

Local Coverage Determination (LCD): MoIDX: GeneSight® Assay for Refractory Depression (L36323)

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Contractor Information

| Contractor Name | Contract Type | Contract Number | Jurisdiction | State(s) |
|--|---------------|-----------------|--------------|--|
| Noridian Healthcare Solutions, LLC | A and B MAC | 01111 - MAC A | J - E | California - Entire State |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01112 - MAC B | J - E | California - Northern |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01182 - MAC B | J - E | California - Southern American Samoa |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01211 - MAC A | J - E | Guam Hawaii Northern Mariana Islands American Samoa |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01212 - MAC B | J - E | Guam Hawaii Northern Mariana Islands |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01311 - MAC A | J - E | Nevada |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01312 - MAC B | J - E | Nevada American Samoa California - Entire State |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01911 - MAC A | J - E | Guam Hawaii Nevada Northern Mariana Islands |

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LCD Information

Document Information

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| LCD ID L36323 | Original Effective Date For services performed on or after 10/01/2015 |
| LCD Title MoIDX: GeneSight® Assay for Refractory Depression | Revision Effective Date For services performed on or after 03/08/2018 |
| Proposed LCD in Comment Period N/A | Revision Ending Date N/A |
| Source Proposed LCD N/A | Retirement Date N/A |
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| | Notice Period End Date N/A |

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CMS National Coverage Policy

Title XVIII of the Social Security Act (the "Act"), Section 1862(a)(1)(A). This section limits coverage and payment to those items and services that are reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Title XVIII of the Social Security Act, Section 1833(e). This section prohibits Medicare payment for any claim that lacks the necessary information to process the claim.

42 C.F.R. § 410.32 "Diagnostic X-ray tests, diagnostic laboratory tests, and other diagnostic tests: Condition."

Medicare Internet Online Manual Pub. 100-2 (Medicare Benefit Policy Manual), Chapter 15, Section 80, "Requirements for Diagnostic X-Ray, Diagnostic Laboratory, and Other Diagnostic Tests"

Medicare Internet Online Manual Pub. 100-4 (Medicare Claims Processing Manual), Chapter 23 (Section 10) "Reporting ICD Diagnosis and Procedure Codes"

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Coverage Indications, Limitations

This LCD provides limited coverage for the GeneSight[®] Psychotropic (AssureRx Health, Inc, Mason, OH) gene panel. GeneSight[®] testing may only be ordered by licensed psychiatrists or neuropsychiatrists contemplating an alteration in neuropsychiatric medication for patients diagnosed with major depressive disorder (MDD) (in accordance with DSM IV/V criteria) who are suffering with refractory moderate to severe depression (based upon DSM-V criteria) after at least one prior neuropsychiatric medication failure.

Note: Provider may have primary boards in internal medicine or neurology and also have boards in psychiatry or neuropsychiatry and the provider has a designated specialty in PECOS as IM/neurology. GeneSight[®] may be ordered, when medically necessary, by these providers and they will affix a KX modifier attesting that they have psychiatry or neuropsychiatry boards. Assurex will maintain the certification and make it available upon request.

Summary of Evidence

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. In multiple prospective clinical studies, the use of GeneSight® to guide neuropsychiatric pharmaceutical selection and prescription has demonstrated an increased patient response to treatment from 60% to 250% (as measured by the standardized 17-item Hamilton Rating Scale for Depression or HAM-17; response is defined as $\geq 50\%$ reduction in HAM-D17 score) versus unguided, empirical treatment (or treatment as usual).

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 make-up 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.

Pine Rest Study

The Pine Rest study was a prospective, patient- and rater-blinded, randomized controlled trial evaluating the clinical impact of GeneSight® on antidepressant selection and treatment outcomes in depressed outpatients (GeneSight®, N=25 vs treatment as usual (TAU), N=24). Patients were assessed for symptom improvement, remission and response from baseline (week 0) and at 2, 4, and 8 weeks, using the HAM-D17 rating.

