Medical Coverage Policy | Genetic Testing for Mental Health Conditions

EFFECTIVE DATE: 11|03|2015
POLICY LAST UPDATED: 07|19|2016

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 effects. Commercially available testing panels include several of these genes and are intended to aid in the diagnosis and treatment 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, and
- Diagnosed with major depressive disorder (MDD) (in accordance with DSM IV/V criteria), and
- Suffering with refractory moderate to severe depression (as defined by the 17-item Hamilton Rating Scale for Depression (HAM-D17) score of 14 or greater), 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

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

Commercial Products

Not applicable

POLICY STATEMENT

BlueCHiP for Medicare

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

Commercial Products

GeneSight Psychotropic gene panel testing is considered not medically necessary due to a lack of scientific literature validating the efficacy of the service.

BlueCHiP for Medicare and Commercial Products

Genetic testing for mutations associated with mental health disorders and 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 considered not medically necessary in all situations due to a lack of peer-reviewed scientific literature proving the efficacy of the service.

COVERAGE

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

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 1 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 potentially be used in several ways including stratifying patients' risks of developing a particular disorder, aiding diagnosis, targeting medication therapy, and optimally dosing medication.

Genes Relevant to Mental Health Disorders

Mental health disorders encompass a wide range of conditions: the *DSM-5* includes more than 300 disorders. However, currently available genetic testing for mental health disorders is primarily related to 2 clinical situations:

1. Risk-stratifying patients for one of several mental health conditions, including schizophrenia and related psychotic disorders, bipolar and related disorders, depressive disorders, obsessive compulsive and related disorders, and substance-related and addictive disorders.
2. Predicting patients' response to, dose requirement for, or adverse effects from one of several medications (or classes of medications) used to treat mental health conditions, including: typical and atypical antipsychotic agents, selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors, and medications used to treat addiction, such as disulfiram.

Panels of genetic tests have been developed and proposed for use in the latter clinical situation. Genes implicated in prediction of mental health disorders or their response to treatment and included in currently available panels are outlined in the following sections.

Several test labs market either panels of tests or individual tests relevant for mental health disorders.

The Genecept™ Assay (Genomind, Chalfont, PA) is a genetic panel test that includes genetic mutations and/or polymorphisms associated with psychiatric disorders and/or response to psychotropic medication. The test consists of a group of individual genes, and the results are reported separately for each gene. There is no summary score derived from this test. The intent of the test is as a decision aid for treatment interventions, particularly in the choice and dosing of medications. However, guidance on specific actions that should be taken following specific results of the test is vague. Interpretation of the results and any management changes as a result of the test are left to the judgment of the treating clinician.

The STA2R (SureGene Test for Antipsychotic and Antidepressant Response; SureGene, Louisville, KY) is a genetic panel that provides information about medication response, adverse event likelihood, and drug metabolism based on the results of the genetic panel. According to the manufacturer's website, the test is recommended for initial medication selection, for patients who have poor efficacy, tolerability, or satisfaction with existing medications, and in cases of severe treatment failure.

GeneSight® Psychotropic (Assurex Health, Mason, OH) is a genetic panel that provides information about genes that may affect a patient's response to antidepressant and antipsychotic pharmacotherapy. According to the manufacturer's website, following testing, the treating provider receives a report with the most common medications for the patient's diagnosed condition categorized by cautionary level, along with a report of the patient's genetic variants. Details are not provided about the algorithm used by the manufacturer to generate risk levels.

The Proove Opioid Risk panel (Proove Biosciences, Irvine, CA) is a panel to evaluate genes involved in the development of substance abuse or dependence and in response to medical therapy for substance abuse or dependence.

Pathway Genomics (San Diego, CA) offers the Mental Health DNA Insight™ panel, which is a single nucleotide polymorphismbased array test that evaluates a number of genes associated with the metabolism and efficacy of psychiatric medications.

AltheaDx (San Diego, CA) offers a number of IDgenetix-branded tests, which include several panels focusing on polymorphisms that affect medication pharmacokinetics for a variety of disorders, including psychiatric disorders. Specific mutations included in the panel were not easily identified from the manufacturer's website.

Commercial Products
The analytic validity of these assays cannot be determined due to a lack of information on the testing methods. The available evidence on clinical validity consists of genome-wide association studies and case-control studies that indicate a correlation between variants of these genes and clinical factors. This evidence shows low-strength associations with a variety of psychiatric and nonpsychiatric conditions. Often the evidence for an association is not consistently reported across all studies, and in many cases, there are correlations of the same genetic variants with other nonpsychiatric disorders. There are also a range of associations reported for response to certain medications and alterations in pharmacokinetics. Evidence on clinical utility is lacking. Management changes that occur as a result of this assay are ill defined, with uncertain impact on clinical outcomes. In addition, it is not well-understood how unexpected results or unknown variants are handled and whether these type of results have an impact on diagnostic work-up, treatment decisions, and health outcomes. Due to these deficiencies in the evidence base, genetic testing panels for mental health disorders are considered investigational for all indications.

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 this testing. Therefore, claims should be filed with unlisted CPT code **81479.**

RELATED POLICIES

Preauthorization via Web-Based Tool for Genetic Testing

PUBLISHED

Provider Update, September 2016
Provider Update, January 2016

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