Status: Updated codes 10/01/2024
Doc ID: GEN09-0223.1-UC1024

Effective Date: 02/12/2023
Last Review Date: 08/29/2022

Approval and implementation dates for specific health plans may vary. Please consult the applicable health plan for more details.

Clinical Appropriateness Guidelines

Genetic Testing

Appropriate Use Criteria: Pharmacogenomic Testing

Proprietary

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Description and Application of the Guidelines

The Carelon Clinical Appropriateness Guidelines (hereinafter “the Carelon Clinical Appropriateness Guidelines” or the “Guidelines”) are designed to assist providers in making the most appropriate treatment decision for a specific clinical condition for an individual. The Guidelines establish objective and evidence-based criteria for medical necessity determinations, where possible, that can be used in support of the following:

- To establish criteria for when services are medically necessary
- To assist the practitioner as an educational tool
- To encourage standardization of medical practice patterns
- To curtail the performance of inappropriate and/or duplicate services
- To address patient safety concerns
- To enhance the quality of health care
- To promote the most efficient and cost-effective use of services

The Carelon guideline development process complies with applicable accreditation and legal standards, including the requirement that the Guidelines be developed with involvement from appropriate providers with current clinical expertise relevant to the Guidelines under review and be based on the most up-to-date clinical principles and best practices. Resources reviewed include widely used treatment guidelines, randomized controlled trials or prospective cohort studies, and large systematic reviews or meta-analyses. Carelon reviews all of its Guidelines at least annually.

Carelon makes its Guidelines publicly available on its website. Copies of the Guidelines are also available upon oral or written request. Additional details, such as summaries of evidence, a list of the sources of evidence, and an explanation of the rationale that supports the adoption of the Guidelines, are included in each guideline document.

Although the Guidelines are publicly available, Carelon considers the Guidelines to be important, proprietary information of Carelon, which cannot be sold, assigned, leased, licensed, reproduced or distributed without the written consent of Carelon.

Carelon applies objective and evidence-based criteria, and takes individual circumstances and the local delivery system into account when determining the medical appropriateness of health care services. The Carelon Guidelines are just guidelines for the provision of specialty health services. These criteria are designed to guide both providers and reviewers to the most appropriate services based on a patient’s unique circumstances. In all cases, clinical judgment consistent with the standards of good medical practice should be used when applying the Guidelines. Guideline determinations are made based on the information provided at the time of the request. It is expected that medical necessity decisions may change as new information is provided or based on unique aspects of the patient’s condition. The treating clinician has final authority and responsibility for treatment decisions regarding the care of the patient and for justifying and demonstrating the existence of medical necessity for the requested service. The Guidelines are not a substitute for the experience and judgment of a physician or other health care professionals. Any clinician seeking to apply or consult the Guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment.

The Guidelines do not address coverage, benefit or other plan specific issues. Applicable federal and state coverage mandates take precedence over these clinical guidelines, and in the case of reviews for Medicare Advantage Plans, the Guidelines are only applied where there are not fully established CMS criteria. If requested by a health plan, Carelon will review requests based on health plan medical policy/guidelines in lieu of the Carelon Guidelines. Pharmaceuticals, radiotracers, or medical devices used in any of the diagnostic or therapeutic interventions listed in the Guidelines must be FDA approved or conditionally approved for the intended use. However, use of an FDA approved or conditionally approved product does not constitute medical necessity or guarantee reimbursement by the respective health plan.

The Guidelines may also be used by the health plan or by Carelon for purposes of provider education, or to review the medical necessity of services by any provider who has been notified of the need for medical necessity review, due to billing practices or claims that are not consistent with other providers in terms of frequency or some other manner.

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General Clinical Guideline

Clinical Appropriateness Framework

Critical to any finding of clinical appropriateness under the guidelines for a specific diagnostic or therapeutic intervention are the following elements:

- Prior to any intervention, it is essential that the clinician confirm the diagnosis or establish its pretest likelihood based on a complete evaluation of the patient. This includes a history and physical examination and, where applicable, a review of relevant laboratory studies, diagnostic testing, and response to prior therapeutic intervention.
- The anticipated benefit of the recommended intervention is likely to outweigh any potential harms, including from delay or decreased access to services that may result (net benefit).
- Widely used treatment guidelines and/or current clinical literature and/or standards of medical practice should support that the recommended intervention offers the greatest net benefit among competing alternatives.
- There exists a reasonable likelihood that the intervention will change management and/or lead to an improved outcome for the patient.

