# Genetic Testing for Diagnosis and Management of Mental Health Conditions

**Policy #** 00402
Original Effective Date: 01/15/2014
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*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

*Note: Cytochrome p450 Genotyping is addressed separately in medical policy 00169.*

*Note: Genetic Testing for Tamoxifen Treatment is addressed separately in medical policy 00269.*

# Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers genetic testing for diagnosis and management of mental health disorders in all situations, including but not limited to the following to be **investigational:***

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

Based on review of available data, the Company considers genetic testing panels for mental health disorders, including but not limited to the Genecept™‡ Assay, STA$^2$R test, the GeneSight®‡ Psychotropic panel, the Proove Opioid Risk assay, and the Mental Health DNA Insight panel for all indications to be **investigational.***

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# Background/Overview

This evidence review assesses whether genetic testing for the diagnosis and management of mental health conditions is clinically useful. To make a clinical management decision that improves the net health outcome; the balance of benefits and harms must be better when the test is used to manage the condition than when another test or no test is used. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

The primary goal of pharmacogenomics testing and personalized medicine is to achieve better clinical outcomes compared to managing the condition with the standard of care. Drug response varies greatly between individuals, and genetic factors are known to play a role. However, in most cases, the genetic variation only explains a modest portion of the variance in the individual response because clinical outcomes are also affected by a wide variety of factors including alternate pathways of metabolism and patient- and disease-related factors that may affect absorption, distribution, and elimination of the drug.

Therefore, assessment of clinical utility of a pharmacogenetic test cannot be made by a chain of evidence from clinical validity data alone. In such cases, evidence evaluation requires studies that directly demonstrate that the use of the pharmacogenomic test to make management decisions alters clinical outcomes; it is not sufficient to demonstrate that the test predicts a disorder or a phenotype. Direct evidence of clinical utility is provided by studies that compare health outcomes for patients managed with or without the test. Because these are intervention studies, the preferred evidence of from randomized controlled trials.

**Study Selection Criteria**

- We sought randomized controlled trials that reported the outcomes of pharmacogenetic testing to diagnose, assess the risk of developing, or to manage a mental health condition.
- We sought evidence on outcomes, with emphasis on efficacy outcomes, as the main purpose of genetic testing in mental health conditions is to achieve clinically meaningful improvement compared with standard of care.
- We also included studies that reported only on adverse events, although for medications where adverse events tend to be mild, efficacy outcomes are of greater importance.

- The specific patient indications, interventions, comparators and outcome measures of interest for each indication are described in the clinical context section.

# FDA or Other Governmental Regulatory Approval

**U.S. Food and Drug Administration (FDA)**

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. The tests discussed in this section are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. FDA has chosen not to require any regulatory review of this test.

Examples of commercially available panels include the following:

- Genecept Assay (Genomind);
- STA$^2$R test (SureGene Test for Antipsychotic and Antidepressant Response; Clinical Reference Laboratory). Specific variants included in the panel were not easily identified from the manufacturer's website.
- GeneSight Psychotropic panel (Assurex Health);
- Mental Health DNA Insight™‡ panel (Pathway Genomics);
- IDgenetix-branded tests (AltheaDx).

Also, many labs offer genetic testing for individual genes, including *MTFHR* (GeneSight Rx and other laboratories), *CYP450* variants, and *SULT4A1*.

AltheaDx offers a number of IDgenetix-branded tests, which include several panels focusing on variants that affect medication pharmacokinetics for a variety of disorders, including psychiatric disorders.

# Rationale/Source

This evidence review assesses whether genetic testing for the diagnosis and management of mental health conditions is clinically useful. To make a clinical management decision that improves the net health outcome; the balance of benefits and harms must be better when the test is used to manage

the condition than when another test or no test is used. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

The primary goal of pharmacogenomics testing and personalized medicine is to achieve better clinical outcomes compared to managing the condition with the standard of care. Drug response varies greatly between individuals, and genetic factors are known to play a role. However, in most cases, the genetic variation only explains a modest portion of the variance in the individual response because clinical outcomes are also affected by a wide variety of factors including alternate pathways of metabolism and patient- and disease-related factors that may affect absorption, distribution, and elimination of the drug.

