Clinical Policy Title: Pharmacogenomic tests for psychiatric medications

Clinical Policy Number: 02.02.01

Effective Date: October 1, 2015
Initial Review Date: April 15, 2015
Most Recent Review Date: May 18, 2016
Next Review Date: May 2017

Policy contains:
- Pharmacogenomic tests.
- Psychiatric medication.
- Genesight.
- SureGene.

Related policies:
None.

ABOUT THIS POLICY: Prestige Health Choice has developed clinical policies to assist with making coverage determinations. Prestige Health Choice’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Prestige Health Choice when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Prestige Health Choice’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Prestige Health Choice’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Prestige Health Choice will update its clinical policies as necessary. Prestige Health Choice’s clinical policies are not guarantees of payment.

Covered policy

Prestige Health Choice considers the use of pharmacogenomics tests for psychiatric medications to be investigational and, therefore, not medically necessary, including but not limited to the use of GeneSightRx or PHARMAchip assay genotyping of CYP1A2, CYP2C9, CYP2C19, CYP2D6, HTR2A, and SCL6A4 to help guide administration of antidepressants and antipsychotics or SureGene (STA2R) for antipsycotic drug response.

Limitations:

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website can be accessed at http://ahca.myflorida.com/Medicaid/.

All other uses of radiofrequency tests are not medically necessary.
Alternative covered services:

Traditional trial and error management.

**Background**

For decades, clinicians have recognized that patients may respond differently to the same dose of a given pharmaceutical agent. Drugs are approved by the Food and Drug Administration (FDA) for sale based upon the general health improvement across a population and considers individual variations only if a subpopulation experiences significant adverse effects. As more of the human genetic makeup is understood, the goal of “personalized medicine” comes closer to realization. There are currently a limited number of genomic tests that can impact the physician selection of therapies and significantly impact the patient outcome. Gervasini et al noted that “despite significant progress in pharmacogenetic research, only a few drugs such as cetuximab, dasatinib, maraviroc and trastuzumab, require a pharmacogenetic test before being prescribed.”

There has been recognition of patterns of behavioral expression, suggesting an inherited predisposition in mental health. More exciting has been the hope that genomics can lead to improved selection of pharmacotherapy. Currently physician selection of anti-depressants or anti-psychotic medications has been based upon physician experience with that drug and not on knowledge of patient-specific medication impact.

Several commercially available genomic tests are currently on the market, with more to come. The intentions of these tests are to enhance positive predictors of medication-specific responders. By using genomic information, the hope is that targeted therapy will replace the current “trial-and-error” approach to medication selection.

Studies sponsored by the genomic test manufacturers have reported inferred success in targeted therapies. However, disinterested researchers, in review of the data, have not found sufficient correlation with genomic test results compared to the test for targeted pharmacologic therapy. In review of the evidence-based clinical literature, the results are superior.

**Searches**

Prestige Health Choice searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services.
We conducted searches on April 28, 2016. Search terms were: “pharmacogenomic drugs,” “depression,” “Psychosis,” “Schizophrenia” and “Psychiatric medication (MeSH).”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.

- **Guidelines based on systematic reviews.**

- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

### Findings

While there have been a number of studies reviewing the statistical association of response to medication in people with varying behavioral health disorders, there are no definitive, validated studies showing that use of pharmacogenomic studies can lead to improved outcomes. In a population there is a greater association of response to specific drug classes (e.g., SSRIs) for the subpopulation with specific behavioral health diagnoses. A number of studies in the published literature are funded by the companies developing these testing tools and/or have principal investigators who are on the boards or are employees of these genetic testing companies. The potential biases in such studies reduce the published data meeting the Prestige Health Choice criteria. Meta-analyses and multi-centered trials have not demonstrated clear outcome improvements with decisions based upon data from pharmacogenomics test data.

### Policy updates:

None.

### Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
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<tbody>
<tr>
<td>Niitsu (2013)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td></td>
<td>• Meta-analysis from three major reviews.</td>
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<tr>
<td></td>
<td>• The findings suggested the BDNF Val66Met as the best single candidate involved in antidepressant response, with a selective effect on SSRI treatment.</td>
</tr>
<tr>
<td></td>
<td>• Our overall results supported no major effect of any single gene variant on AD efficacy.</td>
</tr>
<tr>
<td>GENDEP (2013)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td></td>
<td>• A meta-analysis was performed on data from three genome-wide pharmacogenetic</td>
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</table>
studies (the Genome-Based Therapeutic Drugs for Depression [GENDEP] project, the Munich Antidepressant Response Signature [MARS] project, and the Sequenced Treatment Alternatives to Relieve Depression [STAR*D] study), which included 2,256 individuals of Northern European descent with major depressive disorder.

- There were no reliable predictors of antidepressant treatment outcome, although they did identify modest, direct evidence that common genetic variation contributes to individual differences in antidepressant response.

**Glossary**

**Medically Necessary**— A service or benefit is Medically Necessary if it is compensable under the MA Program and if it meets any one of the following standards:

- The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
- The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
- The service or benefit will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.

**Pharmacogenomics** — The study of how an individual's genetic makeup, or genotype, affects the body's response to drugs. Pharmacogenomics as a science examines associations among variations in genes with individual responses to a drug or medication. In application, pharmacogenomic results (i.e., information on the patient’s genetic variations) can contribute to predicting a patient’s response to a given drug: good, bad or none at all. (CMS definition NCD 90.1)

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


Gardner KR, Brennan FX, Scott R, Lombard J. The potential utility of pharmacogenetic testing in


Clinical trials:

Searched clinicaltrials.gov on April 8, 2015 using terms pharmacogenomics and psychiatry | Open 50 studies found, 6 relevant.


Utility of PharmacoGenomics for Reducing Adverse Drug Effects (UPGRADE) NCT02081872; Companion
“UPGRADE aims to see whether data from Pharmacogenomic Testing (PGx) can help physicians manage patient medication regimens and assess if the testing has an effect on reducing adverse drug reactions, hospitalizations and emergency department visits.”

Impact of GeneSight Psychotropic on Response to Psychotropic Treatment in Outpatients Suffering From a Major Depressive Disorder (MDD) and Having Had an Inadequate Response to at Least One Psychotropic Medication Included in GeneSight Psychotropic (RCT) NCT02109939. University of Michigan and AssureRx Health Inc. Available at: https://clinicaltrials.gov/ct2/show/NCT02109939.

“Evaluate the impact of GeneSight Psychotropic on response to psychotropic treatment as judged by the mean change in the 17-item Hamilton Depression (HAM-D17) score from baseline to end of Week 8 of the study.”

**CMS National Coverage Determinations (NCDs):**

No NCDs identified as of the writing of this policy.

**Local coverage determinations (LCDs):**

No LCDs identified as of the writing of this policy.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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<th>CPT Code</th>
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<tr>
<td>81479</td>
<td>Unlisted molecular pathology procedure</td>
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<table>
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<td>F41.8</td>
<td>Anxiety depression</td>
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<tr>
<td>F28</td>
<td>Other psychotic disorder not due to substance or physiologic disorder</td>
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<table>
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