, 2025. www.cpicpgx.org
14. Clinical Use of Pharmacogenetic Testing in Prescribing Psychotropic Medications for Children and Adolescents. American Academy of Child & Adolescent Psychiatry; 2020. Accessed January 15, 2025. www.aacap.org
15. Clinical Utility Evaluation: MTHRF Genetic Testing for Nondevelopmental Psychiatric Disorders. Hayes; 2023. Reviewed December 10, 2024. Accessed January 15, 2025. www.hayesinc.com
16. Clinical Utility Evaluation: MTHRF Pharmacogenetic Genotyping for Altering Drug Treatment. Hayes; 2017. Reviewed May 23, 2021. Accessed January 15, 2025. www.hayesinc.com
17. Clinical Utility Evaluation: Pharmacogenetic and Pharmacogenomic Testing for Opioid Treatment for Pain in Adults – Selected Single-Gene Variants and

Pharmacogenomic Panels. Hayes; 2019. Reviewed October 26, 2022. Accessed January 15, 2025. www.evidence.hayesinc.com
18. Clinical Utility Evaluation: Pharmacogenetic and Pharmacogenomic Testing to Improve Outcomes Related to Opioid Use Disorder. Hayes; 2020. Reviewed June 30, 2023. Accessed January 15, 2025. www.evidence.hayesinc.com
19. Clinical Utility Evaluation: Pharmacogenomic Testing for Attention-Deficit/Hyperactivity Disorder. Hayes; 2022. Reviewed February 27, 2024. Accessed January 15, 2025. www.evidence.hayesinc.com
20. Clinical Utility Evaluation: Pharmacogenomic Testing of Selected Mental Health Conditions. Hayes; 2021. Reviewed December 9, 2024. Accessed January 15, 2025. www.evidence.hayesinc.com
21. Cytochrome P450 Pharmacogenetics – Gene Tests and Gene Panels: A-0775. MCG Health. 28th ed. Updated March 14, 2024. Accessed January 15, 2025. www.careweb.careguidelines.com
22. Deoxyribonucleic acid (DNA) fact sheet. National Human Genome Research Institute. Updated August 24, 2020. Accessed January 15, 2025. www.genome.gov
23. Diagnostic X-Ray Tests, Diagnostic Laboratory Tests, and Other Diagnostic Tests: Conditions, 42 C.F.R. § 410.32 (2023).
24. Fijal BA, Guo Y, Li SG, et al. CYP2D6 predicted metabolizer status and safety in adult patients with attention-deficit hyperactivity disorder participating in a large placebo-controlled atomoxetine maintenance of response clinical trial. *J Clin Pharmcol*. 2015;55(10):1167-1174. doi:10.1002/jcph.530
25. Guin D, Hasija Y, Kukreti. Assessment of clinically actionable pharmacogenetic markers to stratify anti-seizure medications. *Pharmacogenomics J*. 2023;23:149-160. doi:10.1038/s41397-023-00313-y
26. Hefti E, Blanco JG. Documenting pharmacogenomic testing with CPT codes. *J AHIMA*. 2016;87(1):56-59. Accessed January 15, 2025. www.pubmed.ncbi.nih.gov
27. Hicks JK, Bishop JR, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for CYP2D6 and CYP2C19 genotypes and dosing of selective serotonin reuptake inhibitors. *Clin Pharmacol Ther*. 2015;98(2):127-134. doi:10.1002/cpt.1472
28. Hicks JK, Sangkuhl K, Swen JJ, et al. Clinical Pharmacogenetics Implementation Consortium Guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. *Clin Pharmacol Ther*. 2017;102(1):37-44. doi:10.1002/cpt.597
29. Hicks JK, Swen JJ, Thorn CF, et al. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. *Clin Pharmacol Ther*. 2013;93(5):402-408. doi:10.1038/clpt.2013.2
30. Hippman C, Nislow C. Pharmacogenomic testing: clinical evidence and implementation challenges. *J Pers Med*. 2019;9(3):40. doi:10.3390/jpm9030040
31. Hyperhomocysteinemia – MTHRF Gene: A-0629. MCG Health. 28th ed. Updated March 14, 2024. Accessed January 15, 2025. www.careweb.careguidelines.com
32. Jukic MM, Haslemo T, Molden E. Impact of CYP2C19 genotype on escitalopram exposure and therapeutic failure: a retrospective study based on 2087 patients. *Am J Psych*. 2018;175(5):463-470. doi:10.1176/appi.ajp.2017.17050550
33. Koh A, Pak KC, Choi HY, et al. Quantitative modeling analysis demonstrates the impact of CYP2C19 and CYP2D6 genetic polymorphisms on the pharmacokinetics of

