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

EFFECTIVE DATE: 10|13|2015
POLICY LAST UPDATED: 12|03|2019

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.

MEDICAL CRITERIA

BlueCHiP for Medicare

GeneSight® Psychotropic gene panel testing is covered when all of the following clinical conditions are met:

- Test is ordered by a licensed psychiatrist or neuropsychiatrist, and
- Diagnosed with major depressive disorder (MDD), and
- Suffering with refractory moderate to severe depression (based upon DSM-V criteria), and
- Has had at least one prior neuropsychiatric medication failure, and
- Contemplating an alteration in neuropsychiatric medication.

Commercial Products

Not applicable

PRIOR AUTHORIZATION

BlueCHiP for Medicare and Commercial Products

There is no specific CPT code for this service and 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.

Prior authorization is required for BlueCHiP for Medicare and recommended for Commercial Products and is obtained via the online tool for participating providers. See the Related Policies section.

POLICY STATEMENT

BlueCHiP for Medicare

GeneSight Psychotropic gene panel testing will be considered medically necessary when the medical criteria listed above are met.

Genetic testing panels for mental health disorders, including but not limited to the Genecept Assay, STA2R test, the Proove Opioid Risk assay, and the Mental Health DNA Insight panel, are not covered for all indications as the evidence is insufficient to determine the effects of the technology on health outcomes.

Genetic testing for diagnosis and management of mental health disorders, is not covered in all situations, including but not limited to the following, as the evidence is insufficient to determine the effects of the technology on health outcomes:

- To confirm a diagnosis of a mental health disorder in an individual with symptoms.
- To predict future risk of a mental health disorder in an asymptomatic individual.
- To inform the selection or dose of medications used to treat mental health disorders, including but not limited to the following medications:

o selective serotonin reuptake inhibitors
o selective norepinephrine reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors
o tricyclic antidepressants
o antipsychotic drugs.

Commercial Products
Genetic testing panels for mental health disorders, including but not limited to the GeneSight Psychotropic gene panel testing, Genecept Assay, STA2R test, the Proove Opioid Risk assay, and the Mental Health DNA Insight panel, are considered not medically necessary for all indications as the evidence is insufficient to determine the effects of the technology on health outcomes.

Genetic testing for diagnosis and management of mental health disorders is considered not medically necessary in all situations, including but not limited to the following, as the evidence is insufficient to determine the effects of the technology on health outcomes:

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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
Mental health disorders cover a wide range of clinical phenotypes and are generally classified by symptomatology in systems such as the classification outlined in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5*). In addition to counseling and other forms of behavioral treatment, treatment commonly involves one or more psychotropic medications that are aimed at alleviating symptoms of the disorder. Although there are a wide variety of effective medications, treatment of mental health disorders is characterized by relatively high rates of inadequate response. This often necessitates numerous trials of individual agents and combinations of medications to achieve optimal response.

Knowledge of the physiologic and genetic underpinnings of mental health disorders is advancing rapidly and may substantially alter the way in which these disorders are classified and treated. Genetic testing could be used in several ways including stratifying patients' risks of developing a particular disorder, aiding diagnosis, targeting medication therapy, and optimally dosing medication.

Drug Efficacy and Toxicity
Drug efficacy and toxicity vary substantially across individuals. Because drugs and doses are typically adjusted, if needed, by trial-and-error, clinical consequences may include a prolonged time to optimal therapy. In some cases, serious adverse events may result.

Multiple factors may influence the variability of drug effects, including age, liver function, concomitant diseases, nutrition, smoking, and drug-drug interactions. Inherited (germline) DNA sequence variation in genes coding for drug metabolizing enzymes, drug receptors, drug transporters, and molecules involved in

signal transduction pathways also may have major effects on the activity of those molecules and thus on the efficacy or toxicity of a drug.

Pharmacogenomics studies how an individual's genetic inheritance affects the body's response to drugs. It may be possible to predict therapeutic failures or severe adverse drug reactions in individual patients by testing for important DNA variants (genotyping) in genes related to the metabolic pathway (pharmacokinetics) or signal transduction pathway (pharmacodynamics) of the drug. Potentially, test results could be used to optimize drug choice and/or dose for more effective therapy, avoid serious adverse events, and decrease medical costs.

