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Medicare Advantage Policy Manual **Policy ID:** M-GT10

Pharmacogenomic (PGx) Testing

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IMPORTANT REMINDER

The Medicare Advantage Medical Policy manual is not intended to override the member Evidence of Coverage (EOC), which defines the insured's benefits, nor is it intended to dictate how providers are to practice medicine. Physicians and other health care providers are expected to exercise their medical judgment in providing the most appropriate care for the individual member, including care that may be both medically reasonable and necessary.

The Medicare Advantage medical policies are designed to provide guidance regarding the decision-making process for the coverage or non-coverage of services or procedures in accordance with the member EOC and Centers of Medicare and Medicaid Services (CMS) policies and manuals, along with general CMS rules and regulations. In the event of a conflict, applicable CMS policy or EOC language will take precedence over the Medicare Advantage Medical Policy. In the absence of a specific CMS coverage determination for a requested service, item or procedure, the health plan may apply CMS regulations, as well as their Medical Policy Manual or other applicable utilization management vendor criteria developed with an objective, evidence-based process using scientific evidence, current generally accepted standards of medical practice, and authoritative clinical practice guidelines.

Some services or items may appear to be medically indicated for an individual but they may also be a direct exclusion of Medicare or the member's benefit plan. Medicare and member EOCs exclude from coverage, among other things, services or procedures considered to be investigational (experimental) or cosmetic, as well as services or items considered not medically reasonable and necessary under Title XVIII of the Social Security Act, §1862(a)(1)(A). In some cases, providers may bill members for these non-covered services or procedures. Providers are encouraged to inform members in advance when they may be financially responsible for the cost of non-covered or excluded services. Members, their appointed representative, or a treating provider can request coverage of a service or item by submitting a pre-service organization determination prior to services being rendered.

DESCRIPTION

Pharmacogenomic (PGx) testing may assist health care professionals to tailor drug selection and dosing for patients based on their predicted drug metabolism. The goal of this testing is to allow selection and optimal dosing of the most effective drugs while minimizing treatment failures or toxicities. PGx testing can include single genes, multi-gene panels, and combinatorial tests.

MEDICARE ADVANTAGE POLICY CRITERIA

Notes: This policy does not apply to genetic testing for the purpose of selecting a targeted cancer therapy or diagnosing a hereditary disorder (see Cross References).

The Medicare references in this policy represent the guidance available at publication; please see the Medicare Coverage Database for the latest guidance. This policy includes links to external webpages that are not maintained by the health plan.

Genes/Test Name:	HCPCS Code(s)	Criteria For Medicare Coverage Determinations and Articles, see the *Medicare Coverage Database*
***CYP2C9*, *VKORC1* for Warfarin Dosing**	0030U 81227 81355 81479 G9143	**National Coverage Determinations (NCD)** Pharmacogenomic Testing for Warfarin Response (NCD 90.1)
Other PGx Testing	See Coding section	**National Coverage Determinations (NCD)** None **Noridian Healthcare Solutions (Noridian) Local Coverage Determinations (LCDs) and Articles** *Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY:* ✓ MolDX: Pharmacogenomics Testing (L38337) ✓ Billing and Coding: MolDX: Pharmacogenomics Testing (A57385) *(See tables for specific guidance)* Links to prior versions can be found at the bottom of the LCD. Additional research may be needed to determine coverage for tests or indications not addressed in the LCD and article. **LCDs and Articles for Other Jurisdictions:** **Note:** The health plan is required to use LCDs and articles published by the contractor with jurisdiction over the service area in which the tests are performed.[1,2] See below for contractor guidance in other jurisdictions: *Laboratories in CA and NV:* ✓ MolDx: Pharmacogenomics Testing (L38335) and associated article *(See article tables for specific guidance)* *Laboratories in AL, GA, TN, SC, NC, VA, WV:* ✓ MolDx: Pharmacogenomics Testing (L38294) and associated article *(See article tables for specific guidance)* *Laboratories in IA, KS, MO, NE, IN, MI:*

Genes/Test Name:	HCPCS Code(s)	Criteria For Medicare Coverage Determinations and Articles, see the Medicare Coverage Database
		✓ MolDx: Pharmacogenomics Testing (L38435) and associated article *(See article tables for specific guidance)* *Laboratories in KY, OH:* ✓ MolDx: Pharmacogenomics Testing (L38394) and associated article *(See article tables for specific guidance)* *Laboratories in FL, PR, and VI:* ✓ Pharmacogenomics Testing (L39073) and associated article *(See article tables for specific guidance)* *Laboratories in CO, NM, OK, TX, AR, LA, MS, DE, MD, NJ, PA:* ✓ Pharmacogenomics Testing (L39063) *(See article tables for specific guidance)* *Laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, or VT:* ✓ Pharmacogenomics Testing (L39995) *(See article tables for specific guidance)* Additional research may be needed to determine coverage for tests or indications not addressed in the LCD and article. **Additional Information** The MolDX program requires that tests complete a technical assessment (TA) for coverage. The following tests have completed a MolDX TA and are listed as "**covered**": • GeneSight® Psychotropic Panel (Myriad Genetics) [0345U] • IDgenetix® (Castle Biosciences) [0411U] • Tempus nP (Tempus) [0419U] The following tests have completed a TA and are listed as "**not covered**": • Medication Management Neuropsychiatric Panel (GENETWORx) • EffectiveRX (GENETWORx)

POLICY GUIDELINES

REQUIRED DOCUMENTATION

The following information is required in order to determine medical necessity and potential Medicare coverage for a genetic or molecular diagnostic test. *[See Title XVIII of the Social Security Act, §1833(e), which states no payment may be made unless information necessary to determine payment has been submitted)]*

1. The specific name of the genetic or molecular diagnostic test or panel;
2. Name of the performing laboratory;
3. The exact gene(s) and/or variants being tested;
4. Applicable CPT and/or HCPCS code(s);
5. Brief explanation of how the results of genetic testing are necessary to guide treatment decisions relevant to the member's personal medical history.
6. Medical records relevant to the testing being performed. This includes:
   - History and physical examinations by the referring physician;
   - Conventional testing and outcomes; and
   - Conservative treatment provided, if applicable.