Subjects in the GeneSight® arm had a greater average decrease in the 17-item Hamilton Rating Scale for Depression (HAM-D17) scores from baseline at 8 weeks ($p = 0.30$) and a higher response rate ($p = 0.055$) and significantly higher remission rate ($p = 0.012$) at any time point. Response rates in the GeneSight®-guided arm were 73% higher compared to the unguided TAU arm. Retrospective analysis of the TAU subjects at the end of the study after un-blinding and stratifying by GeneSight® results proved the clinical validity of GeneSight® with 30% of subjects unknowingly on red bin medications showing a significant worsening of depressive symptoms in contrast to significant improvements in depressive symptoms experienced by 30% of subjects unknowingly on green bin medications ($p = 0.07$). Additionally, surveys from the treating clinicians revealed that the GeneSight® composite report had a significant influence on treatment decisions for 65% of the GeneSight® subjects.

Hamm Study

The Hamm Clinic prospective cohort study with two arms (GeneSight® (n = 22) vs. TAU (n = 22)) enrolled adult patients with a primary diagnosis of major depressive disorder utilizing DSM-IV criteria for depression not otherwise specified. GeneSight® subjects achieved greater reductions in depression symptoms between the baseline and the week 8 visits compared to TAU subjects using the Quick Inventory of Depressive Symptomatology – Clinician version (QIDS-C16) ($p = 0.0024$) and HAM-D17 ($p = 0.042$) ratings. Both the response and remission rate were more than doubled in the GeneSight® arm compared to the TAU arm. Upon unblinding the TAU group at the end of 8 weeks, TAU subjects were being prescribed significantly more red and yellow bin medications and less green bin medications compared to the GeneSight® guided subjects ($p = 0.02$).

La Crosse

In the La Crosse prospective cohort study (GeneSight® (n = 72) vs. TAU (n = 93)) at the Franciscan Skemp Hospital in La Crosse, Wisconsin, patients with a primary diagnosis of MDD or depression not otherwise specified with a minimum score of 14 on HAM-D17 were enrolled. Diagnosis was confirmed by checking the diagnosis reported in the physician clinical notes in the electronic medical record (EMR). Samples were collected at baseline

in both arms, while only the physicians in the GeneSight® arm were provided with test results to inform treatment decisions. In addition to the prospective comparisons, retrospective analysis in the TAU subjects at the end of the study was implemented after un-blinding the GeneSight® results to test for clinical validity.

A greater reduction in depression scores from baseline to the week 8 visit was observed in the GeneSight® arm for all three measures of depression: QIDS-C16 ($p < 0.0001$), HAM-D17 ($p < 0.0001$), and PHQ-9 ($p < 0.0001$). In all measures, a faster reduction of symptoms was observed in the GeneSight® arm subjects compared to the TAU arm subjects (QIDS-C16 and HAM-D17 ($p < 0.0001$), PHQ-9 ($p = 0.002$)). The GeneSight® arm had a significantly higher remission rate based on the QIDS-C16 score ($p = 0.03$), and significantly higher response rates based on QIDS-C16 ($p = 0.005$), HAM-D17 ($p = 0.03$), and PHQ-9 ($p = 0.01$).

Physicians changed medications more often for subjects in the GeneSight®- guided group (57.9%) than the unguided group (25.9%) ($p = 0.0007$). Of the 15 GeneSight® - guided subjects classified in the red bin category at baseline, fourteen (93.3%) experienced a medication change or dose adjustment during the eight week study period, compared with 8 out of 18 subjects in the unguided group (44.4%) in the red bin category ($p = 0.002$). A significant association between bin status and outcome was observed within the unguided group ($p = 0.028$). Subjects classified in the red bin category had less improvement (11%) than those classified in the green or yellow categories (31.9%, $p = 0.047$), further demonstrating the deleterious effects of red bin medications on patient outcomes.

Dayton Study

This retrospective study, in collaboration with Union Health Services (UHS, a staff model HMO located in Chicago, Illinois), examined healthcare utilization in relation to medication categories (binning) using GeneSight®. Ninety-six patients previously diagnosed with a depressive disorder or anxiety disorder and treated with one of the medications included in the GeneSight® panel were included in the study. The GeneSight® bin assignments of patient psychiatric medications were compared to the medical records for patient medication prescriptions, healthcare utilization, medical absence days, and disability claims for the previous 12 months.

Subjects whose medication regimen included a medication in the GeneSight® red bin ("use with caution and more frequent monitoring") had 69% more total healthcare visits ($p = 0.005$), 67% more general medical visits ($p = 0.02$), greater than 3-fold more medical absence days ($p = 0.06$), and greater than 4-fold more disability claims ($p = 0.004$) than subjects taking drugs in the green ("use as directed") or yellow bin ("use with caution"). The mean healthcare utilization cost calculated for red bin subjects during the previous 12 month period was higher at \$8,627, compared to \$3,453 calculated for green bin subjects ($p = 0.024$) and \$3,426 for yellow bin subjects ($p = 0.027$), yielding an average annual increase in healthcare cost of \$5,188 for subjects on GeneSight® red bin medications.

