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HCPCS Codes & Clinical Laboratory Improvement Amendments Edits: April 2025

Related CR Release Date: March 13, 2025	**MLN Matters Number:** MM13959
Effective Date: April 1, 2025	**Related Change Request (CR) Number:** CR 13959
Implementation Date: April 7, 2025	**Related CR Transmittal Number:** R13102CP
Related CR Title: Healthcare Common Procedure Coding System (HCPCS) Codes Subject to and Excluded from Clinical Laboratory Improvement Amendments (CLIA) Edits	

Affected Providers

- Laboratories
- Physicians
- Hospitals billing Medicare Administrative Contractors (MACs) for services they provide to Medicare patients

Action Needed

Make sure your billing staff knows about:

- Discontinued HCPCS codes
- New HCPCS codes
- HCPCS codes subject to and excluded from Clinical Laboratory Improvement Amendments (CLIA) edits

Background

CLIA regulations require a facility to be appropriately certified for each test it performs. To make sure that Medicare & Medicaid only pay for laboratory tests performed in certified facilities, CMS edits each claim for a HCPCS code that's considered a CLIA laboratory test at the CLIA certificate level.

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We discontinued the following HCPCS codes on October 1, 2024:

- 0167U – Gonadotropin, chorionic (hCG), immunoassay with direct optical observation, blood
- 0396U – Obstetrics (pre-implantation genetic testing), evaluation of 300000 DNA single-nucleotide polymorphisms (SNPs) by microarray, embryonic tissue, algorithm reported as a probability for single-gene germline conditions

We discontinued the following HCPCS codes on January 1, 2025:

- 0346U – Beta amyloid, Aβ40 and Aβ42 by liquid chromatography with tandem mass spectrometry (LC-MS/MS), ratio, plasma
- 0352U – Infectious disease (bacterial vaginosis and vaginitis), multiplex amplified probe technique, for detection of bacterial vaginosis-associated bacteria (BVAB-2, Atopobium vaginae, and Megasphera type 1), algorithm reported as detected or not detected and separate detection of Candida species (C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis), Candida glabrata/Candida krusei, and trichomonas vaginalis, vaginal-fluid specimen, each result reported as detected or not detected
- 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
- 0428U – Oncology (breast), targeted hybrid-capture genomic sequence analysis panel, circulating tumor DNA (ctDNA) analysis of 56 or more genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability, and tumor mutation burden
- 0448U – Oncology (lung and colon cancer), DNA, qualitative, next-generation sequencing detection of single-nucleotide variants and deletions in EGFR and KRAS genes, formalin-fixed paraffin-embedded (FFPE) solid tumor samples, reported as presence or absence of targeted mutation(s), with recommended therapeutic options
- 0456U – Autoimmune (rheumatoid arthritis), next-generation sequencing (NGS), gene expression testing of 19 genes, whole blood, with analysis of anti-cyclic citrullinated peptides (CCP) levels, combined with sex, patient global assessment, and body mass index (BMI), algorithm reported as a score that predicts nonresponse to tumor necrosis factor inhibitor (TNFi) therapy

We subject the following HCPCS codes to CLIA edits. We don't include new HCPCS codes for waived tests or provider-performed microscopy procedures in these lists. These HCPCS codes all require a facility to have either a:

- CLIA certificate of registration (certificate type code 9)
- CLIA certificate of compliance (certificate type code 1)
- CLIA certificate of accreditation (certificate type code 3)

We don't pay for tests at a facility without a valid, current, CLIA certificate, with a current CLIA certificate of waiver (certificate type code 2), or with a current CLIA certificate for provider-performed microscopy procedures (certificate type code 4), unless a facility with a current CLIA certificate of waiver or CLIA certificate for provider-performed microscopy procedures bills the appropriate HCPCS code with a QW modifier.