CROSS REFERENCES

1. Genetic and Molecular Diagnostics – Next Generation Sequencing, Genetic Panels, and Biomarker Testing, Genetic Testing, Policy No. M-64
2. Genetic and Molecular Diagnostics – Testing for Cancer Diagnosis, Prognosis, and Treatment Selection, Genetic Testing, Policy No. M-83
3. Laboratory and Genetic Testing for Use of Fluoropyrimidine Chemotherapy (5-FU and Capecitabine) in Patients with Cancer, Laboratory, Policy No.M-64

REFERENCES

1. Medicare Claims Processing Manual, Chapter 1 - General Billing Requirements, §10.1.5.4 - Independent Laboratories
2. Medicare Managed Care Manual, Chapter 4 - Benefits and Beneficiary Protections, §90.4.1 - MAC with Exclusive Jurisdiction over a Medicare Item or Service

CODING

NOTE: See relevant Billing and Coding Articles reference above for additional information about appropriate coding for pharmacogenomic testing.

Codes	Number	Description
CPT	0029U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis (ie, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 and rs12777823)
	0030U	Drug metabolism (warfarin drug response), targeted sequence analysis (ie, CYP2C9, CYP4F2, VKORC1, 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])
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)
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)
0169U	NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants
0173U	Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes
0175U	Psychiatry (eg, depression, anxiety), genomic analysis panel, variant analysis of 15 genes
0286U	CEP72 (centrosomal protein, 72-KDa), NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants
0345U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6
0347U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 16 gene report, with variant analysis and reported phenotypes
0348U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 25 gene report, with variant analysis and reported phenotypes
0349U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 27 gene report, with variant analysis, including reported phenotypes and impacted gene-drug interactions

0350U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 27 gene report, with variant analysis and reported phenotypes
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
0411U	Psychiatry (eg, depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6
0419U	Neuropsychiatry (eg, depression, anxiety), genomic sequence analysis panel, variant analysis of 13 genes, saliva or buccal swab, report of each gene phenotype
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
0434U	Drug metabolism (adverse drug reactions and drug response), genomic analysis panel, variant analysis of 25 genes with reported phenotypes
0438U	Drug metabolism (adverse drug reactions and drug response), buccal specimen, gene-drug interactions, variant analysis of 33 genes, including deletion/duplication analysis of CYP2D6, including reported phenotypes and impacted genedrug interactions
0460U	Oncology, whole blood or buccal, DNA single-nucleotide polymorphism (SNP) genotyping by real-time PCR of 24 genes, with variant analysis and reported phenotypes
0461U	Oncology, whole blood or buccal, DNA single-nucleotide polymorphism (SNP) genotyping by real-time PCR of 24 genes, with variant analysis and reported phenotypes
0476U	Drug metabolism, psychiatry (eg, major depressive disorder, general anxiety disorder, attention deficit hyperactivity disorder [ADHD], schizophrenia), whole blood, buccal swab, and pharmacogenomic genotyping of 14 genes and CYP2D6 copy number variant analysis and reported phenotypes
0477U	Drug metabolism, psychiatry (eg, major depressive disorder, general anxiety disorder, attention deficit hyperactivity disorder [ADHD], schizophrenia), whole blood, buccal swab, and pharmacogenomic genotyping of 14 genes and CYP2D6 copy number variant analysis, including impacted gene-drug interactions and reported phenotypes
0516U	Drug metabolism, whole blood, pharmacogenomic genotyping of 40 genes and CYP2D6 copy number variant analysis, reported as metabolizer status
0533U	Drug metabolism (adverse drug reactions and drug response), genotyping of 16 genes (ie, ABCG2, CYP2B6, CYP2C9, CYP2C19, CYP2C, CYP2D6, CYP3A5, CYP4F2, DPYD, G6PD, GGCX, NUDT15, SLCO1B1, TPMT, UGT1A1, VKORC1), reported as metabolizer status and transporter function
81225	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)
81230	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22)

	81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7)
	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)
	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, hyperbilirubinemia [Gilbert syndrome]), gene analysis, common variants (eg, *28, *36, *37)
	81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G>A, c. 173+1000C>T)
	81374	HLA Class I typing, low resolution (eg, antigen equivalents); one antigen equivalent (eg, B*27), each
	81377	HLA Class II typing, low resolution (eg, antigen equivalents); one antigen equivalent, each
	81381	HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each
	81383	HLA Class II typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, HLA-DQB1*06:02P), each
	81400	Molecular pathology procedure, Level 1
	81401	Molecular pathology procedure, Level 2
	81402	Molecular pathology procedure, Level 3
	81403	Molecular pathology procedure, Level 4
	81404	Molecular pathology procedure, Level 5
	81405	Molecular pathology procedure, Level 6
	81406	Molecular pathology procedure, Level 7
	81407	Molecular pathology procedure, Level 8
	81408	Molecular pathology procedure, Level 9
	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
	81479	Unlisted molecular pathology procedure
HCPCS	G9143	Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)