MEDICAL POLICY	Genetic Testing: Pharmacogenetic Testing (Medicare Only)
Effective Date: 1/1/2022  1/1/2022 Medical Officer Date	Medical Policy Number: 217 Medical Policy Committee Approved Date: 8/18; 12/18; 3/19; 6/19; 9/19; 11/19; 07/2020; 12/2020; 7/2021; 9/2021; 11/2021

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:

Medicare only

DOCUMENTATION REQUIREMENTS:

In order to review for medical necessity under *Social Security Act, §1862(a)(1)(A),* the following documentation **must** be provided. If any of these items are not submitted, the review may be delayed and the decision outcome could be affected:

- Clinical documentation supporting the diagnosis for which pharmacologic therapy is requested.
- Clinical documentation that an initial personalized decision has been made for the patient based on the patient's diagnosis, other medical conditions, other medications the patient is taking, professional judgement, clinical science and basic science pertinent to the drug (e.g. mechanism of action, side effects), the patient's past medical history and if applicable, relevant family history, patient preferences and values.
- Clinical record of what drug(s) is/are being considered and for what indication(s).

MEDICARE POLICY CRITERIA

The following Centers for Medicare & Medicaid Service (CMS) guidelines should be utilized for medical necessity coverage determinations. Click the link provided in the table below to access applicable medical necessity criteria. All listed guidelines apply.

Notes:

- This policy does not address genetic tests to determine drug therapy for the following indications:
  - Non-small cell lung cancer targeted therapies (e.g., EGFR, ALK, ROS1, RET genes).
  - BCR-ABL1 fusion gene testing, which may be considered medically necessary.

  Please see Medical Policy Cross References section below for medical policies that may apply to these pharmacogenetic tests.
- This policy does not address genetic testing of mutations in the MTHFR, CYP450, or VKORC1 genes (See Medical Policy Cross References section below for relevant policy information).

See "Policy Guidelines" for specific panel test information.

Service	Medicare Guidelines
Next Generation Sequencing (e.g. FoundationOne® CDx)	National Coverage Determination (NCD) for Next Generation Sequencing (NGS) (90.2) • *Note*: See Policy Guidelines for assistance with FDA-approved companion diagnostic (CDx) tests.[1] Criteria from NCD 90.2 must still be met. Based on their regulatory status, few tests will actually use this NCD. • ***Note:** This NCD is limited to NGS *DNA* sequencing tests which are FDA-approved or cleared as a companion diagnostic (CDx) test **and** only when used for cancer-related purposes. For all other tests, including tests which are **not** FDA-approved or cleared as a CDx test, tests which have a specific local coverage determination (LCD) or article (LCA) available, NGS *RNA* sequencing tests, or for tests related to *non*-cancer indications, see separate Medicare references below.
Pharmacogenomic Testing – General *Including multi-gene panels not otherwise specified in this policy*	All of the below LCDs require successful completion of a technical assessment (TA) by the MolDX Program contractor. See "Policy Guidelines" below for outcomes of TA reviews for specific panel tests. If a test is not listed in this policy, further research may be required. • Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD for MolDX: Pharmacogenomics Testing (L38337)