We added the following HCPCS code on July 1, 2024, and it's subject to CLIA edits:

0020M – Oncology (central nervous system), analysis of 30000 DNA methylation loci by methylation array, utilizing DNA extracted from tumor tissue, diagnostic algorithm reported as probability of matching a reference tumor subclass

We added the following HCPCS codes on October 1, 2024, and they're subject to CLIA edits:

- 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
- 0478U – Oncology (non-small cell lung cancer), DNA and RNA, digital PCR analysis of 9 genes (EGFR, KRAS, BRAF, ALK, ROS1, RET, NTRK 1/2/3, ERBB2, and MET) in formalin-fixed paraffin-embedded (FFPE) tissue, interrogation for single-nucleotide variants, insertions/deletions, gene rearrangements, and reported as actionable detected variants for therapy selection
- 0479U – Tau, phosphorylated, pTau217
- 0480U – Infectious disease (bacteria, viruses, fungi, and parasites), cerebrospinal fluid (CSF), metagenomic next-generation sequencing (DNA and RNA), bioinformatic analysis, with positive pathogen identification
- 0481U – IDH1 (isocitrate dehydrogenase 1 [NADP+]), IDH2 (isocitrate dehydrogenase 2 [NADP+]), and TERT (telomerase reverse transcriptase) promoter (eg, central nervous system [CNS] tumors), next-generation sequencing (single-nucleotide variants [SNV], deletions, and insertions)
- 0482U – Obstetrics (preeclampsia), biochemical assay of soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PlGF), serum, ratio reported for sFlt-1/PlGF, with risk of progression for preeclampsia with severe features within 2 weeks
- 0483U – Infectious disease (Neisseria gonorrhoeae), sensitivity, ciprofloxacin resistance (gyrA S91F point mutation), oral, rectal, or vaginal swab, algorithm reported as probability of fluoroquinolone resistance
- 0484U – Infectious disease (Mycoplasma genitalium), macrolide sensitivity (23S rRNA point mutation), oral, rectal, or vaginal swab, algorithm reported as probability of macrolide resistance

- 0485U – Oncology (solid tumor), cell-free DNA and RNA by next-generation sequencing, interpretative report for germline mutations, clonal hematopoiesis of indeterminate potential, and tumor-derived single-nucleotide variants, small insertions/deletions, copy number alterations, fusions, microsatellite instability, and tumor mutational burden
- 0486U – Oncology (pan-solid tumor), next-generation sequencing analysis of tumor methylation markers present in cell-free circulating tumor DNA, algorithm reported as quantitative measurement of methylation as a correlate of tumor fraction
- 0487U – Oncology (solid tumor), cell-free circulating DNA, targeted genomic sequence analysis panel of 84 genes, interrogation for sequence variants, aneuploidy-corrected gene copy number amplifications and losses, gene rearrangements, and microsatellite instability
- 0488U – Obstetrics (fetal antigen noninvasive prenatal test), cell-free DNA sequence analysis for detection of fetal presence or absence of 1 or more of the Rh, C, c, D, E, Duffy (Fya), or Kell (K) antigen in alloimmunized pregnancies, reported as selected antigen(s) detected or not detected
- 0489U – Obstetrics (single-gene noninvasive prenatal test), cell-free DNA sequence analysis of 1 or more targets (eg, CFTR, SMN1, HBB, HBA1, HBA2) to identify paternally inherited pathogenic variants, and relative mutation-dosage analysis based on molecular counts to determine fetal inheritance of maternal mutation, algorithm reported as a fetal risk score for the condition (eg, cystic fibrosis, spinal muscular atrophy, beta hemoglobinopathies [including sickle cell disease], alpha thalassemia)
- 0490U – Oncology (cutaneous or uveal melanoma), circulating tumor cell selection, morphological characterization and enumeration based on differential CD146, high molecular–weight melanoma-associated antigen, CD34 and CD45 protein biomarkers, peripheral blood
- 0491U – Oncology (solid tumor), circulating tumor cell selection, morphological characterization and enumeration based on differential epithelial cell adhesion molecule (EpCAM), cytokeratins 8, 18, and 19, CD45 protein biomarkers, and quantification of estrogen receptor (ER) protein biomarker–expressing cells, peripheral blood
- 0492U – Oncology (solid tumor), circulating tumor cell selection, morphological characterization and enumeration based on differential epithelial cell adhesion molecule (EpCAM), cytokeratins 8, 18, and 19, CD45 protein biomarkers, and quantification of PD-L1 protein biomarker–expressing cells, peripheral blood
- 0493U – Transplantation medicine, quantification of donor-derived cell-free DNA (cfDNA) using next-generation sequencing, plasma, reported as percentage of donor-derived cell-free DNA
- 0494U – Red blood cell antigen (fetal RhD gene analysis), next-generation sequencing of circulating cell-free DNA (cfDNA) of blood in pregnant individuals known to be RhD negative, reported as positive or negative
- 0495U – Oncology (prostate), analysis of circulating plasma proteins (tPSA, fPSA, KLK2, PSP94, and GDF15), germline polygenic risk score (60 variants), clinical information (age, family history of prostate cancer, prior negative prostate biopsy), algorithm reported as risk of likelihood of detecting clinically significant prostate cancer