amitriptyline and its metabolite, nortriptyline. *J Clin Pharmacol*. 2019;59(4):532-540. doi:10.1002/jcph.1344
34. Kohlmann W, Slavotinek A. Genetic testing. UpToDate. Updated October 7, 2022. Accessed January 15, 2025. www.uptodate.com
35. Laboratory Requirements, 42 C.F.R. § 493 (2024).
36. Lagishetty CV, Deng J, Lesko LJ, et al. How informative are drug-drug interactions of gene-drug interactions? *J Clin Pharmacol*. 2016;56(10):1221-1231. doi:10.1002/jcph.743
37. Leckband SG, Kelso JR, Dunnenberger HM, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for HLA-B genotype and carbamazepine dosing. *Clin Pharmacol Ther*. 2013;94(3):324-328. doi:10.1038/clpt.2013.103
38. Li D, Pain O, Chiara F, et al. Metabolic activity of CYP2C19 and CYP2D6 on antidepressant response from 13 clinical studies using genotype imputation: a meta-analysis. *Transl Psychiatry*. 2024;14(1):296. doi:10.1038/s41398-024-02981-1
39. List of cleared or approved companion diagnostic devices (in vitro and imaging tools). Food and Drug Administration. Updated November 15, 2024. Accessed January 15, 2025. www.fda.gov
40. Lu ML, Chen TT, Kuo PH, et al. Effects of adjunctive fluvoxamine on metabolic parameters and psychopathology in clozapine-treated patients with schizophrenia: A 12-week, randomized, double-blind, placebo-controlled study. *Schizophr Res*. 2018;193:126-133. doi:10.1016/j.schres.2017.06.030
41. McCormack M, Bourgeois S, Farrell JJ, et al. HLA-A*3101 and carbamazepine-induced hypersensitivity reactions in Europeans. *N Engl J Med*. 2011;364(12):1134-1143. doi:10.1056/NEJMoa1013297
42. Medical Code Brief: 0345U-PLA (U Codes). Hayes; 2022. Accessed January 15, 2025. www.evidence.hayesinc.com
43. Medical Code Brief: 0347U-PLA (U Codes). Hayes; 2022. Accessed January 15, 2025. www.evidence.hayesinc.com
44. Medical Code Brief: 0348U-PLA (U Codes). Hayes; 2022. Accessed January 15, 2025. www.evidence.hayesinc.com
45. Medical Code Brief: 0349U-PLA (U Codes). Hayes; 2022. Accessed January 15, 2025. www.evidence.hayesinc.com
46. Medical Code Brief: 0350U-PLA (U Codes). Hayes; 2022. Accessed January 15, 2025. www.evidence.hayesinc.com
47. Medical Code Brief: 0392U-PLA (U Codes). Hayes; 2023. Accessed January 15, 2025. www.evidence.hayesinc.com
48. Medical Code Brief: 0411U-PLA (U Codes). Hayes; 2023. Accessed January 15, 2025. www.evidence.hayesinc.com
49. Medical Code Brief: 0419U-PLA (U Codes). Hayes; 2023. Accessed January 15, 2025. www.evidence.hayesinc.com
50. Medical Code Brief: 0423U-PLA (U Codes). Hayes; 2023. Accessed January 15, 2025. www.evidence.hayesinc.com
51. Medical Code Brief: 0434U-PLA (U Codes). Hayes; 2024. Accessed January 15, 2025. www.evidence.hayesinc.com
52. Medical Code Brief: 0438U-PLA (U Codes). Hayes; 2023. Accessed January 15, 2025. www.evidence.hayesinc.com