	• Testing performed in CA or NV: LCD for MolDX: Pharmacogenomics Testing (L38335) • Testing performed in NC, SC, AL, GA, TN, VA, WV: LCD for MolDX: Pharmacogenomics Testing (L38294)
BCR-ABL1 Genetic Testing (81206, 81207, 81208, 81479, 0016U)	• Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD: MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (L36186) • Testing performed in NC, SC, AL, GA, TN, VA, WV (e.g., BCR-ABL1 major and minor breakpoint fusion transcripts by the University of Iowa; PLA code 0016U): LCD: MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (L36815) For the above LCDs: If a treating physician suspects a patient has myeloproliferative neoplasms (MPN) or myelodysplastic syndromes (MDS), it would be clinically appropriate to test BCR-ABL. No specific criteria are provided for this gene directly as this is considered "step one" in the LCD, and would be considered "medically reasonable and necessary" for these and related indications, as outlined in the LCDs. If performed with other genes (e.g., JAK2), this would be considered panel testing. • Testing performed in TX (e.g., BCR-ABL1 major and minor breakpoint fusion transcripts by Asuragen in Texas; 0016U): LCD: Biomarkers for Oncology (L35396)
BRAF Genetic Testing (81210)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCA: Billing and Coding: MolDX: FDA-Approved BRAF Tests (A54420)
BRCA1 and BRCA2 Genetic Testing (81162, 81163, 81164, 81165, 81166, 81167, 81212, 81215, 81216, 81217)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD: MolDX: BRCA1 and BRCA2 Genetic Testing (L36163)
BRACAnalysis CDx® Test (81162)	LCA: Billing and Coding: MolDX: Myriad's BRACAnalysis CDx® (A55295)
CFTR Genetic Testing (81220, 81221, 81222, 81223, 81224)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD: MolDX: Pharmacogenomics Testing (L38337)
FLT3 Genetic Testing (81245, 81246, 81479, 0023U, 0046U)	See the Noridian J-F web page for Approved Gene Testing, where FLT3 testing is listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for laboratories in CA and NV). Coverage for the FLT3 gene testing requires that the medical documentation clearly states how test results are actionable, and how they will promptly and directly be used for treatment decisions or diagnosis (e.g., if being used

	for treatment decision-making, the considered drugs/medications must be noted in the records).
KRAS Genetic Testing (81275)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCA: Billing and Coding: MolDX: FDA-Approved KRAS Tests (A54500)
*HLA Class Typing (for **non**-transplant testing, performed either as single gene tests or in panels, such as the High Risk HLA Panel by Genelex) (81370, 81371, 81372, 81373, 81374, 81375, 81376, 81377, 81378, 81379, 81380, 81381, 81382, 81383)*	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD: MolDX: Pharmacogenomics Testing (L38337) *(The companion article provides gene/drug information)* For ***HLA transplant*** testing, see the separate Genetic and Molecular Testing (MP# 317).
NRAS Genetic Testing (81311, 81479)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD: MolDX: NRAS Genetic Testing (L36339)
PIK3CA Genetic Testing (81309, 81404, 0155U, 0177U)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: Local Coverage Article: Billing and Coding: MolDX: PIK3CA Gene Tests (A55602)
SULT4A1 Genetic Testing (81479)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: Local Coverage Article: Billing and Coding: MolDX: SULT4A1 Genetic Testing (A55601)
SLC6A4 (also known as HTTLPR) Genetic Testing (81479)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: Local Coverage Article: Billing and Coding: MolDX: HTTLPR Gene Testing (A55265)
DMD (81161), DPYD (81232), SMN1 (81329, 81400, 81403, 81405, 0236U), SLCO1B1 (81328), TYMS (81346) NUDT15 (81306), or UGT1A1 (81350) Genetic Testing	• Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD for MolDX: Pharmacogenomics Testing (L38337) • Testing performed in CA or NV: LCD for MolDX: Pharmacogenomics Testing (L38335) • Testing performed in NC, SC, AL, GA, TN, VA, WV: LCD for MolDX: Pharmacogenomics Testing (L38294)
VEGFR2 Genetic Testing (81479)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCA: Billing and Coding: MolDX: VEGFR2 Tests (A55469)
MMACHC Genetic Testing (81404)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCA: Billing and Coding: MolDX: MMACHC Test (A55289)
KIF6 Genetic Testing (81479)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCA: Billing and Coding: MolDX: KIF6 Genotype (A55273)
IDH2 Genetic Testing (81120, 81121)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCA: Billing and Coding: MolDX: Abbott RealTime IDH1 and IDH2 testing for Acute Myeloid Leukemia (AML) (A55712)