Providers may be required to submit clinical documentation in support of a request for services. Such documentation must a) accurately reflect the clinical situation at the time of the requested service, and b) sufficiently document the ordering provider's clinical intent.

If these elements are not established with respect to a given request, the determination of appropriateness will most likely require a peer-to-peer conversation to understand the individual and unique facts that would justify a finding of clinical appropriateness. During the peer-to-peer conversation, factors such as patient acuity and setting of service may also be taken into account to the extent permitted by law.

Simultaneous Ordering of Multiple Diagnostic or Therapeutic Interventions

Requests for multiple diagnostic or therapeutic interventions at the same time will often require a peer-to-peer conversation to understand the individual circumstances that support the medical necessity of performing all interventions simultaneously. This is based on the fact that appropriateness of additional intervention is often dependent on the outcome of the initial intervention.

Additionally, either of the following may apply:

- Current literature and/or standards of medical practice support that one of the requested diagnostic or therapeutic interventions is more appropriate in the clinical situation presented; or
- One of the diagnostic or therapeutic interventions requested is more likely to improve patient outcomes based on current literature and/or standards of medical practice.

Repeat Diagnostic Intervention

In general, repeated testing of the same anatomic location for the same indication should be limited to evaluation following an intervention, or when there is a change in clinical status such that additional testing is required to determine next steps in management. At times, it may be necessary to repeat a test using different techniques or protocols to clarify a finding or result of the original study.

Repeated testing for the same indication using the same or similar technology may be subject to additional review or require peer-to-peer conversation in the following scenarios:

- Repeated diagnostic testing at the same facility due to technical issues
- Repeated diagnostic testing requested at a different facility due to provider preference or quality concerns

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- Repeated diagnostic testing of the same anatomic area based on persistent symptoms with no clinical change, treatment, or intervention since the previous study
- Repeated diagnostic testing of the same anatomic area by different providers for the same member over a short period of time

Repeat Therapeutic Intervention

In general, repeated therapeutic intervention in the same anatomic area is considered appropriate when the prior intervention proved effective or beneficial and the expected duration of relief has lapsed. A repeat intervention requested prior to the expected duration of relief is not appropriate unless it can be confirmed that the prior intervention was never administered. Requests for on-going services may depend on completion of previously authorized services in situations where a patient's response to authorized services is relevant to a determination of clinical appropriateness.

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Pharmacogenomic Testing

Clinical Indications

For each of the following FDA-approved therapies and associated biomarkers (see Table 1), one genotyping for the appropriate biomarker is considered **medically necessary** when **ALL** the following conditions are met:

- The medication for which genotyping is being done is the most appropriate treatment for the individual's underlying condition
- The pharmacogenomic test has demonstrated analytical and clinical validity and clinical utility for the individual, including consideration of the frequency of relevant alleles in the individual's subgroup (when applicable)
- The biomarker testing is focused on the specific genetic polymorphisms relevant to guiding treatment for the individual's condition and expected treatment

Table 1. Therapies and associated biomarkers

Biomarker	Drug	Therapeutic Area
CFTR	ivacaftor	Pediatrics
CYP2C19	clopidogrel	Cardiology
CYP2C9	siponimod	Neurology
CYP2D6	eliglustat	Pediatrics
CYP2D6	tetrabenazine	Neurology
G6PD	rasburicase	Hematology
G6PD	tafenoquine, primaquine	Infectious Diseases
HLA-B*1502	carbamazepine, oxcarbazepine	Neurology
HLA-B*5701	abacavir	Infectious Diseases
HLA-B*58:01	allopurinol	Rheumatology
NAGS	carglumic acid	Gastroenterology
POLG	divalproex sodium, valproic acid	Neurology
TPMT	mercaptopurine, thioguanine	Hematology