Therefore, assessment of clinical utility of a pharmacogenomic test cannot be made by a chain of evidence from clinical validity data alone. In such cases, evidence evaluation requires studies that directly demonstrate that the use of the pharmacogenomic test to make management decisions alters clinical outcomes; it is not sufficient to demonstrate that the test predicts a disorder or a phenotype. Direct evidence of clinical utility is provided by studies that compare health outcomes for patients managed with or without the test. Because these are intervention studies, the preferred evidence of from randomized controlled trials.

Individual genes have been shown to be associated with the 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.

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 (cohort, case-control, genome-wide association study). Relevant outcomes are changes in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. Most studies evaluated the association between genotype and mental health disorders or gene-drug interactions among patients with risk for mental health conditions. 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 adult patients with major depressive disorder who have had inadequate response to antidepressant therapy who receive GeneSight testing guided drug treatment, the evidence includes 2 randomized controlled trials (RCT). Relevant outcomes are symptoms, changes in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The 2 RCTs compared response (≥50% decrease in HAM-D17) and remission (HAMD-17≤7) with antidepressant therapy informed by GeneSight test results to standard of care (SOC)—antidepressant therapy selected without GeneSight test results. The Genomics Used to Improve DEpression Decisions (GUIDED) trial by Greden *et al* (2019) reported statistically significant improvement in response (26% of 560 vs 20% of 607, p=0.01) and remission (15% of 560 vs 10% of 607, p=0.007) in the GeneSight arm compared to SOC at 8 weeks among patients with MDD using per protocol analysis. Per protocol cohort excluded 401 (22%) of 1799 randomized patients, and additional 231 patients from the per protocol cohort did not complete the study through the blinded week 8 endpoint. The extent of missing data following randomization (35%) precludes conclusions on outcomes at 8 weeks. In the small single center study by Winner *et al* (2013), depression outcomes did not differ significantly between guided care and SOC groups at the 10-week follow-up and the study was underpowered to detect significant differences in outcomes between study arms. None of these trials provided adequate evidence. Both studies have major limitations in design and conduct and in consistency and precision. The evidence is insufficient to determine the effects of the technology on health outcomes.

For adult patients with major depressive disorder who have had inadequate response to antidepressant therapy who receive NeuroIDgenetix®‡ testing guided drug treatment, the evidence includes 2 randomized controlled trials (RCT). Relevant outcomes are symptoms, changes in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. Bradley *et al* (2018) conducted a double-blind RCT among patients with MDD and reported statistically significant improvement in response (≥50% decrease in HAM-D17) in the NeuroIDgenetix arm (64% of 140) compared to SOC (46% of 121) at 12 weeks among moderate and severe group of patients (p=0.01) and significant improvement in remission (HAMD-17≤7) in the NeuroIDgenetix arm (35% of 40) compared to SOC (13% of 53) at 12 weeks among severe group of patients only (p=0.02). There was evidence suggesting selective reporting, as remission was reported for only those with severe depression and contrary to the listing in clinicaltrials.gov adverse drug events was not reported as the primary outcome. It was unclear if the analysis was based on intention-to-treat population and there was high loss to follow-up (15%). In the RCT conducted by Olson *et al* (2017), among patients with neuropsychiatric disorders those receiving

SOC reported significantly more adverse events (53%) than those receiving NeuroIDgenetix guided care (28%), however, the study did not report the number of patients included in this analysis. The study did not describe the randomization procedure and in ClinicalTrials.gov neurocognitive measures were listed as co-primary outcomes, which were not reported, suggesting possible selective reporting. None of these trials provided adequate evidence. The Olson et al (2017) study had major relevance limitations and both the studies have major limitations in design and conduct and in consistency and precision. The evidence is insufficient to determine the effects of the technology on health outcomes.

