

## Medical Coverage Policy | Genetic Testing for Mental Health Conditions



**EFFECTIVE DATE:** 10|13|2015

**POLICY LAST UPDATED:** 09|05|017

### 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 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

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 as the evidence is insufficient to determine the effects of the technology on health outcomes.

#### 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 as the evidence is insufficient to determine the effects of the technology on health outcomes.

## 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.

Several test labs market either panels of tests or individual tests relevant for mental health disorders, which may include a variety of genes relevant to psychopharmacology or risk of mental illness. Some of the panels (eg, the GeneSight panel) provide an overall risk score or summary score.

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, Chalfont, PA)
- STA2R test (SureGene Test for Antipsychotic and Antidepressant Response; Clinical Reference Laboratory, Lenexa, KS)
- GeneSight® Psychotropic panel (Assurex Health, Mason, OH)
- Proove Opioid Risk panel (Proove Biosciences, Irvine, CA)
- Mental Health DNA Insight™ panel (Pathway Genomics, San Diego, CA)
- IDgenetix-branded tests (AltheaDx, San Diego, CA)

For individuals who are evaluated for diagnosis or risk of a mental illness who receive genetic testing for risk of that disorder, the evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have a mental illness who are undergoing drug treatment who receive genetic testing for genes associated with medication pharmacokinetics and pharmacodynamics, 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 this testing. Therefore, claims should be filed with unlisted CPT code **81479**.

### **RELATED POLICIES**

Genetic Testing Services

### **PUBLISHED**

Provider Update, November 2017

Provider Update, September 2016

Provider Update, January 2016

### **REFERENCES**

1. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): MolDX: GENESIGHT<sup>®</sup> Assay for Refractory Depression (L35443). CGS Administrators, LLC.
2. Gatt JM, Burton KL, Williams LM, et al. Specific and common genes implicated across major mental disorders: a review of meta-analysis studies. *J Psychiatr Res.* Jan 2015;60:1-13. PMID 25287955

3. Hariri AR, Mattay VS, Tessitore A, et al. Serotonin transporter genetic variation and the response of the human amygdala. *Science*. Jul 19 2002;297(5580):400-403. PMID 12130784
4. Lasky-Su JA, Faraone SV, Glatt SJ, et al. Meta-analysis of the association between two polymorphisms in the serotonin transporter gene and affective disorders. *Am J Med Genet B Neuropsychiatr Genet*. Feb 5 2005; 133B(1):110-115. PMID 15578606
5. Enoch MA, Gorodetsky E, Hodgkinson C, et al. Functional genetic variants that increase synaptic serotonin and 5-HT<sub>3</sub> receptor sensitivity predict alcohol and drug dependence. *Mol Psychiatry*. Nov 2011;16(11):1139-1146.PMID 20838391
6. Sen S, Burmeister M, Ghosh D. Meta-analysis of the association between a serotonin transporter promoter polymorphism (5-HTTLPR) and anxiety-related personality traits. *Am J Med Genet B Neuropsychiatr Genet*. May15 2004;127B(1):85-89. PMID 15108187
7. Allen JD, et al. **GENESIGHT**® psychotropic reduces overall medication costs in patients treated with psychiatric medications. Poster presentation. American Psychiatric Association; May 2014. New York, NY.
8. American Psychiatric Association (APA). Practice guidelines for the treatment of patients with major depressive disorder. 3rd ed. *Am Psychiatry* 2010;167(suppl):1-152.
9. Furmaga K, et al. The clinical impact of an antidepressant pharmacogenomic algorithm. NCDEU poster, 2012.
10. Hall-Flavin DK, et al. Using a pharmacogenomic algorithm to guide the treatment of depression. *Transl Psychiatry*. 2012;2, e172; doi:10.1038/tp.2012.99

**CLICK THE ENVELOPE ICON BELOW TO SUBMIT COMMENTS**

This medical policy is made available to you for informational purposes only. It is not a guarantee of payment or a substitute for your medical judgment in the treatment of your patients. Benefits and eligibility are determined by the member's subscriber agreement or member certificate and/or the employer agreement, and those documents will supersede the provisions of this medical policy. For information on member-specific benefits, call the provider call center. If you provide services to a member which are determined to not be medically necessary (or in some cases medically necessary services which are non-covered benefits), you may not charge the member for the services unless you have informed the member and they have agreed in writing in advance to continue with the treatment at their own expense. Please refer to your participation agreement(s) for the applicable provisions. This policy is current at the time of publication; however, medical practices, technology, and knowledge are constantly changing. BCBSRI reserves the right to review and revise this policy for any reason and at any time, with or without notice. Blue Cross & Blue Shield of Rhode Island is an independent licensee of the Blue Cross and Blue Shield Association.

