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## OVERVIEW

Several commercially available testing panels include genes related to neurotransmitter function and pharmacokinetics of psychiatric drugs. They are intended to be an aid in clinical decision making regarding interventions for psychiatric conditions.

Panels of multiple genetic tests have been developed to aid the diagnosis and treatment of mental health disorders. Genes included in the panels have shown some association with psychiatric disorders or with the pharmacokinetics of psychotropic medications.

## MEDICAL CRITERIA

### BlueCHiP for Medicare

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

### 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 GeneSight Psychotropic panel, 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

Psychiatric 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 psychiatric disease 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 psychiatric 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. Better understanding of these factors may lead to an improved ability to target medications to the specific underlying abnormalities, with potential improvement in the efficiency and efficacy of treatment.

The Genecept™ Assay (Genomind, Chalfont, PA) is a genetic panel test that includes a range of genetic mutations and/or polymorphisms that have been 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 or aggregate results 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.

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.<sup>2</sup> Details are not provided about the algorithm used by the manufacturer to generate risk levels.

## BlueCHiP for Medicare

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.

### 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.

### 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, January 2016

### REFERENCES

1. 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.
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3. Assurex. GeneSight Informative Letter. <http://assurexhealth.com/>. Accessed March, 2015.
4. 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
5. 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
6. Jiang H, Qiao F, Li Z, et al. Evaluating the association between CACNA1C rs1006737 and schizophrenia risk: A meta-analysis. *Asia Pac Psychiatry.* Jan 15 2015. PMID 25588813

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