For adult patients with major depressive disorder who have had inadequate response to antidepressant therapy who receive Neuropharmagen®‡ testing guided drug treatment, the evidence includes 2 randomized controlled trials (RCT). Relevant outcomes are symptoms, changes in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The 2 RCTs compared response (≥50% decrease in HAM-D17) and remission (HAMD-17≤7) with antidepressant therapy informed by Neuropharmagen test results to standard of care (SOC)—antidepressant therapy selected without Neuropharmagen test results. The single-blinded RCT by Han *et al* (2018) reported statistically significant improvement in response (72% of 52 vs 44% of 48, p=0.01) and not statistically significant improvement in remission (46% of 52 vs 26% of 48, p=0.07) in the Neuropharmagen arm compared to SOC at 8 weeks among patients with MDD. The study reported early dropout of 25% in guided-care and 38% in the standard care arm and used last observation carried forward (LOCF) approach in intention to treat analysis of effectiveness. Use of LOCF assumes data are missing completely at random (MCAR), which is unlikely to hold in this analysis. Also, the study did not report registration in any clinical trial database. The single-blinded RCT by Perez *et al* (2017) reported statistically not significant improvement in response (45% of 141 vs 40% of 139, p=0.39) and remission (34% of 141 vs 33% of 139, p=0.87) in the Neuropharmagen arm compared to SOC at 12 weeks among patients with MDD. Response and remission data were missing for 9% patients in the guided care group and 14% of the standard care group. None of these trials provided adequate evidence. Both studies have major limitations in design and conduct and in consistency and precision. 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 a systematic review and meta-analysis and RCTs

evaluating associations between specific genes and outcomes of drug treatment. 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 and meta-analysis by Hartwell *et al* (2020) included 7 RCTs and reported no significant moderating effect of rs1799971, a single nucleotide polymorphism (SNP) that encodes a non-synonymous substitution (Asn40Asp) in the mu-opioid receptor gene, *OPRM1* on response to naltrexone treatment of alcohol use disorder. Bradley *et al* (2018) conducted a double-blind RCT among patients with anxiety disorders and reported statistically significant improvement in response (≥50% decrease in HAM-A17) in the NeuroIDgenetix arm (63% of 82) compared to SOC (50% of 95) at 12 weeks among moderate and severe group of patients (p=0.04). There was evidence suggesting selective reporting, as anxiety remission was not reported and contrary to the listing in clinicaltrials.gov adverse drug events was not reported as the primary outcome. It was unclear if the analysis was based on intention-to-treat population and among the randomized moderate and severe anxiety patients with only anxiety, 25% in the experimental arm and 17% in the standard care arm were lost to follow up over the 12 week period. The evidence is insufficient to determine the effects of the technology on health outcomes.

# Supplemental Information

**Practice Guidelines and Position Statements**

**Clinical Pharmacogenetics Implementation Consortium**

In 2009, the Clinical Pharmacogenetics Implementation Consortium (CPIC) was established to develop practice guidelines on the use of genetic laboratory results to inform prescribing decisions. The panel consists of experts from the U. S., Europe, and Asia.

In 2015, the CPIC conducted a systematic literature review on the influence of *CYP2D6* and *CYP2C19* genotyping on selective serotonin reuptake inhibitor (SSRI) therapy. The CPIC provided dosing recommendations for SSRIs based on phenotypes that classified patients as ultrarapid metabolizers, extensive metabolizers, intermediate metabolizers, and poor metabolizers. However, CPIC noted that patients on an effective and stable dose of SSRIs would not benefit from dose modifications based on *CYP2D6* and *CYP2C19* genotype results. Additionally, CPIC asserted that genetic testing is only one factor among several clinical factors that should be considered when determining a therapeutic approach.

