Subject: Pharmacogenomics Testing, Behavioral Health for Medicare

Medical Policy #: 30.0

Original Effective Date: 01/23/2019

Status: Reviewed

Last Annual Review Date: 05/22/2024

Disclaimer

Refer to the member's specific benefit plan and Schedule of Benefits to determine coverage. This may not be a benefit on all plans or the plan may have broader or more limited benefits than those listed in this Medical Policy.

Description

This is a limited coverage policy for pharmacogenomics testing (PGx) including single gene, multi-gene panels, and combinatorial tests.

PGx tests must demonstrate analytical validity, clinical validity, and clinical utility to be considered reasonable and necessary for coverage. This is demonstrated through a required technical assessment of the test. PGx Tests are considered germline tests and must adhere to other relevant germline testing policies published by this contractor.

Coverage Determination

Prior Authorization is required. Logon to Pres Online to submit a request: https://ds.phs.org/preslogin/index.jsp

Not covered for Medicaid and Commercial, it is considered investigational and not a covered benefit.

For Medicare, PHP follows Novitas LCD Pharmacogenomics Testing (L39063) and related article LCA (A58801).

Coverage for IDgenetix (code 0411U) maybe reviewed on a case-by-case basis for Medicare. IDgenetix is considered investigational for commercial and Medicaid.

Coverage for GeneSight® Psychotropic, Assurex Health, Inc, Myriad Genetics, Inc (code 0345U) is considered investigational for Medicare, Commercial and Medicaid.

**Testing should not be the sole basis for clinical decision-making regarding Rx.

Coding

The coding listed in this medical policy is for reference only. Covered and non-covered codes are within this list.

Please visit the prior authorization for consideration of other test(s) which may not be listed in this table. Not all test(s) meet coverage described in this policy, those test(s) will be considered on a case-by-case basis.

CPT Codes	Description
81479	Unlisted Molecular Pathology Procedure
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (EG, cystic fibrosis) gene analysis; common variants (EG, ACMG/ACOG guidelines) (Prior authorization is not required)
81225	Gene CYP2C19 (cytochrome p450, family 2, subfamily c, polypeptide 19) (EG, drug metabolism), gene analysis, common variants (EG, *2, *3, *4, *8, *17)
81226	CYP2D6 (cytochrome p450, family 2, subfamily d, polypeptide 6) (eg, drug metabolism), gene analysis, common variants (EG, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)
81227	CYP2C9 (cytochrome p450, family 2, subfamily c, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (EG, *2, *3, *5, *6)
81231	CYP3A5 (cytochrome p450 family 3 subfamily a member 5) (eg, drug metabolism), gene analysis, common variants (EG, *2, *3, *4, *5, *6, *7)
81232	DPYD (dihydropyrimidine dehydrogenase) (EG, 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (EG, *2A, *4, *5, *6)