Meta-analysis of GeneSight® Prospective 2-Armed Studies

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.

Analysis of Evidence (Rationale for Determination)

Level of Evidence

Quality of Evidence – Moderate
Strength of Evidence – Moderate
Weight of Evidence - Limited

The evidence of clinical utility to support the use of the GeneSight assay is limited to patients diagnosed with major depressive disorder (MDD) who are suffering with refractory moderate to severe depression (based upon DSM-V criteria) after at least one prior neuropsychiatric medication failure when ordered by a licensed psychiatrist or neuropsychiatrist contemplating an alteration in neuropsychiatric medication. Claims submitted by non-physician providers (NPPs) and physician extenders as "incident to" services will be denied. The GeneSight assay is limited to once in a life-time.

[Coding Information](#)

Bill Type Codes:

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

N/A

Revenue Codes:

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

N/A

CPT/HCPCS Codes

Group 1 Paragraph: N/A

Group 1 Codes:

81479 UNLISTED MOLECULAR PATHOLOGY PROCEDURE

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph: N/A

Group 1 Codes:

ICD-10 Codes

Description

| | |
|--------|--|
| F32.1 | Major depressive disorder, single episode, moderate |
| F32.2 | Major depressive disorder, single episode, severe without psychotic features |
| F32.3 | Major depressive disorder, single episode, severe with psychotic features |
| F32.4 | Major depressive disorder, single episode, in partial remission |
| F32.9 | Major depressive disorder, single episode, unspecified |
| F33.1 | Major depressive disorder, recurrent, moderate |
| F33.2 | Major depressive disorder, recurrent severe without psychotic features |
| F33.3 | Major depressive disorder, recurrent, severe with psychotic symptoms |
| F33.40 | Major depressive disorder, recurrent, in remission, unspecified |
| F33.41 | Major depressive disorder, recurrent, in partial remission |
| F33.9 | Major depressive disorder, recurrent, unspecified |

ICD-10 Codes that DO NOT Support Medical Necessity N/A

ICD-10 Additional Information [Back to Top](#)

[General Information](#)

Associated Information

N/A

Sources of Information

N/A

Bibliography

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Revision History Information

| Revision History Date | Revision History Number | Revision History Explanation | Reason(s) for Change |
|------------------------------|--------------------------------|---|--|
| 03/08/2018 | R4 | Updated LCD for 21st Century Act requirements. | <ul style="list-style-type: none">• Creation of Uniform LCDs With Other MAC Jurisdiction |
| 03/08/2018 | R3 | Replaced "...as defined by the 17-item Hamilton Rating Scale for Depression (HAM-D17) score of 14 or greater..." with "based upon DSM-V criteria" in the first paragraph of Indications and Limitations. Added information relating to physician boards and KX modifier billing requirements. Under Sources of Information, added 2. American Psychiatric Association (APA). Removed the section on documentation requirements. 03/06/2018: At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy. | <ul style="list-style-type: none">• Creation of Uniform LCDs With Other MAC Jurisdiction |
| 11/17/2016 | R2 | This final LCD, effective 10/01/2015, combines JEA L36322 into the JEB LCD L36323 so that both JEA and JEB contract numbers will have the same final MCD LCD number. | <ul style="list-style-type: none">• Creation of Uniform LCDs Within a MAC Jurisdiction |
| 10/01/2015 | R1 | The LCD is revised to add 'or neuropsychiatrists' to Coverage Indications, Limitations section. | <ul style="list-style-type: none">• Reconsideration Request |

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Associated Documents

Attachments N/A

Related Local Coverage Documents Article(s) [A54219](#) - (MCD Archive Site)

Related National Coverage Documents N/A

Public Version(s) Updated on 06/20/2018 with effective dates 03/08/2018 - N/A [Updated on 03/06/2018 with effective dates 03/08/2018 - N/A Updated on 11/13/2016 with effective dates 11/17/2016 - 03/07/2018](#) Some older versions have been archived. Please visit the [MCD Archive Site](#) to retrieve them. [Back to Top](#)

Keywords

- GeneSight
- Assay
- Refractory
- Depression
- 81479

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