Medical Coverage Policy | Genetic Testing for Diagnosis and Management of Mental Health Conditions

EFFECTIVE DATE: 01|01|2025
POLICY LAST REVIEWED: 09|18|2024

OVERVIEW

Individual genes have been shown to be associated with risk of psychiatric disorders and specific aspects of psychiatric drug treatment such as drug metabolism, treatment response, and risk of adverse events. Commercially available testing panels include several of these genes and are intended to aid in the diagnosis and management of mental health disorders.

The following tests are addressed in this policy:

- Cytochrome P450 1A2 Genotype (Mayo Clinic) CPT code 0031U
- Genecept Assay (Genomind) CPT code 81479
- Genomind® Professional PGx Express™ CORE (Genomind, Inc.) CPT code 0175U
- Mental Health DNA Insight panel (Pathway Genomics) CPT code 81479
- Neuropharmagen (AB-Biotics) CPT code 81479
- Proove Opioid Risk Assay (Proove Biosciences) CPT code 81479
- Psych HealthPGx Panel (RPRD Diagnostics) CPT code 0173U
- Psychotropic Pharmacogenomics Gene Panel (Mayo Clinic) CPT code 81479
- STA²R - SureGene Test for Antipsychotic and Antidepressant Response (SureGene) CPT code 81479

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Medicare Advantage Plans and Commercial Products

For services in this policy that do not have a specific CPT code an Unlisted CPT code should be used (See Coding Section for details). All Unlisted genetic testing CPT codes require prior authorization to determine what service is being rendered and if the service is covered or not medically necessary. See the Related Policies section.

Note: Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

POLICY STATEMENT

Medicare Advantage Plans and Commercial Products

The following test is covered:

- Psychotropic Pharmacogenomics Gene Panel – CPT code 81479

The following tests are not covered for Medicare Advantage Plans and not medically necessary for Commercial Products as the evidence is insufficient to determine that the technology results in an improvement in the net health outcome:

- Cytochrome P450 1A2 Genotype (Mayo Clinic)
- Genecept Assay (Genomind)
- Genomind® Professional PGx Express™ CORE (Genomind, Inc.)
- Mental Health DNA Insight Panel (Pathway Genomics)
- Neuropharmagen (AB-Biotics)
- Proove Opioid Risk Assay (Proove Biosciences)
- Psych HealthPGx Panel (RPRD Diagnostics)
- STA²R - SureGene Test for Antipsychotic and Antidepressant Response (SureGene)

Commercial Products
Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L**. §27-19-81** described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for laboratory tests or not medically necessary/not covered benefits/coverage.

BACKGROUND

This policy assesses whether genetic testing for the diagnosis and management of mental health conditions is clinically useful. To make a clinical management decision that improves the net health outcome; the balance of benefits and harms must be better when the test is used to manage the condition than when another test or no test is used. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

The primary goal of pharmacogenomics testing and personalized medicine is to achieve better clinical outcomes compared to managing the condition with the standard of care. Drug response varies greatly between individuals, and genetic factors are known to play a role. However, in most cases, the genetic variation only explains a modest portion of the variance in the individual response because clinical outcomes are also affected by a wide variety of factors including alternate pathways of metabolism and patient- and disease-related factors that may affect absorption, distribution, and elimination of the drug.

Therefore, assessment of clinical utility of a pharmacogenetic test cannot be made by a chain of evidence from clinical validity data alone. In such cases, evidence evaluation requires studies that directly demonstrate that the use of the pharmacogenomic test to make management decisions alters clinical outcomes; it is not sufficient to demonstrate that the test predicts a disorder or a phenotype. Direct evidence of clinical utility is provided by studies that compare health outcomes for patients managed with or without the test. Because these are intervention studies, the preferred evidence is from randomized controlled trials.

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). The tests discussed in this section are available under the auspices of

CLIA. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

Examples of commercially available panels include the following:

- Cytochrome P450 1A2 Genotype (Mayo Clinic)
- Genecept™ Assay (Genomind)
- Genomind® Professional PGx Express™ CORE (Genomind, Inc.)
- Mental Health DNA Insight™ panel (Pathway Genomics)
- Neuropharmagen (AB-Biotics)
- Proove Opioid Risk Assay (Proove Biosciences)
- Psych HealthPGx Panel (RPRD Diagnostics)
- Psychotropic Pharmacogenomics gene panel (Mayo Clinic)
- STA2R test (SureGene Test for Antipsychotic and Antidepressant Response; Clinical Reference Laboratory)

Documentation Requirements

The medical record must clearly reflect the following:

- The patient has a diagnosis for which pharmacologic therapy is reasonable and necessary, and the drug or drugs that the clinician is considering using must be reasonable and necessary for the treatment of the patient's diagnosis.
- The clinician has made an initial personalized decision for the patient based on the patient's diagnosis, the patient's other medical conditions, other medications the patient is taking, professional judgement, clinical science and basic science pertinent to the drug (e.g. mechanism of action, side effects), the patient's past medical history and when pertinent family history and the patient's preferences and values.
- The provider performing the service must have a record of what drug(s) is/are being considered and for what indication(s).