FGFR3 Genetic Testing (81400, 81401, 81403, 81404, 0154U)	Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD: MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer (L38684)
TPMT Testing (81335, 81401)	• For the Prometheus IBD sgi Diagnostic® test (Prometheus Laboratories; California): LCD: MolDX: Prometheus IBD sgi Diagnostic® Policy (L37299) • For all other *TPMT* Testing: ○ Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD for MolDX: Pharmacogenomics Testing (L38337) ○ Testing performed in CA or NV: LCD for MolDX: Pharmacogenomics Testing (L38335) ○ Testing performed in NC, SC, AL, GA, TN, VA, WV: LCD for MolDX: Pharmacogenomics Testing (L38294)
GeneSight® Psychotropic (AssureRx Health, Inc.; Ohio) (81479)	Testing performed in OH and KY: LCD for MolDX: Pharmacogenomics Testing (L38394) *(LCA A58324 includes GeneSight® as an approved multi-gene test, but LCD criteria must still be met)* This LCD requires successful completion of a technical assessment (TA) by the MolDX Program contractor. Tests which have been reviewed and considered "not covered" OR tests which have not been reviewed at all include the following: The LCD above requires successful completion of a technical assessment (TA) by the MolDX Program contractor. See "Policy Guidelines" below for outcomes of TA reviews for specific panel tests. If a test is not listed in this policy, further research may be required.
MDS FISH Testing (88271-88275)	• Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: LCD for MDS FISH (L37622) • Testing performed in CA or NV: LCD for MDS FISH (L37620)

For tests performed within a Medicare jurisdiction which has **NOT** adopted MolDX guidelines:

- LCDs for these service areas (National Government Services [NGS] LCD L35000, Novitas LCDs L35062 and L35396, and First Coast Service Options [FCSO] LCD L34519) all require tests undergo evaluation to establish clinical utility and analytical validity in order to be eligible for coverage.
- In the absence of a Medicare policy or reference, the PHP Commercial medical policy criteria may be applied to panel tests to provide the required review for clinical utility and analytical validity.
    - The Company policy *PHA Medicare Medical Policy Development and Application* (MP# 50) describes the Plan's hierarchy with respect to Medicare medical policy development. Medicare rules and regulations state that when no NCD, LCD, LCA, or other Medicare coverage guideline exists, Medicare allows Medicare Advantage

Organizations (MAOs) to make coverage determinations based on an objective, evidenced-based process.

- Thus, the non-coverage outcome found in the PHP Commercial medical policy *Genetic Testing: Non-Covered Genetic Panel Tests* may be applied to the following panel tests which do not have clinical utility or analytical validity documented within an LCD directly.

  - Genecept™ Assay (Genomind; Pennsylvania)
  - GenoMind Professional PGx Express™, Full Mental Health Report (24 Genes) (Genomind; Pennsylvania)
  - GenoMind Professional PGx Express™, CORE Anxiety & Depression Report (15 Genes) (Genomind; Pennsylvania)
  - PGxOne™ Plus Pharmacogenomics Test Admera Health (New Jersey)
  - RightMed Comprehensive Test OneOme (Minnesota)
  - Focused Pharmacogenomics Panel (0029U) (Mayo Clinic, Mayo Medical Laboratories, headquartered in Minnesota)
  - Warfarin Response Genotype (0030U) (Mayo Clinic, Mayo Medical Laboratories, headquartered in Minnesota)
  - Catechol-O-Methyltransferase (COMT) Genotype (0032U) (Mayo Clinic, Mayo Medical Laboratories, headquartered in Minnesota)
  - Serotonin Receptor Genotype (HTR2A and HTR2C) (0033U) (Mayo Clinic, Mayo Medical Laboratories, headquartered in Minnesota)

CNT (CEP72, TPMT and NUDT15) genotyping panel (0286U) (RPRD Diagnostics)

POLICY GUIDELINES

Companion Diagnostic Devices (In Vitro and Imaging Tools)

Please see the FDA website "List of Cleared or Approved Companion Diagnostic Devices" for the most current information on these tests and new tests as they are approved.

PLEASE READ: For any test within a service area which follows and uses MolDX Program policies and coverage guidance, all tests and assays require evaluation to determine if the test meets Medicare's reasonable and necessary requirement. Only tests which demonstrate analytical and clinical validity, and clinical utility at a level that meets the Medicare reasonable and necessary requirement are eligible for coverage under Medicare.

The outcome of MolDX TA reviews is maintained in the DEX™ Diagnostics Exchange registry catalog.