CPT Codes	Description
81247	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (EG, A, A-)
81283	IFNL3 (interferon, lambda 3) (EG, drug response), gene analysis, RS12979860 variant
81306	NUDT15 (NUDIX HYDROLASE 15) (EG, DRUG METABOLISM) GENE ANALYSIS, COMMON VARIANT(S) (EG, *2, *3, *4, *5, *6) (Prior Authorization is not required)
81328	SLCO1B1 (SOLUTE CARRIER ORGANIC ANION TRANSPORTER FAMILY, MEMBER 1B1) (EG, ADVERSE DRUG REACTION), GENE ANALYSIS, COMMON VARIANT(S) (EG, *5)
81335	TPMT (THIOPURINE S-METHYLTRANSFERASE) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3)
81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide a1) (eg, drug metabolism, hereditary unconjugated hyperbilirubinemia [gilbert syndrome]) gene analysis, common variants (EG, *28, *36, *37)
81374	HLA CLASS I TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); ONE ANTIGEN EQUIVALENT (EG, B*27), EACH
81381	HLA CLASS I TYPING, HIGH RESOLUTION (IE, ALLELES OR ALLELE GROUPS); ONE ALLELE OR ALLELE GROUP (EG, B*57:01P), EACH
81406	MOLECULAR PATHOLOGY PROCEDURE, LEVEL 7 (EG, ANALYSIS OF 11-25 EXONS BY DNA SEQUENCE ANALYSIS, MUTATION SCANNING OR DUPLICATION/DELETION VARIANTS OF 26-50 EXONS, CYTOGENOMIC ARRAY ANALYSIS FOR NEOPLASIA)
81418	Drug metabolism (eg, pharmacogenomics) genomic sequence analysis panel, must include testing of at least 6 genes, including CYP2C19, CYP2D6, and CYP2D6 duplication/deletion analysis
0070U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, common and select rare variants (ie, *2, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14A, *14B, *15, *17, *29, *35, *36, *41, *57, *61, *63, *68, *83, *xN)
0071U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, full gene sequence (List separately in addition to code for primary procedure)
0072U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D6-2D7 hybrid gene) (List separately in addition to code for primary procedure)
0073U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D7-2D6 hybrid gene) (List separately in addition to code for primary procedure)
0074U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, non-duplicated gene when duplication/multiplication is trans) (List separately in addition to code for primary procedure)
0075U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 5' gene duplication/multiplication) (List separately in addition to code for primary procedure)
0076U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 3' gene duplication/multiplication) (List separately in addition to code for primary procedure)
0193U	Red cell antigen (JR blood group) genotyping (JR), gene analysis, ABCG2 (ATP binding cassette subfamily G member 2 [Junior blood group]) exons 2-26
0286U	CEP72 (CENTROSOMAL PROTEIN, 72-KDA), NUDT15 (NUDIX HYDROLASE 15) AND TPMT (THIOPURINE S-METHYLTRANSFERASE) (EG, DRUG METABOLISM) GENE ANALYSIS, COMMON VARIANTS

CPT Codes	Description
0411U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6 Includes: IDgenetix®, Castle Biosciences, Inc, Castle Biosciences, Inc
81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
0392U	Drug metabolism (depression, anxiety, attention deficit hyperactivity disorder [ADHD]), gene-drug interactions, variant analysis of 16 genes, including deletion/duplication analysis of CYP2D6, reported as impact of gene-drug interaction for each drug Includes: Medication Management Neuropsychiatric Panel, RCA Laboratory Services LLC d/b/a GENETWORx, GENETWORx
0423U	Psychiatry (eg, depression, anxiety), genomic analysis panel, including variant analysis of 26 genes, buccal swab, report including metabolizer status and risk of drug toxicity by condition Includes: Genomind® Pharmacogenetics Report - Full, Genomind®, Inc, Genomind®, Inc

CPT codes	NON-Covered for pharmacogenomic testing:
81230	Cyp3a4 gene common variants
81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (EG, warfarin metabolism), gene analysis, common variant(s) (EG, -1639G>A, C.173+1000C>T)
81407	MOLECULAR PATHOLOGY PROCEDURE LEVEL 8
0029U	DRUG METABOLISM (ADVERSE DRUG REACTIONS AND DRUG RESPONSE), TARGETED SEQUENCE ANALYSIS (IE, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 AND RS12777823)
0031U	CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7)
0032U	COMT (catechol-O-methyltransferase)(drug metabolism) gene analysis, c.472G>A (rs4680) variant
0033U	HTR2A (5-hydroxytryptamine receptor 2A), HTR2C (5-hydroxytryptamine receptor 2C) (eg, citalopram metabolism) gene analysis, common variants (ie, HTR2A rs7997012 [c.614-2211T>C], HTR2C rs3813929 [c.-759C>T] and rs1414334 [c.551-3008C>G])
0173U	Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes
0345U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6 Includes: GeneSight® Psychotropic, Assurex Health, Inc, Myriad Genetics, Inc

Reviewed by / Approval Signatures

Population Health & Clinical Quality Committee (PHCQC): Gray Clarke MD
Medical Director: Ana Maria Rael MD
Date Approved: 05-22-2024
Reviewed by:

Not every Presbyterian health plan contains the same benefits. Please refer to the member's specific benefit plan and Schedule of Benefits to determine coverage [MPMPPC051001].