53. Medical Code Brief: 0476U-PLA (U Codes). Hayes; 2024. Accessed January 15, 2025. www.evidence.hayesinc.com
54. Medical Code Brief: 0477U-PLA (U Codes). Hayes; 2024. Accessed January 15, 2025. www.evidence.hayesinc.com
55. Medical Code Brief: 81418-PLA (U Codes). Hayes; 2023. Accessed January 15, 2025. www.evidence.hayesinc.com
56. Methotrexate Pharmacogenetics-MTHFR Gene: A-1009. MCG Health. 28th ed. Updated March 14, 2024. Accessed January 15, 2025. www.careweb.careguidelines.com
57. Milosavljevic F, Bukvic N, Pavlovic Z, et al. Association of CYP2C19 and CYP2D6 poor and intermediate metabolizer status with antidepressant and antipsychotic exposure: a systematic review and meta-analysis. *JAMA Psychiatry*. 2021;78(3):270-280. doi:10.1001/jamapsychiatry.2020.3643
58. Molecular Test Assessment: GeneSight Psychotropic (Assurex Health Inc/Myriad Neuroscience). Hayes; 2021. Reviewed September 17, 2024. Accessed January 15, 2025. www.evidence.hayesinc.com
59. Nahid NA, Johnson JA. CYP2D pharmacogenetics and phenoconversion in personalized medicine. *Expert Opin Drug Metab Toxicol*. 2022;18(11):769-785. doi:10.1080/17425255.2022.2160317
60. National Cancer Institute (NCI). NCI Dictionary of Genetics Terms. National Institute of Health. Accessed January 15, 2025. www.cancer.gov
61. National Center for Biotechnology Information. Genetic testing registry. National Library of Medicine. Accessed January 15, 2025. www.ncbi.nlm.nih.gov
62. *National Correct Coding Initiative Policy Manual For Medicaid Services*. Centers for Medicaid and Medicare Services. Effective January 1, 2025. Accessed January 15, 2025. www.medicaid.gov
63. Ozeki T, Mushiroda T, Yowang A, et al. Genome-wide association study identifies HLA-A*3101 allele as a genetic risk factor for carbamazepine-induced cutaneous adverse drug reactions in Japanese population. *Hum Mol Genet*. 2011;20(5):1034-1041. doi:10.1093/hmg/ddq537
64. Patel JN, Morris SA, ,Torres R, et al. Pharmacogenomic insights in psychiatric care: uncovering novel actionability, allele-specific CYP2D6 copy number variation, and phenoconversion in 15,000 patients. *Mol Psychiatry*. 2024. doi:10.1038/s41380024-0
65. Pharmacogenetic testing. American Academy of Child and Adolescent Psychiatry. Updated December 2019. Accessed January 15, 2025. www.aacap.org
66. Phillips EJ, Sukasem C, Whirl-Carrillo M, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for HLA genotype and use of carbamazepine and oxcarbazepine: 2017 update. *Clin Pharmaco Ther*. 2018. doi:10.1002/cpt.1004
67. Precision Medicine Research Brief: Genecept Assay (Genomind). Hayes; 2016. Accessed January 15, 2025. www.evidence.hayesinc.com
68. Precision Medicine Research Brief: PGxOne Plus (Admera Health). Hayes; 2017. Accessed January 15, 2025. www.evidence.hayesinc.com
69. Precision Medicine Research Brief: Proove Opioid Risk Test (Proove Biosciences). Hayes; 2016. Accessed January 15, 2025. www.evidence.hayesinc.com
70. Pritchard D, Patel JN, Stephens LE, et al. Comparison of FDA table of Pharmacogenetic Associations and Clinical Pharmacogenetics Implementation