For adult individuals with Major Depressive Disorder (MDD) who receive Neuropharmagen testing guided drug treatment, the evidence includes 2 RCTs. Relevant outcomes are symptoms, changes in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The 2 RCTs compared response (≥50% decrease in HAM-D17) and remission (HAM-D17 ≤7) with antidepressant therapy informed by Neuropharmagen test results to antidepressant therapy selected without Neuropharmagen test results (i.e. SOC). The single-blinded RCT by Han et al (2018) reported statistically significant improvement in response (72% of 52 vs. 44% of 48; p=.01) but no statistically significant improvement in remission (46% of 52 vs. 26% of 48; p=.07) in the Neuropharmagen arm compared to SOC at 8 weeks among patients with MDD. The study reported early dropout of 25% in guided-care and 38% in the standard care arm and used last observation carried forward (LOCF) approach in the ITT analysis of effectiveness. Use of LOCF assumes data are missing completely at random, which is unlikely to hold in this analysis. Also, the study did not report registration in any clinical trial database. The single-blinded RCT by Perez et al (2017) reported non-statistically significant improvement in response (45% of 141 vs. 40% of 139; p=.39) and remission (34% of 141 vs. 33% of 139; p=.87) in the Neuropharmagen arm compared to SOC at 12 weeks among patients with MDD. Response and remission data were missing for 9% of patients in the guided care group and 14% in the SOC group. None of these trials provided adequate evidence. Both studies have major limitations in design and conduct and in consistency and precision. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are evaluated for diagnosis or risk of a mental illness who receive genetic testing for risk of that disorder, the evidence includes various observational studies (cohort, case-control, genome-wide association study). Relevant outcomes are changes in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. Most studies evaluated the association between genotype and mental health disorders or gene-drug interactions among patients with risk for mental health conditions. No studies were identified that evaluated whether testing for variants changed clinical

management or affected health outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with a mental illness other than depression who are undergoing drug treatment who receive genetic testing for genes associated with medication pharmacokinetics and pharmacodynamics, the evidence includes a systematic review and meta-analysis and RCTs evaluating associations between specific genes and outcomes of drug treatment. Relevant outcomes are symptoms, changes in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The systematic review and meta-analysis by Hartwell et al (2020) included 7 RCTs and reported no significant moderating effect of rs1799971, a single nucleotide polymorphism (SNP) that encodes a non-synonymous substitution (Asn40Asp) in the mu-opioid receptor gene, OPRM1 on response to naltrexone treatment of alcohol use disorder. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Specific variants included in the STA²R test (SureGene Test for Antipsychotic and Antidepressant Response; Clinical Reference Laboratory) were not easily identified from the manufacturer's website.

CODING

Medicare Advantage Plans and Commercial Products
The following CPT code(s) are not covered for Medicare Advantage Plans and not medically necessary for Commercial Products:

Psych HealthPGx Panel
0173U Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes

Genomind® Professional PGx Express™ CORE
0175U Psychiatry (eg, depression, anxiety), genomic analysis panel, variant analysis of 15 genes

Cytochrome P450 1A2 Genotype
0031U CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7)

*For all other testing referenced in this policy:
There is not a specific CPT code, therefore, claims should be filed with Unlisted CPT code **81479.**
81479 Unlisted molecular pathology procedure

While there may be specific CPT codes for some of the components of the panel testing in this policy, claims for the entire panel must be filed with the Unlisted CPT code noted above.

RELATED POLICIES

Biomarker Testing Mandate
Genetic Testing Services
Proprietary Laboratory Analyses (PLA)
Unlisted Procedures

PUBLISHED

Provider Update, November 2024
Provider Update, January/September/November 2023
Provider Update, February 2022
Provider Update, March 2021
Provider Update, February 2020

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3. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): Pharmacogenomics Testing, Novitas Solutions, Inc (L39063)
4. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article: Billing and Coding: MolDX: Pharmacogenomics Testing, Novitas Solutions, Inc (A58801)
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