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:

- Genecept™ Assay (Genomind)
- STA2R test (SureGene Test for Antipsychotic and Antidepressant Response; Clinical Reference Laboratory)
- GeneSight® Psychotropic panel (Assurex Health)
- Proove Opioid Risk panel (Proove Biosciences)
- Mental Health DNA Insight™ panel (Pathway Genomics)
- IDgenetix-branded tests (AltheaDx)

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 (case-control, genome-wide association study) evaluating the association between the mental illness of interest and candidate genes. The relevant outcomes are test validity, other test performance measures, and changes in disease status. Most studies have evaluated the association between genotype and mental health disorders without a clinical perspective; thus diagnostic characteristics and validated risk predictions among specific clinical populations are unknown. The associations are inconsistent across studies. There is no clear clinical strategy for how the associations of specific genes and mental health disorders would be used to diagnose a specific patient or to manage a patient at higher risk of a specific disorder. No studies were identified that evaluated whether testing for variants changed clinical management or affected health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with depression who are inadequately controlled with drug treatment who receive genetic testing for genes associated with medication pharmacokinetics and pharmacodynamics, the evidence includes a large number of observational studies evaluating associations between specific genes and outcomes of drug treatment, as well as six randomized controlled trials comparing outcomes for patients who received treatment guided by genetic testing with patients who received standard of care treatment. The relevant outcomes are symptoms, changes in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The largest randomized trial did not find significant differences in the primary outcome of change in Hamilton Depression score among patients managed by results from a pharmacogenomic test compared with patients managed by the standard of care. The remaining trials reported inconsistent results, with some reporting significant improvements in Hamilton Depression and other depression measures, and other trials finding no difference among patients managed with pharmacogenomic tests vs standard of care. Observational studies comparing patients who have had and have not had genetic testing reported that testing may be associated with differences in depression treatment outcomes, though methodologic shortcomings such as lack of randomization, small sample sizes, and large

loss to follow-up limit the conclusions that can be drawn. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 studies evaluating associations between specific genes and outcomes of drug treatment, as well as a systematic review and observational studies. The 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 of observational studies included patients with schizophrenia and reported associations between gene variants and treatment response; however, many of the studies were retrospective and had small sample sizes. No randomized controlled trials comparing health outcomes among patients undergoing guided and unguided management were identified. The evidence is insufficient to determine the effects of the technology on health outcomes.

BlueCHiP for Medicare
GeneSight Psychotropic is a multiplex pharmacogenomic test involving the analysis of fifty alleles (SNPs) from six different genes and a clinical outcomes-based decision support modeling tool that weights the influence of the various alleles/SNPs with respect to thirty-two different psychotropic pharmaceutical agents. The test results in the differentiation of psychoactive drugs that are likely to be effective and well-tolerated by a particular patient versus those that are not.

GeneSight has particular relevance for Medicare beneficiaries, 26% of whom experience a mental disorder each year. Additionally, six out of ten disabled Medicare beneficiaries (~3.7 million) under age 65, representing roughly 17% of all beneficiaries, have a diagnosis of mental disorder. Furthermore, the American Psychiatric Association (APA) recognizes depression as the most common mental disorder in people aged 65 and older. It frequently appears as a co-morbid symptom to other conditions and can even mimic the symptoms of dementia. As a group, seniors generally take more medications than other age groups, increasing their risk of drug-drug interactions and adverse drug events (ADEs).

The GeneSight report segments and displays these psychotropic medications into three "traffic light" categories or "bins"—green, yellow, and red. Based on the patient's genetic makeup and the drug's metabolic and therapeutic pathways, the green bin identifies drugs that will likely be well tolerated and efficacious for the tested patient; the yellow bin identifies drugs with an intermediate effect; and the red bin identifies drugs likely to be poorly tolerated and/or ineffective. The report also identifies common drug-drug interactions that are similarly influenced by the patient's genetic composition.

In a meta-analysis of three prospective, 2-armed clinical trials (Pine Rest, Hamm, and La Crosse), use of the test to aid in therapeutic selection has improved patient responses to treatment by 73% on average, which is consistent with the results from each study individually, and is highly significant ($p=0.004$). These findings support the value of the GeneSight test in improving patient outcomes.

CODING

BlueCHiP for Medicare and Commercial Products
There is not a specific CPT code for the testing referenced in this policy. Therefore, claims should be filed with Unlisted CPT code **81479.**

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

RELATED POLICIES

Genetic Testing Services

PUBLISHED

Provider Update, February 2020
Provider Update, January 2019
Provider Update, November 2017
Provider Update, September 2016
Provider Update, January 2016

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