In 2016, the CPIC conducted a systematic literature review of the influence of *CYP2D6* and *CYP2C19* genotype on the dosing of tricyclic antidepressants. Dosing recommendations for tricyclic antidepressants were provided, based on patient classifications of ultrarapid metabolizers, extensive metabolizers, intermediate metabolizers, and poor metabolizers.

**Table 1. Dosing Recommendations for Antidepressants Based on *CYP2D6* and *CYP2C19* Phenotype**

| **Recommendations for Tricyclic Antidepressants** | | | | |
|---|---|---|---|---|
| **Phenotype** | **Implications** | **Recommendation** | **Class of recommendation for amitriptyline and nortripyline** | **Class of recommendation for other TCAs[a]** |
| *CYP2D6* ultrarapid metabolizer | Increased metabolism to less active compound results in lower plasma concentrations of active drug and decreased probability of drug effectiveness. | Avoid TCA due to potential lack of efficacy. If TCA warranted, consider higher dose with monitoring to guide dose adjustments. | strong | optional |
| *CYP2D6* rapid metabolizer | Normal metabolism of TCAs | Initiate TCA with recommended steady-state dose. | strong | strong |
| *CYP2D6* intermediate metabolizer | Reduced metabolism | Consider 25% reduced starting | moderate | optional |

| | | | | |
|---|---|---|---|---|
| | to less active compound results in higher plasma concentrations of active drug and increased probability of side effects. | dose with monitoring to guide dose adjustments. | | |
| *CYP2D6* poor metabolizer | Greatly reduced metabolism to less active compound results in higher plasma concentrations of active drug and increased probability of side effects. | Avoid TCA due to potential side effects. If TCA is warranted, consider 50% reduced starting dose with monitoring to guide dose adjustments. | strong | optional |
| **Recommendations for Tertiary Amines Amytriptyline, Clomipramine, Doxepin, Imipramine, and Trimipramine** | | | | |
| **Phenotype** | **Implications** | **Recommendation** | **Class of recommendation for amitriptyline** | **Class of recommendation for other tertiary amine TCAs** |

| | | | | |
|---|---|---|---|---|
| *CYP2C19* ultrarapid and rapid metabolizer | Increased metabolism of tertiary amines to secondary amines may affect efficacy and side effects | Avoid tertiary amines due to potential sub-optimal response. Consider secondary amines. If tertiary amines warranted, use monitoring to guide dose adjustments. | optional | optional |
| *CYP2C19* normal metabolizer | Normal metabolism of tertiary amines | Initiate tertiary amine with recommended steady-state dose. | strong | strong |
| *CYP2C19* intermediate metabolizer | Reduced metabolism of tertiary amines | Initiate tertiary amine with recommended steady-state dose. | strong | optional |
| *CYP2C19* poor metabolizer | Greatly reduced metabolism of tertiary amines to secondary amines may affect efficacy and side effects | Avoid tertiary amines due to potential sub-optimal response. Consider secondary amines. If tertiary amines warranted, consider 50% reduced starting dose with | moderate | optional |

| | | | | |
|---|---|---|---|---|
| | | monitoring to guide dose adjustments. | | |

[a] There is less clinical and pharmacokinetic evidence to support genotype-guided dose adjustments for TCAs other than amitriptyline or nortriptyline, though it may be reasonable to apply the same recommendations.

TCA: tricyclic antidepressants.