Excerpted from https://cpicpgx.org/genes-drugs/

Rationale

Pharmacogenomic testing refers to genotype testing for polymorphisms in order to identify variants of specific genes associated with drug pharmacodynamics or metabolism. Such testing is sometimes used to guide the dosing or choice of particular drugs in an individual with the goal of optimizing the response to therapy and/or minimizing the likelihood of an adverse drug effect. Polymorphisms in the genes encoding the drug target can influence the drug pharmacodynamics. Moreover, genetic determinates of excretion or drug metabolism influence pharmacokinetics.[1] Although about 15% of all prescriptions in the United States have potential influence from pharmacogenetics, evidence is available to support genotype-guided prescribing for a limited number of drugs, and sometimes only for specific subpopulations. In some cases, there are race-based screening recommendations that can be difficult to apply because of wide variability in allele frequencies even within ethnic groups along with difficulty in discerning race ancestry and due to mixed ancestry. At the same time, imperatives to use resources judiciously warrant selective screening to target high prevalence groups when they can be accurately identified.[2]

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The Clinical Pharmacogenetics Implementation Consortium (CPIC) was developed in 2009 as a shared project between the Pharmacogenomics Knowledge Base (PharmGKB, http://www.pharmgkb.org) and the National Institutes of Health (NIH). The CPIC is focused on facilitation the translation of research findings into clinical actions for selected gene/drug pairs with sufficient evidence.[3] With notable exceptions, pharmacogenomics is best used to assess the risk of general suboptimal response. This type of testing does not override the need for clinical assessment and judgement.[4]

While there is considerable enthusiasm for pharmacogenomic testing and tremendous growth in direct-to-consumer marketing, there has also been actions taken by the FDA and other groups to warn patients that selecting or changing drug treatment in response to genetic test results can also lead to potentially serious health consequences (see FDA warning letter, April 4, 2019; FDA warning letter November 1, 2018). One area where there has been particular enthusiasm is the realm of psychiatry, particularly with the use of pharmacogenetic testing to guide antidepressant therapy. While it is known that genetic variants contribute to the variance in response to drug treatments for depression, rigorously conducted clinical trials have not yet shown the clinical utility of such testing. Meta-analyses and non-industry technical assessments of the existing literature have shown notable risks of bias in existing studies, a high degree of between study heterogeneity, and significant methodological limitations. In particular, the randomized, double-blind, clinical trial evaluating the GeneSight pharmacogenomic intervention did not find a statistically significant difference in response rates or remission rates when those tested were compared to those without testing.[5] Systematic reviews of the available studies in this realm are unequivocal that the evidence of clinical utility are lacking in this realm.[6, 7]

One area of controversy in the field of pharmacogenomics is the role of DPYD testing for patients being treated with cytolytic chemotherapy using 5-fluorouracil. 5-fluorouracil (5-FU) and capecitabine are commonly used in solid tumors including colorectal, pancreatic, esophageal, head and neck, and breast cancer, and use of these drugs is associated with infrequent severe, life-threatening toxicities including neutropenia, diarrhea, and mucositis. Fluoropyrimidine toxicity is due in part to inherited polymorphisms in the dihydropyrimidine dehydrogenase enzyme, encoded by DPYD, which is responsible for 5-FU elimination. Approximately 5% of patients carry one of five DPYD polymorphisms that increase toxicity risk. DPYD variant carriers who receive standard fluoropyrimidine doses have ~70% risk of severe toxicity and ~3% risk of fatal toxicity, and these risks are even higher in the ~1/250 patients who carry two DPYD variants.[8, 9] The NCCN and the FDA recognize the increased risk of severe fluoropyrimidine toxicity in known DPYD carriers but do not recommend routine testing. While some countries have mandated preemptive DPYD testing for patients scheduled to receive a fluoropyrimidine, preemptive DPYD testing is rarely conducted for a variety of reasons.[10] In the SWOG cancer research group, a survey was conducted of 59 US-based medical oncologists within the SWOG gastrointestinal and breast committees. Those data indicate that the primary reasons for not testing are the perceived low prevalence of DPYD deficiency, lack of clinical guidelines recommending testing, and a lack of knowledge around which test to order and what to do with the result. There is also concern among the oncology community related to the potential for dose reduction resulting from this testing, leading ultimately to reduced treatment efficacy.

The clinical utility of pharmacogenomic testing is not established for most instances of its use, and thus it is considered not medically necessary unless otherwise specified. There are some instances where the FDA is explicit in recommending genotyping ahead of prescribing.

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8. Meulendijks D, Henricks LM, Sonke GS, et al. Clinical relevance of DPYD variants c.1679T>G, c.1236G>A/HapB3, and c.1601G>A as predictors of severe fluoropyrimidine-associated toxicity: a systematic review and meta-analysis of individual patient data. Lancet Oncol. 2015;16(16):1639-50.