1. Gray Clarke, MD, Senior Medical Director, VP-Chief Medical Officer-PHP Administration
2. Anjali Yeolekar-Dasari, Medical Director Behavior Health

References

1. Local Coverage Determination by Novitas LCD Pharmacogenomics Testing (L39063), December 12, 2021, updated 10-22-2021; Related article LCA (A58801), Date 01/01/2024, R10 [Cited 01/19/2024]
2. Hayes, TractManager Company, GeneSight Psychotropic (Assurex Health Inc./Myriad Neuroscience), Molecular Test Assessment Sep 10, 2021 Annual Review Nov 13, 2023. [Cited 04/25/2024]
3. Hayes, Tract Manger Company, Pharmacogenomic Testing of Selected Mental Health Conditions, Clinical Utility Evaluation Dec 06, 2021Annual review: Dec 01, 2023. [Cited 04-25-2024]
4. Hayes, Pharmacogenomic Testing for Attention-Deficit/Hyperactivity Disorder Treatment, clinical Utility Evaluation Jan 12, 2022, Annual review: Feb 27, 2024 [Cited 04/25/2024]
5. Hayes, Pharmacogenetic and Pharmacogenomic Testing to Improve Outcomes Related to Opioid Use Disorder, Clinical Utility Evaluation, Apr 27, 2020, Annual Review: June 30, 2023 [Cited 04/25/2024]
6. Hayes, Pharmacogenetic and Pharmacogenomic Testing for Opioid Treatment for Pain in Adults – Selected Single-Gene Variants and Pharmacogenomic Panels, Clinical Utility Eval: Dec 11, 2019, Annual review Oct 26, 2022 [Cited]
7. Hayes, Pharmacogenetic and Pharmacogenomic Testing for Opioid Treatment for Pain -OPRM1 and COMT Variants – Clinical Utility Evaluation Dec 3, 2019 | Annual Review: Oct 24, 2022 [Cited 04/25/2024]
8. Aetna, Pharmacogenetic and Pharmacodynamic Testing, number: 0715, Effective: 09-16-2005, Next review: 08/08/2024 [Cited 04/25/2024]
9. Local Coverage Determination by Novitas LCD (L35062) Biomarkers Overview, revision date: 12/12/2021, R22; and related LCA (A58917), last updated 10-01-2023. [Cited 01/19/2024]
10. Local Coverage Determination by WPS, MolDX: Pharmacogenomics Testing, LCD (L38435), updated: 08/23/2023, R4 [Cited 04/25/2024]
11. MCG, Behavioral Health Medication Pharmacogenetics – Gene Panels- ACG: A-0861 (AC), 28th Edition, Last Update: 3/14/2024. [Cited 04/25/2024]

Publication History

01-23-2019 Policy created

05-20-2020 Annual review. Reviewed by Dr. Clark then PHP. Medical Policy Committee on 04-16-2020. Also, other payers were reviewed, and all consider GeneSight Testing as investigational. Agreed, PHP will continue coverage for Medicare only using LCD L36799, therefore no change to policy. Prior authorization is required.

05-26-2021 Annual review. Reviewed by PHP Medical Policy Committee on 05/14/2021. CMS announced the retirement of the LCD GeneSight Assay for Refractory Depression, (LCD L36799) because the language conflicted with and is superseded by Wisconsin Physicians, LCD L38435 MolDX: Pharmacogenomics Testing and policy Article LCA A58395. Due to this change the following was decided:

- Removed the retired LCD GeneSight Assay for Refractory Depression, (LCD L36799) from policy.
- PHP will now follow Wisconsin Physicians, LCD L38435 MolDX: Pharmacogenomics Testing and policy Article LCA A5839 for Medicare.
- Continue no coverage for Medicaid and Commercial, since it's considered investigational and is not a covered benefit
- Title changed from "Genesight Assay for Refractory Major Depression, for Medicare" to "Pharmacogenomics Testing for Behavioral Health".
- Add new CPT codes: 81374, 81381, 81479, 81225, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U. These codes will require prior authorization for all LOB
- All the CPT codes listed in Pharmacogenomics Testing (A58395) will be listed on the PA grid as well.

05-25-2022 Annual review. Reviewed by PHP Medical Policy Committee on 04/08/2022. Coverage will continue for Medicare only. Change: Removed to follow Wisconsin, Pharmacogenomics Testing LCD L38435 and will now follow the newly released Novitas LCD Pharmacogenomics Testing LCD (L39063) and related LCA (A58801). Novitas LCA (A58801) does not list code: 0030U which will be listed in MPM 7.1. New codes added to policy: 0286U, 81230, 81346, 81407, 81408, 0029U, 0031U, 0032U, 0033U, 0117U, 0173U, 0175U, 0289U, 0290U, 0291U, 0292U, 0293U and 0294U. All of these codes will require PA after adding: 0286U, 0117U, 0173U, 0175U, 0289U, 0290U, 0291U, 0292U, 0293U and 0294U to the PA grid.