- 0496U – Oncology (colorectal), cell-free DNA, 8 genes for mutations, 7 genes for methylation by real-time RT-PCR, and 4 proteins by enzyme-linked immunosorbent assay, blood, reported positive or negative for colorectal cancer or advanced adenoma risk
- 0497U – Oncology (prostate), mRNA gene-expression profiling by real-time RT-PCR of 6 genes (FOXM1, MCM3, MTUS1, TTC21B, ALAS1, and PPP2CA), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a risk score for prostate cancer
- 0498U – Oncology (colorectal), next-generation sequencing for mutation detection in 43 genes and methylation pattern in 45 genes, blood, and formalin-fixed paraffin-embedded (FFPE) tissue, report of variants and methylation pattern with interpretation
- 0499U – Oncology (colorectal and lung), DNA from formalin-fixed paraffin-embedded (FFPE) tissue, next-generation sequencing of 8 genes (NRAS, EGFR, CTNNB1, PIK3CA, APC, BRAF, KRAS, and TP53), mutation detection
- 0500U – Autoinflammatory disease (VEXAS syndrome), DNA, UBA1 gene mutations, targeted variant analysis (M41T, M41V, M41L, c.118-2A>C, c.118-1G>C, c.118-9_118-2del, S56F, S621C)
- 0501U – Oncology (colorectal), blood, quantitative measurement of cell-free DNA (cfDNA)
- 0502U – Human papillomavirus (HPV), E6/E7 markers for high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68), cervical cells, branched-chain capture hybridization, reported as negative or positive for high risk for HPV
- 0503U – Neurology (Alzheimer disease), beta amyloid (Aβ40, Aβ42, Aβ42/40 ratio) and tau-protein (ptau217, np-tau217, ptau217/np-tau217 ratio), blood, immunoprecipitation with quantitation by liquid chromatography with tandem mass spectrometry (LC-MS/MS), algorithm score reported as likelihood of positive or negative for amyloid plaques
- 0504U – Infectious disease (urinary tract infection), identification of 17 pathologic organisms, urine, real-time PCR, reported as positive or negative for each organism
- 0505U – Infectious disease (vaginal infection), identification of 32 pathogenic organisms, swab, real-time PCR, reported as positive or negative for each organism
- 0506U – Gastroenterology (Barrett's esophagus), esophageal cells, DNA methylation analysis by next-generation sequencing of at least 89 differentially methylated genomic regions, algorithm reported as likelihood for Barrett's esophagus
- 0507U – Oncology (ovarian), DNA, whole-genome sequencing with 5-hydroxymethylcytosine (5hmC) enrichment, using whole blood or plasma, algorithm reported as cancer detected or not detected
- 0508U – Transplantation medicine, quantification of donor-derived cell-free DNA using 40 single-nucleotide polymorphisms (SNPs), plasma, and urine, initial evaluation reported as percentage of donor-derived cell-free DNA with risk for active rejection
- 0509U – Transplantation medicine, quantification of donor-derived cell-free DNA using up to 12 single-nucleotide polymorphisms (SNPs) previously identified, plasma, reported as percentage of donor-derived cell-free DNA with risk for active rejection