- Genetic tests noted as "covered" within this registry **may be medically reasonable and necessary** when all other Medicare coverage requirements are met, including criteria found in LCDs or LCAs.

- In contrast, if a test does **not** have a coverage determination noted within the registry, clinical validity or utility has not been established via the TA review process and the test **not considered medically reasonable and necessary** under *SSA §1862(a)(1)(A)* until a MolDX review is complete and coverage is indicated by MolDX or any other Medicare contractor (MAC) that uses MolDX policies or coverage guidance.

Related panel tests include:

Note: This list was accurate at the time of publication, but it is subject to change at any time by the Medicare MolDX Program contractor.

Proprietary Test Name	Laboratory	MolDX TA Review Outcome (as found in the DEX™ Diagnostics Exchange registry catalog)
High Risk HLA Panel *(this test consists of HLA-A*31:01, HLA-B*15:02, HLA-B*57:01, HLA-B*58:01)*	Genelex Corporation (Washington)	Covered
GeneSight® ADHD	AssureRx health, Inc. (Ohio)	Not Covered
GeneSight® Analgesic Panel		Not Covered
SureGene Test for Antipsychotic and Antidepressant Response (STA2R)	SureGene LLC. (Kentucky)	Not Covered
Mental Health DNA Insight™	Pathway Genomics® (California)	Covered
Neuro IDGenetix	(AltheaDx, Inc.; California)	Covered
Pain Panel (aka, "Pain/Psychiatry Panel")	Alpha Genomix (Georgia)	Not Covered
Pain Medication DNA Insight™	Pathway Genomics® (California)	Not Covered
Personalized Medicine Panel	Alpha Genomix (Georgia)	Not Covered
Polypharmacy Panel	Genelex Corporation (Washington)	Not Covered
Polypharmacy Comprehensive Panel	Genelex Corporation (Washington)	Not Covered
Psychiatry/ADHD Panel	Alpha Genomix (Georgia)	Not Covered

For tests performed within a Medicare jurisdiction which has **NOT** adopted MolDX guidelines, in the absence of a Medicare policy or reference, the PHP Commercial medical policy associated with the review of evidence for the test in question may be applied to provide the required review for clinical utility and analytical validity. Tests which are considered "investigational" in a PHP Commercial policy will be denied as **not medically reasonable or necessary** under *Social Security Act, §1862(a)(1)(A)* for Medicare members.

Related panel tests include:

Note: This list was accurate at the time of publication, but it is subject to change at any time by a Medicare contractor.

Proprietary Test Name	Laboratory	Coverage/Non-coverage Outcome
Focused Pharmacogenomics Panel (0029U)	Mayo Clinic, Mayo Medical Laboratories (Headquartered in Minnesota)	Not Covered
Genecept™ Assay	Genomind (Pennsylvania)	Not Covered
GenoMind Professional PGx Express™, Full Mental Health Report (24 Genes)	Genomind (Pennsylvania)	Not Covered
GenoMind Professional PGx Express™, CORE Anxiety & Depression Report (15 Genes)	Genomind (Pennsylvania)	Not Covered
PGxOne™ Plus Pharmacogenomics Test	Admera Health (New Jersey)	Not Covered
RightMed Comprehensive Test	OneOme (Minnesota)	Not Covered
Warfarin Response Genotype (0030U)	Mayo Clinic, Mayo Medical Laboratories (Headquartered in Minnesota)	Not Covered
CNT (CEP72, TPMT and NUDT15) genotyping panel	RPRD Diagnostics	Not Covered

BILLING GUIDELINES

For additional coding and billing guidance, see related local coverage articles (LCAs):

- LCA: Billing and Coding: MolDX: Pharmacogenomics Testing (A57385)
- LCA: Billing and Coding: MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (A57422)
- LCA: Billing and Coding: MolDX: BCR-ABL (A55600)
- LCA: Billing and Coding: MolDX: BRCA1 and BRCA2 Genetic Testing (A57355)
- LCA: Billing and Coding: MolDX: BRCA1 and BRCA2 Genetic Testing (A57355)
- LCA: Billing and Coding: MolDX: NRAS Genetic Testing (A57487)
- LCA: Billing and Coding: MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer (A58211)
- LCA: Billing and Coding: MolDX: Next-Generation Sequencing Lab-Developed Tests for Myeloid Malignancies and Suspected Myeloid Malignancies (A57892)
- LCA: Billing and Coding: MolDX: Targeted and Comprehensive Genomic Profile Next-Generation Sequencing Testing in Cancer (A56518)
- LCA: Billing and Coding: MolDX: Genetic Testing for Lynch Syndrome (A54996)