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9. Lee AM, Shi Q, Pavey E, et al. DPYD variants as predictors of 5-fluorouracil toxicity in adjuvant colon cancer treatment (NCCTG N0147). J Natl Cancer Inst. 2014;106(12).
10. Ciccolini J. DPD deficiency in patients treated with fluorouracil. Lancet Oncol. 2015;16(16):1574-6.

Codes

The following code list is not meant to be all-inclusive. Authorization requirements will vary by health plan. Please consult the applicable health plan for guidance on specific procedure codes.

Specific CPT codes for services should be used when available. Nonspecific or not otherwise classified codes may be subject to additional documentation requirements and review.

CPT/HCPCS

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May Be Medically Necessary When Criteria are Met

Code	May Be Medically Necessary When Criteria are Met
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17) [for clopidogrel metabolism]
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) [for eliglustat or tetrabenazine metabolism]
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6) [for siponimod (Mayzent) metabolism]
81247	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, A, A-)
81248	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; known familial variant(s)
81249	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; full gene sequence
81335	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)
81380	HLA Class I typing, high resolution (ie, alleles or allele groups); HLA Class I typing, high resolution (ie, alleles or allele groups)
81381	HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each [when specified as Human Leukocyte Antigen B*57:01P (HLA-B*5701) for abacavir metabolism, Human Leukocyte Antigen B*58:01 (HLA-B*58:01) for allopurinol metabolism, or Human Leukocyte Antigen B*1502 (HLA-B*1502) for carbamazepine metabolism]
81479	Unlisted molecular pathology procedure
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
0072U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D6-2D7 hybrid gene)
0073U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D7-2D6 hybrid gene)
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)
0075U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 5' gene duplication/multiplication)
0076U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 3' gene duplication/ multiplication)

Not Medically Necessary

Code	Not Medically Necessary
81230	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22)

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Code	Not Medically Necessary
81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variant(s) (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)
81240	F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant
81241	F5 (coagulation Factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant
81283	IFNL3 (interferon, lambda 3) (eg, drug response), gene analysis, rs12979860 variant
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (eg, hereditary hypercoagulability) gene analysis, common variants (eg, 677T, 1298C)
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)
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, drug metabolism, hereditary unconjugated hyperbilirubinemia [Gilbert syndrome]), gene analysis, common variants (eg, *28, *36, *37) [when specified for drug metabolism (irinotecan)]
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G>A, c.173+1000C>T)
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
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)
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
0205U	Ophthalmology (age-related macular degeneration), analysis of 3 gene variants (2 CFH gene, 1 ARMS2 gene), using PCR and MALDI-TOF, buccal swab, reported as positive or negative for neovascular agerelated macular-degeneration risk associated with zinc supplements
0286U	CEP72 (centrosomal protein, 72-KDa), NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants - CNT (CEP72, NUDT15 and TPMT) Genotyping Panel
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
0380U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis, 20 gene variants and CYP2D6 deletion or duplication analysis with reported genotype and phenotype
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

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Code	Not Medically Necessary
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 gene-drug 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, pharmacogenomic analysis of single-nucleotide polymorphism (SNP) genotyping by real-time PCR of 24 genes, whole blood or buccal swab, with variant analysis, including impacted gene-drug interactions 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
G9143	Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)

ICD-10 Diagnosis

Refer to the ICD-10 CM manual

History

Status	Review Date	Effective Date	Action
Updated codes 10/01/2024	n/a	Unchanged	Added CPT codes 81380 (MNWCM), 0476U, 0477U, 0516U (NMN). Removed 0078U (NMN).
Updated codes 07/01/2024	n/a	Unchanged	Added CPT codes 0460U and 0461U (NMN).
Updated codes 03/17/2024	n/a	Unchanged	Split code list into those considered medically necessary when criteria are met (MNWCM) and not MN. Added NMN CPT codes 81240, 81241, 81291, 0205U, 0380U, 0392U, 0411U, 0419U, 0423U, 0434U, 0438U. Removed 81250, 0258U, 0290U, 0291U, 0292U, 0293U. Added required language to General Clinical Guideline per new Medicare regulations.
Created	08/29/2022	02/12/2023	Independent Multispecialty Physician Panel (IMPP) review. Original effective date.

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