- 0510U – Oncology (pancreatic cancer), augmentative algorithmic analysis of 16 genes from previously sequenced RNA whole-transcriptome data, reported as probability of predicted molecular subtype
- 0511U – Oncology (solid tumor), tumor cell culture in 3D microenvironment, 36 or more drug panel, reported as tumor-response prediction for each drug
- 0512U – Oncology (prostate), augmentative algorithmic analysis of digitized whole-slide imaging of histologic features for microsatellite instability (MSI) status, formalin-fixed paraffin-embedded (FFPE) tissue, reported as increased or decreased probability of MSI-high (MSI-H)
- 0513U – Oncology (prostate), augmentative algorithmic analysis of digitized whole-slide imaging of histologic features for microsatellite instability (MSI) and homologous recombination deficiency (HRD) status, formalin-fixed paraffin-embedded (FFPE) tissue, reported as increased or decreased probability of each biomarker
- 0514U – Gastroenterology (irritable bowel disease [IBD]), immunoassay for quantitative determination of adalimumab (ADL) levels in venous serum in patients undergoing adalimumab therapy, results reported as a numerical value as micrograms per milliliter (µg/mL)
- 0515U – Gastroenterology (irritable bowel disease [IBD]), immunoassay for quantitative determination of infliximab (IFX) levels in venous serum in patients undergoing infliximab therapy, results reported as a numerical value as micrograms per milliliter (µg/mL)
- 0516U – Drug metabolism, whole blood, pharmacogenomic genotyping of 40 genes and CYP2D6 copy number variant analysis, reported as metabolizer status
- 0517U – Therapeutic drug monitoring, 80 or more psychoactive drugs or substances, LC-MS/MS, plasma, qualitative and quantitative therapeutic minimally and maximally effective dose of prescribed and non-prescribed medications
- 0518U – Therapeutic drug monitoring, 90 or more pain and mental health drugs or substances, LC-MS/MS, plasma, qualitative and quantitative therapeutic minimally effective range of prescribed and non-prescribed medications
- 0519U – Therapeutic drug monitoring, medications specific to pain, depression, and anxiety, LC-MS/MS, plasma, 110 or more drugs or substances, qualitative and quantitative therapeutic minimally effective range of prescribed, non-prescribed, and illicit medications in circulation
- 0520U – Therapeutic drug monitoring, 200 or more drugs or substances, LC-MS/MS, plasma, qualitative and quantitative therapeutic minimally effective range of prescribed and non-prescribed medications

We added the following HCPCS codes on January 1, 2025, and they're subject to CLIA edits:

- 81195 – Cytogenomic (genome-wide) analysis, hematologic malignancy, structural variants and copy number variants, optical genome mapping (OGM)