CPT/HCPCS CODES

Medicare Only	
Prior Authorization Required	
0023U	Oncology (acute myelogenous leukemia), DNA, genotyping of internal tandem duplication, p.D835, p.I836, using mononuclear cells, reported as detection or non-detection of FLT3 mutation and indication for or against the use of midostaurin
0030U	Drug metabolism (warfarin drug response), targeted sequence analysis (ie, CYP2C9, CYP4F2, VKORC1, rs12777823)
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])
0034U	TPMT (thiopurine S-methyltransferase), NUDT15 (nudix hydroxylase 15)(eg, thiopurine metabolism) gene analysis, common variants (ie, TPMT *2, *3A, *3B, *3C, *4, *5, *6, *8, *12; NUDT15 *3, *4, *5)
0037U	Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden
0046U	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia) internal tandem duplication (ITD) variants, quantitative
0078U	Pain management (opioid-use disorder) genotyping panel, 16 common variants (ie, ABCB1, COMT, DAT1, DBH, DOR, DRD1, DRD2, DRD4, GABA, GAL, HTR2A, HTTLPR, MTHFR, MUOR, OPRK1, OPRM1), buccal swab or other germline tissue sample, algorithm reported as positive or negative risk of opioid-use disorder
0111U	Oncology (colon cancer), targeted KRAS (codons 12, 13, and 61) and NRAS (codons 12, 13, and 61) gene analysis, utilizing formalin-fixed paraffin-embedded tissue
0154U	FGFR3 (fibroblast growth factor receptor 3) gene analysis (ie, p.R248C [c.742C>T], p.S249C [c.746C>G], p.G370C [c.1108G>T], p.Y373C [c.1118A>G], FGFR3-TACC3v1, and FGFR3-TACC3v3)
0155U	PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha) (eg, breast cancer) gene analysis (ie, p.C420R, p.E542K, p.E545A, p.E545D [g.1635G>T only], p.E545G, p.E545K, p.Q546E, p.Q546R, p.H1047L, p.H1047R, p.H1047Y)
0172U	Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score
0177U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha) gene analysis of 11 gene variants utilizing plasma, reported as PIK3CA gene mutation status

0239U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free DNA, analysis of 311 or more genes, interrogation for sequence variants, including substitutions, insertions, deletions, select rearrangements, and copy number variations
0286U	CEP72 (centrosomal protein, 72-KDa), NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants *(Used for the CNT (CEP72, TPMT and NUDT15) Genotyping Panel, by RPRD Diagnostics)*
81121	IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (eg, glioma), common variants (eg, R140W, R172M)
81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene rearrangements)
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81164	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81165	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81166	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81167	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)
81232	DPYD (dihydropyrimidine dehydrogenase) (eg, 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (eg, *2A, *4, *5, *6)
81233	BTK (Bruton's tyrosine kinase) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F)

81236	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence
81237	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, diffuse large B-cell lymphoma) gene analysis, common variant(s) (eg, codon 646)
81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13)
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146)
81283	IFNL3 (interferon, lambda 3) (eg, drug response), gene analysis, rs12979860 variant
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (eg, glioblastoma multiforme), methylation analysis
81306	NUDT15 (nudix hydrolase 15) (eg, drug metabolism) gene analysis, common variant(s) (eg, *2, *3, *4, *5, *6)
81309	PIK3CA (phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (eg, colorectal and breast cancer) gene analysis, targeted sequence analysis (eg, exons 7, 9, 20)
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (eg, colorectal carcinoma), gene analysis, variants in exon 2 (eg, codons 12 and 13) and exon 3 (eg, codon 61)
81315	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative
81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; single breakpoint (eg, intron 3, intron 6 or exon 6), qualitative or quantitative
81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (eg, adverse drug reaction), gene analysis, common variant(s) (eg, *5)
81329	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed
81335	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)
81336	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence
81337	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)
81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)
81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (eg, irinotecan metabolism), gene analysis, common variants (eg, *28, *36, *37)
81400	Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg, SNP] by techniques such as restriction enzyme digestion or melt curve analysis)