**Table 2. Dosing Recommendations for Amitriptyline Based on Both *CYP2D6* and *CYP2C19* Phenotypes[a,b]**

| **Phenotype** | ***CYP2D6* ultrarapid metabolizer** | ***CYP2D6* normal metabolizer** | ***CYP2D6* intermediate metabolizer** | ***CYP2D6* poor metabolizer** |
|---|---|---|---|---|
| *CYP2C19* ultrarapid or rapid metabolizer | Avoid amitryptyline, (optional) | Consider alternative drug. (optional) | Consider alternative drug. (optional) | Avoid amitryptyline. (optional) |
| *CYP2C19* normal metabolizer | Avoid amitryptyline. If amitryptyline is warranted, consider higher target dose, (strong) | Initiate therapy with recommended starting dose. (strong) | Consider 25% reduction of recommended starting dose. (moderate) | Avoid amitryptyline. If amitryptyline is warranted, consider 50% reduction of recommended starting dose. (strong) |

| | | | | |
|---|---|---|---|---|
| *CYP2C19* intermediate metabolizer | Avoid amitryptyline. (optional) | Initiate therapy with recommended starting dose. (strong) | Consider 25% reduction of recommended starting dose.(optional) | Avoid amitryptyline. If amitryptyline is warranted, consider 50% reduction of recommended starting dose. (optional) |
| *CYP2C19* poor metabolizer | Avoid amitryptyline. (optional) | Avoid amitryptyline. If amitryptyline is warranted, consider 50% reduction of recommended starting dose. (moderate) | Avoid amitryptyline. (optional) | Avoid amitryptyline. (optional) |

[a] classification of recommendation appears in parenthesis after every recommendation
[b] Recommendations from studies focused on amitryptyline; however, since tricyclic antidepressants have comparable pharmacokinetic properties, these guidelines may apply to other tertiary amines.

**Evaluation of Genomic Applications in Practice and Prevention**
In 2007, the EGAPP Working Group commissioned the Agency for Healthcare Research and Quality to conduct a systematic review on *CYP450* testing in patients receiving SSRIs. Based on results from the review, EGAPP "found insufficient evidence to support a recommendation for or against use of CYP450 testing in adults beginning SSRI treatment for non-psychotic depression. In the absence of supporting evidence, and with consideration of other contextual issues, EGAPP discourages use of CYP450 testing for patients beginning SSRI treatment until further clinical trials are complete."

**International Society of Psychiatric Genetics**
In 2018, the International Society of Psychiatric Genetics published a review and recommendations from its Residency Education Committee regarding genetic issues relevant to psychiatric training programs. The Committee only recommends genetic testing as part of a diagnostic workup for patients with autism spectrum disorders or intellectual disability. In regards to pharmacogenetic testing, the Committee states that the "efficacy of these pharmacogenomic profiles requires further investigation in controlled studies."

**U.S. Preventive Services Task Force Recommendations**
Not applicable.

**Medicare National Coverage**
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**Ongoing and Unpublished Clinical Trials**
Some currently ongoing and unpublished trials that might influence this policy are listed in Table 3.

**Table 3. Summary of Key Trials**

| NCT Number | Title | Enrollment | Completion Date |
|---|---|---|---|
| *Ongoing* | | | |
| NCT04207385 | Accurate Clinical Study of Medication in Patients With Depression Via Pharmacogenomics (PGx) and Therapeutic Drug Monitoring (TDM) of Venlafaxine | 160 | November 20, 2021 |
| NCT03952494 | Individualizing Antidepressant Treatment Using Pharmacogenomics and EHR-driven Clinical Decision Support | 500 | April 30, 2021 |

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|---|---|---|---|
| NCT03907124 | Clinical Utility of Pharmacogenomics of Psychotropic Medications | 60 | February 1, 2021 |
| NCT03749629 | Comparative Effectiveness of Pharmacogenomics for Treatment of Depression | 400 | February 28, 2022 |
| NCT03674138 | Pharmacogenomic-Guided Antidepressant Drug Prescribing in Cancer Patients | 300 | December 10, 2021 |
| NCT03591224[a] | Pharmacogenomic Testing to Optimize Antidepressant Drug Therapy | 200 | April 17, 2019 |
| NCT03537547[a] | Combinatorial Pharmacogenomics Testing in Treatment-NaÃ¯ve Major Depressive Disorder | 120 | May 31, 2021 |
| NCT03302364 | A Research in Pharmacogenomics and Accurate Medication of Risperidone | 800 | June 1, 2020 |
| NCT03228953 | Pharmacogenomic Testing in Major Depressive Disorder | 206 | May 15, 2021 |
| NCT02573168[a] | Pharmacogenomic Decision Support With GeneSight Psychotropic to Guide the Treatment of Schizophrenia/Schizoaffective Disorder | 531 | September 1, 2020 |
| NCT03270891 | | | |
| *Unpublished* | | | |
| NCT02497027 | Pharmacogenetic Testing in an Outpatient Population of Patients With Depression | 83 | April 1, 2017 |