- 81515 – Infectious disease, bacterial vaginosis and vaginitis, real-time PCR amplification of DNA markers for Atopobium vaginae, Atopobium species, Megasphaera type 1, and Bacterial Vaginosis Associated Bacteria-2 (BVAB-2), utilizing vaginal-fluid specimens, algorithm reported as positive or negative for high likelihood of bacterial vaginosis, includes separate detection of Trichomonas vaginalis and Candida species (C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis), Candida glabrata/Candida krusei, when reported
- 81558 – Transplantation medicine (allograft rejection, kidney), mRNA, gene expression profiling by quantitative polymerase chain reaction (qPCR) of 139 genes, utilizing whole blood, algorithm reported as a binary categorization as transplant excellence, which indicates immune quiescence, or not transplant excellence, indicating subclinical rejection
- 82233 – Beta-amyloid; 1-40 (Abeta 40)
- 82234 – Beta-amyloid; 1-42 (Abeta 42)
- 83884 – Neurofilament light chain (NfL)
- 84393 – Tau, phosphorylated (eg, pTau 181, pTau 217), each
- 84394 – Tau, total (tTau)
- 86581 – Streptococcus pneumoniae antibody (IgG), serotypes, multiplex immunoassay, quantitative
- 87513 – Infectious agent detection by nucleic acid (DNA or RNA); Helicobacter pylori (H. pylori), clarithromycin resistance, amplified probe technique
- 87564 – Infectious agent detection by nucleic acid (DNA or RNA); Mycobacterium tuberculosis, rifampin resistance, amplified probe technique
- 87594 – Infectious agent detection by nucleic acid (DNA or RNA); Pneumocystis jirovecii, amplified probe technique
- 87626 – Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), separately reported high-risk types (eg, 16, 18, 31, 45, 51, 52) and high-risk pooled result(s)
- 0521U – Rheumatoid factor IgA and IgM, cyclic citrullinated peptide (CCP) antibodies, and scavenger receptor A (SR-A) by immunoassay, blood
- 0522U – Carbonic anhydrase VI, parotid specific/secretory protein and salivary protein 1 (SP1), IgG, IgM, and IgA antibodies, chemiluminescence, semiqualitative, blood
- 0523U – Oncology (solid tumor), DNA, qualitative, next-generation sequencing (NGS) of single-nucleotide variants (SNV) and insertion/deletions in 22 genes utilizing formalin-fixed paraffin-embedded tissue, reported as presence or absence of mutation(s), location of mutation(s), nucleotide change, and amino acid change
- 0524U – Obstetrics (preeclampsia), sFlt-1/PlGF ratio, immunoassay, utilizing serum or plasma, reported as a value
- 0525U – Oncology, spheroid cell culture, 11-drug panel (carboplatin, docetaxel, doxorubicin, etoposide, gemcitabine, niraparib, olaparib, paclitaxel, rucaparib, topotecan, veliparib) ovarian, fallopian, or peritoneal response prediction for each drug

- 0526U – Nephrology (renal transplant), quantification of CXCL10 chemokines, flow cytometry, urine, reported as pg/mL creatinine baseline and monitoring over time
- 0527U – Herpes simplex virus (HSV) types 1 and 2 and Varicella zoster virus (VZV), amplified probe technique, each pathogen reported as detected or not detected
- 0528U – Lower respiratory tract infectious agent detection, 18 bacteria, 8 viruses, and 7 antimicrobial-resistance genes, amplified probe technique, including reverse transcription for RNA targets, each analyte reported as detected or not detected with semiquantitative results for 15 bacteria
- 0529U – Hematology (venous thromboembolism [VTE]), genome-wide single-nucleotide polymorphism variants, including F2 and F5 gene analysis, and Leiden variant, by microarray analysis, saliva, report as risk score for VTE
- 0530U – Oncology (pan-solid tumor), ctDNA, utilizing plasma, next-generation sequencing (NGS) of 77 genes, 8 fusions, microsatellite instability, and tumor mutation burden, interpretative report for single-nucleotide variants, copy-number alterations, with therapy association

CR 13959 doesn't rescind or replace any previous instructions indicating that we allow a laboratory with a valid CLIA certificate of waiver or CLIA certificate for provider-performed microscopy procedures to bill the above codes with the QW modifier.

Your MAC won't search their files to either retract payment for claims already paid or to retroactively pay claims. However, they'll adjust claims you bring to their attention.

More Information

We issued CR 13959 to your MAC as the official instruction for this change. For more information, find your MAC's website.

Document History

Date of Change	Description
March 14, 2025	Initial article released.