CareSource

ADMINISTRATIVE POLICY STATEMENT
Nevada Medicaid

Policy Name & Number	Date Effective
Pharmacogenomics-Gene Testing for Behavioral Health Indications-NV MCD-AD-1614	01/01/2026
Policy Type	
ADMINISTRATIVE	

Administrative 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.

Administrative 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 Administrative Policy Statement. Except as otherwise required by law, if there is a conflict between the Administrative 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 refers to 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 (BH) 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 and 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 evidence is high quality, and desirable effects outweigh undesirable. In an optional recommendation, the desirable effects are closely balanced with undesirable, or the evidence is weak or based on extrapolations. Opinions differ as to the recommended course of action. With no recommendation, there is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical 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 stating, “The relationship between DNA variations and effectiveness of antidepressant medications has never been established.” The entity cautions that changes in patient medications based on test results “could potentially lead to patient harm.” In 2024, Baum, et al., updated the APA’s position by reviewing new clinical trials and meta-analyses published from 2017 to 2022 using PGx tools for treatment with depression and found “addition of these new data do not alter the recommendations of the 2018 report, or the advice of the US FDA, that the evidence does not support the use of currently available combinatorial PGx tools for treatment.” In 2019, the International Society of Psychiatric Genetics published the following: “Pharmacogenetic testing should be viewed as a decision-support tool to assist in thoughtful implementation of good clinical care, enhancing rather than offering an alternative to standard protocols… 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.”

CareSource covers items and services with sufficient medical/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/services with insufficient data to determine net health impact. Insufficient data includes support that testing 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. CareSource provides appeal rights to members or providers on behalf of members who disagree with denial decisions. Tests should be chosen to maximize the likelihood of identifying mutations in genes of interest for specific medical reasons, 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 actionable use.
- **Adherence** – Consumption of a drug at the maximum or near maximum FDA approved dosage and duration (eg, antidepressant for 4-6 weeks) for the specific medication, or documentation that higher doses are not tolerated when less than the FDA-approved maximum.

- **Biomarker** – A characteristic objectively measured/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** – 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 the 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 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 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).

B. Coverage of biomarker testing for the purpose of screening a member prior to initiating diagnostic testing or care for a disease or condition for which biomarker testing is appropriate is not considered medically necessary.

C. Any biomarker testing with clinical significance and evidence supported by scientific and medical evidence may be subject to medical necessity review.

II. Based on a review of existing evidence, there are currently no clinical indications for the high-volume tests below. The current role remains uncertain. Therefore, CareSource considers these requests not medically necessary. There is not sufficient evidence for use in medical/scientific evidence (not an all-inclusive list):

CPT Code and Description	
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17)

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)
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)
81291	MTHFR (5, 10-methylenetetrahydrofolate reductase) (eg, hereditary hypercoagulability) gene analysis, common variants (eg,677T, 1298C)
0345U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6
0411U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6

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

IV. CareSource 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 of 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 (eg, pain management, cardiovascular drugs, anthracyclines, or polypharmacy) for evaluating drug-metabolizer status
- C. broad symptom-based panels when a narrower panel is available and more appropriate based on clinical findings
- 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

CareSource 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 procedures 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 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 requested, only testing for the medically necessary, previously untested genes is reimbursable. Only the most appropriate procedure codes for additional genes will be considered for reimbursement.

F. Related Policies/Rules

Medical Necessity Determinations
Experimental and Investigational Items and Services

G. Review/Revision History

	DATE	ACTION
Date Issued	08/27/2025	New policy. Approved at Committee.
Date Revised		
Date Effective	01/01/2026	
Date Archived		

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