| | | | |
|---|---|---|---|
| NCT02474680 | Evaluation of Pharmacogenetic Testing In a Mental Health Population and Economic Outcomes | 84 | January 1, 2017 |
| NCT02479464 | Clinical Impact of the Antidepressant Pharmacogenomic Algorithm in an Outpatient Therapy-based Clinical Setting | 60 | August 1, 2014 |
| NCT02466477[a] | Pharmacogenomic Decision Support With GeneSight Psychotropic to Guide the Treatment of Major Depressive Disorder | 570 | September 1, 2019 |
| NCT02443584 | Pharmacogenetic Testing on an Outpatient Population With a Depression Diagnosis | 84 | April 1, 2017 |
| NCT01610063 | Evaluation of an Antidepressant Pharmacogenomic Algorithm in an Outpatient Clinical Setting | 227 | May 1, 2013 |
| NCT01261364 | Pharmacogenetic-Directed Treatment for Major Depression | 50 | September 1, 2011 |
| NCT02855580 | Integrating Pharmacogenomic Testing Into a Child Psychiatry Clinic | 71 | July 6, 2017 |

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Current Effective Date: 11/09/2020

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|---|---|
| 01/09/2014 | Medical Policy Committee review |
| 01/15/2014 | Medical Policy Implementation Committee approval. New policy. |
| 08/07/2014 | Medical Policy Committee review |
| 08/20/2014 | Medical Policy Implementation Committee approval. Title changed from Genecept Assay to Genetic Testing for Mental Health Conditions. Entire policy rewritten to track BCBSA. |
| 08/06/2015 | Medical Policy Committee review |
| 08/19/2015 | Medical Policy Implementation Committee approval. Policy statements changed to clarify which categories of genetic testing the policy addresses. |
| 08/04/2016 | Medical Policy Committee review |
| 08/17/2016 | Medical Policy Implementation Committee approval . No change to coverage. |
| 01/01/2017 | Coding update: Removing ICD-9 Diagnosis Codes |
| 08/03/2017 | Medical Policy Committee review |
| 08/23/2017 | Medical Policy Implementation Committee approval . No change to coverage. |
| 08/09/2018 | Medical Policy Committee review |
| 08/15/2018 | Medical Policy Implementation Committee approval. Policy statements changed to specify drugs used to treat mental health conditions (SSRIs, SNRIs, tricyclic antidepressants, and antipsychotic drugs). Title changed to "Genetic Testing for Diagnosis and Management of Mental Health Conditions." |
| 08/01/2019 | Medical Policy Committee review |
| 08/14/2019 | Medical Policy Implementation Committee approval. No change to coverage. |
| 10/01/2020 | Medical Policy Committee review |
| 10/07/2020 | Medical Policy Implementation Committee approval. No change to coverage. |

Next Scheduled Review Date: 10/2021

# Coding

*The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2019 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of*

*descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.*

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

| Code Type | Code |
|---|---|
| CPT | 0029U, 0031U, 0032U, 0033U, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U, 81225, 81226, 81230, 81231, 81291, 81401, 81479<br>Add codes eff 7/1/2020: 0173U, 0175U |
| HCPCS | No codes |
| ICD-10 Diagnosis | All related diagnoses |

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

**NOTICE:** If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.