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)
81402	Molecular pathology procedure, Level 3 (eg, >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD])
81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
81404	Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
81405	Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)
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)
81407	Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)
81408	Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis)
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
81450	Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
G9143	Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)

No Prior Authorization Required

The following codes do not require routine review for medical necessity, but they may be subject to audit. If there is uncertainty regarding the medical necessity and reasonableness of a test, an advance benefit determination request may be submitted.

81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s)
81245	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; internal tandem duplication (ITD) variants (ie, exons 14, 15)
81246	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (eg, D835, I836)
81301	Microsatellite instability analysis (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (eg, BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed
81370	HLA Class I and II typing, low resolution (eg, antigen equivalents); HLA-A, -B, -C, -DRB1/3/4/5, and -DQB1
81371	HLA Class I and II typing, low resolution (eg, antigen equivalents); HLA-A, -B, and -DRB1 (eg, verification typing)
81372	HLA Class I typing, low resolution (eg, antigen equivalents); complete (ie, HLA-A, -B, and -C)
81373	HLA Class I typing, low resolution (eg, antigen equivalents); one locus (eg, HLA-A, -B, or -C), each
81374	HLA Class I typing, low resolution (eg, antigen equivalents); one antigen equivalent (eg, B*27), each
81375	HLA Class II typing, low resolution (eg, antigen equivalents); HLADRB1/3/4/5 and -DQB1
81376	HLA Class II typing, low resolution (eg, antigen equivalents); one locus (eg, HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
81377	HLA Class II typing, low resolution (eg, antigen equivalents); one antigen equivalent, each
81378	HLA Class I and II typing, high resolution (ie, alleles or allele groups), HLA-A, -B, -C, and -DRB1
81379	HLA Class I typing, high resolution (ie, alleles or allele groups); complete (ie, HLA-A, -B, and -C)
81380	HLA Class I typing, high resolution (ie, alleles or allele groups); one locus (eg, HLA-A, -B, or -C), each
81381	HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each
81382	HLA Class II typing, high resolution (ie, alleles or allele groups); one locus (eg, HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
81383	HLA Class II typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, HLA-DQB1*06:02P), each
88271	Molecular cytogenetics; DNA probe, each (eg, FISH)

88272	Molecular cytogenetics; chromosomal in situ hybridization, analyze 3-5 cells (eg, for derivatives and markers)
88273	Molecular cytogenetics; chromosomal in situ hybridization, analyze 10-30 cells (eg, for microdeletions)
88274	Molecular cytogenetics; interphase in situ hybridization, analyze 25-99 cells
88275	Molecular cytogenetics; interphase in situ hybridization, analyze 100-300 cells
Unlisted Codes All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then **prior-authorization is required.**	
81479	Unlisted Molecular pathology procedure
81599	Unlisted multianalyte assay with algorithmic analysis
84999	Unlisted chemistry procedure

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

MEDICAL POLICY CROSS REFERENCES

Providence Health Plans Medical Policies

- Genetic Studies and Counseling
- Genetic Testing: Cytochrome P450 and VKORC1 Polymorphisms (Medicare Only)
- Genetic Testing: Hereditary Breast and Ovarian Cancer (Medicare Only)
- Genetic Testing: Inherited Susceptibility to Colorectal Cancer (Medicare Only)
- Genetic Testing: MTHFR (Medicare Only)
- Genetic Testing: Non-covered Genetic Panel Tests (Medicare Only)
- Inflammatory Bowel Disease (IBD) Serologic Testing and Therapeutic Monitoring
- Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (Medicare Only)

REFERENCES

1. U.S. Food and Drug Administration. List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools). 2021; https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools. Accessed 7/2/2021.