05-24-2023 Annual review. Reviewed by PHP Medical Policy Committee on 03-29-2023. Coverage will continue for Medicare only. Continue to follow Novitas LCD Pharmacogenomics Testing LCD (L39063) and related LCA (A58801). Added codes (81418 and 0193U) to policy. Codes 81418 and 0193U and previously listed code 81306 will require PA for ALOB. Code 81220 (cystic fibrosis) will continue to not require PA as per our response to HSD.

Update on 02/07/2024:

Test **IDgenetix** code (0411U) will be covered for Medicare and PA will continue to be required. Coverage language added "IDgenetix maybe reviewed on a case-by-case basis for Medicare". The test name and code is not mentioned in Pharmacogenomics Testing LCA (A58801), but are mentioned in Novitas, Biomarkers Overview LCD (L35062) & LCA (A58917) and WPS, MolDX: Repeat Germline Testing LCD (L38429) & related LCA (A57100). IDgenetix is considered experimental for commercial and Medicaid and code 0411U) and will be

	configured as investigation and the PA requirement will be removed for non-Medicare. Code (0411U) was moved from MPM 7.1 and added code to this policy. Other update that was erroneously left out during review date 05-25-22: For all LOBs the following code 81335 will be configured to allow Rheumatology and Gastroenterologist to by-pass PA requirement and all other specialties will continue to require PA.
05-22-2024	Annual review. Reviewed by PHP Medical Policy Committee on 04/26/2024. Continue to cover for Medicare only and follow Novitas LCD (L39063) and LCA (A58801). Added coverage for GeneSight® Psychotropic, Assurex Health, Inc, Myriad Genetics, Inc (code 0345U) is considered investigational for ALOB and will be config as I&E for ALOB and remove PA requirement. Add to require PA for **0423U** for ALOB. Code 81220 (cystic fibrosis) will continue to not require PA as per our response to HSD, May 2023. Add: 81401, 0392U, 0423U, and 0345U. Remove codes: 0289U, 0290U, 0291U, 0292U, 0293U and 0294U which were erroneously listed incorrectly by Novitas LCA (A58801), then moved code to MPM 7.1. IDgenetic (0411U) was reviewed on 02/07/2024: Continue review on a case-by-case basis for Medicare and non-covered for non-Medicare. Continue PA requirement for all codes. **Update 08/21/2024**: MPC meeting on 07-26-2024, determined that prior auth requirement will be removed for ALOB when Laboratory Benefit Management (LBM), Routine Testing Management (RTM) product becomes effective for policies which includes Q1 and 07/01/2024 updates. The following CPT code(s) will no longer be managed in this policy and may have previously required PA as part of this policy, are now listed in the LBM policy which can be found in the PHP Administrative Claims Edits Guide under Appendix A, LBM Program Policy. The policy can be found at this weblink: CORRECT CODING MEDICAL REVIEW GUIDES/ Administrative Claims Edits Guide. CPT code(s) include: 81377, 81383, 81408, 0117U, 0173U and 0175U. These codes have been removed from the policy. No other codes were identified.

This Medical Policy is intended to represent clinical guidelines describing medical appropriateness and is developed to assist Presbyterian Health Plan and Presbyterian Insurance Company, Inc. (Presbyterian) Health Services staff and Presbyterian medical directors in determination of coverage. The Medical Policy is not a treatment guide and should not be used as such.

For those instances where a member does not meet the criteria described in these guidelines, additional information supporting medical necessity is welcome and may be utilized by the medical director in reviewing the case. Please note that all Presbyterian Medical Policies are available online at: ***Click here for Medical Policies***

Web links:

At any time during your visit to this policy and find the source material web links has been updated, retired or superseded, PHP is not responsible for the continued viability of websites listed in this policy.

When PHP follows a particular guideline such as LCDs, NCDs, MCG, NCCN etc., for the purposes of determining coverage; it is expected providers maintain or have access to appropriate documentation when requested to support coverage. See the References section to view the source materials used to develop this resource document.