Consortium guidelines. *Am J Health Syst Pharm*. 2022;79(12):993-1005. doi:10.1093/ajhp/zxac064
71. Raby B. Personalized medicine. UpToDate. Updated September 06, 2023. Accessed January 15, 2025. www.uptodate.com
72. Rehder C, Bean LJH, Bick D, et al. Next-generation sequencing for constitutional variants in the clinical laboratory, 2021 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2021;23(8):1399-1415. doi:10.1038/s41436-021-01139-4
73. Rosenblat JD, Lee Y, McIntyre RS. Does pharmacogenomic testing improve clinical outcomes for major depressive disorder? a systematic review of clinical trials and cost-effectiveness studies. *J Clin Psychiatry*. 2017;78(6):720-729. doi:10.4088/JCP.15r10583
74. Roy S, LaFramboise WA, Nikiforov YE, et al. Next-generation sequencing informatics: challenges and strategies for implementation in a clinical environment. *Arch Pathol Lab Med*. 2016;140(9):958-975. doi:10.5858/arpa.2015-0507-RA
75. Royal College of Psychiatrists. *College Report CR237: The Role of Genetic Testing in Mental Health Settings*. Royal College of Psychatrists; 2023. Accessed January 15, 2025. www.rcpsych.ac.uk
76. Saadullah Khani NS, Hudson G, Mills G, et al. A systematic review of pharmacogenetic testing to guide antipsychotic treatment. *Nat Mental Health*. 2024;2(5):616-626. doi:10.1038/s44220-024-00240-2
77. Swen JJ, van der Wouden CH, Manson LE, et al. A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study. *Lancet*. 2023;401(10374):347-356. doi:10.1016/S0140-6736(22)01841-4
78. Tangamornsuksan W, Chaiyakunapruk N, Somkrua R, et al. Relationship between the HLA-B*1502 allele and carbamazepine-induced Stevens-Johnson syndrome and toxic epidermal necrolysis: a systematic review and meta-analysis. *JAMA Dermatol*. 2013;149(9):1025-1032. doi:10.1001/jamadermatol.2013.4114
79. Tantisira K. Overview of pharmacogenomics. UpToDate. Updated July 05, 2024. Accessed January 15, 2025. www.uptodate.com
80. Ter Hark S, Vos CF, Aarnoutse RE, et al. Biomarkers as predictors of treatment response to tricyclic antidepressants in major depressive disorder: a systematic review. *J Psych Res*. 2022;150:202-213. doi:10.1016/j.jpsychires.2022.03.057
81. US Food and Drug Administration. Warning letter: MARC-CMS 577422. 2019. Accessed January 15, 2025. www.fda.gov
82. Vos CF, Ter Hark SE, Schelleken AFA, et al. Effectiveness of genotype-specific tricyclic antidepressant dosing in patients with major depressive disorder: a randomized clinical trial. *JAMA Netw Open*. 2023;6(5):e2312443. doi:10.1001/jamanetworkopen.2023.12443
83. Wang Q, Sun S, Xie M, et al. Association between the HLA-B alleles and carbamazepine-induced SJS/TEN: a meta-analysis. *Epilepsy Res*. 2017;135:19-28. doi:10.1016/j.eplepsyres.2017.05.015
84. Warfarin Pharmacogenetics-CYP2C9, CYP4F2, and VKORC1 Genes: A-0587. MCG Health. 28th ed. Updated March 14, 2024. Accessed January 15, 2025. www.careweb.careguidelines.com

85. Wu X, Zhang H, Miah MK, et al. Physiologically based pharmacokinetic approach can successfully predict pharmacokinetics of citalopram in different patient populations. *J Clin Pharmacol*. 2020;60(4):477-488. doi:10.1002/jcph.1541
86. Zeier Z, Carpenter L, Kalin N, et al. Clinical implementation of pharmacogenetic decision support tools for antidepressant drug prescribing. *Am J Psychiatry*. 2018;175(9):873-886. doi:10.1176/appi.ajp.2018.17111282
87. Zubenko G, Sommer B, Cohen B. On the marketing and use of pharmacogenetic tests for psychiatric treatment. *JAMA Psychiatry.* 2018;75(8):769-770. doi:10.1001/jamapsychiatry.2018.0834

Reviewed by AllMed 09/2024

Approved by Mississippi Division of Medicaid 04/18/2025