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MEDICAL POLICY – 2.04.520

Laboratory Testing Investigational Services

BCBSA Ref. Policy:	2.04.159
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Replaces:	N/A

RELATED MEDICAL POLICIES:

2.04.26	Fecal Analysis in the Diagnosis of Intestinal Dysbiosis
2.04.73	Intracellular Micronutrient Analysis
2.04.119	Multibiomarker Disease Activity Blood Test for Rheumatoid Arthritis
2.04.123	Serum Biomarker Panel Testing for Systemic Lupus Erythematosus and Other Connective Tissue Diseases
2.04.152	Maternal Serum Biomarkers for Prediction of Adverse Obstetric Outcomes
2.04.509	Cardiovascular Risk Panels
2.04.514	Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | REFERENCES | HISTORY

Clicking this icon returns you to the hyperlinks menu above.

Introduction

There are many tests available to check for diseases or future health risks using genes and molecules. This policy focuses on tests that diagnose diseases that were not discussed in other policies. If there is another review about the same test, its conclusions are more important than the ones here. The main reason for including a test in this review is because there isn't much evidence showing how useful it is for doctors and patients. This policy gives information about several laboratory tests that have not been proven to be helpful in treating people's health, there isn't enough evidence to say they make a positive difference.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Test	Investigational
Tests identified in this policy	**All tests listed in this policy are considered investigational as there is insufficient evidence to determine that the technology results in an improvement in the net health outcome**

Coding

Code	Description
CPT	
0002U	Oncology (colorectal), quantitative assessment of three urine metabolites (ascorbic acid, succinic acid and carnitine) by liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring acquisition, algorithm reported as likelihood of adenomatous polyps (use to report: PolypDX)
0016M	Oncology (bladder), mRNA, microarray gene expression profiling of 209 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as molecular subtype (luminal, luminal infiltrated, basal, basal claudin-low, neuroendocrine-like) (use to report: Decipher Bladder TURBT+G54)
0019M	Cardiovascular disease, plasma, analysis of protein biomarkers by aptamer-based microarray and algorithm reported as 4-year likelihood of coronary event in high-risk populations
0112U	Infectious agent detection and identification, targeted sequence analysis (16S and 18S rRNA genes) with drug-resistance gene (use to report: MicroGenDx)
0163U	Oncology (colorectal) screening, biochemical enzyme-linked immunosorbent assay (ELISA) of 3 plasma or serum proteins (teratocarcinoma derived growth factor-1 [TDGF-1, Cripto-1], carcinoembryonic antigen [CEA], extracellular matrix protein [ECM]), with demographic data (age, gender, CRC-screening compliance) using a proprietary algorithm and reported as likelihood of CRC or advanced adenomas (use to report: BeScreened-CRC test)
0174U	Oncology (solid tumor), mass spectrometric 30 protein targets, formalin-fixed paraffin-embedded tissue, prognostic and predictive algorithm reported as likely, unlikely, or uncertain benefit of 39 chemotherapy and targeted therapeutic oncology agents (use to report: LC-MS/MS Targeted Proteomic Assay)
0176U	Cytolethal distending toxin B (CdtB) and vinculin IgG antibodies by immunoassay (i.e., ELISA) (use to report: IBSchek)

Code	Description
0180U	Red cell antigen (ABO blood group) genotyping (ABO), gene analysis Sanger/chain termination/conventional sequencing, ABO (ABO, alpha 1-3-N-acetylgalactosaminyltransferase and alpha 1-3-galactosyltransferase) gene, including subtyping, 7 exons (use to report: Navigator ABO Sequencing)
0181U	Red cell antigen (Colton blood group) genotyping (CO), gene analysis, AQP1 (aquaporin 1 [Colton blood group]) exon 1(use to report: Navigator CO Sequencing)
0182U	Red cell antigen (Cromer blood group) genotyping (CROM), gene analysis, CD55 (CD55 molecule [Cromer blood group]) exons 1-10 (use to report: Navigator CROM Sequencing)
0183U	Red cell antigen (Diego blood group) genotyping (DI), gene analysis, SLC4A1 (solute carrier family 4 member 1 [Diego blood group]) exon 19 (use to report: Navigator DI Sequencing)
0184U	Red cell antigen (Dombrock blood group) genotyping (DO), gene analysis, ART4 (ADP-ribosyltransferase 4 [Dombrock blood group]) exon 2 (use to report: Navigator DO Sequencing)
0185U	Red cell antigen (H blood group) genotyping (FUT1), gene analysis, FUT1 (fucosyltransferase 1 [H blood group]) exon 4 (use to report: Navigator FUT1 Sequencing)
0186U	Red cell antigen (H blood group) genotyping (FUT2), gene analysis, FUT2 (fucosyltransferase 2) exon 2 (use to report: Navigator FUT2 Sequencing)
0187U	Red cell antigen (Duffy blood group) genotyping (FY), gene analysis, ACKR1 (atypical chemokine receptor 1 [Duffy blood group]) exons 1-2 (use to report: Navigator FY Sequencing)
0188U	Red cell antigen (Gerbich blood group) genotyping (GE), gene analysis, GYPC (glycophorin C [Gerbich blood group]) exons 1-4 (use to report: Navigator GE Sequencing)
0189U	Red cell antigen (MNS blood group) genotyping (GYPA), gene analysis, GYPA (glycophorin A [MNS blood group]) introns 1, 5, exon 2 (use to report: Navigator GYPA Sequencing)
0190U	Red cell antigen (MNS blood group) genotyping (GYPB), gene analysis, GYPB (glycophorin B [MNS blood group]) introns 1, 5, pseudoexon 3 (use to report: Navigator GYPB Sequencing)
0191U	Red cell antigen (Indian blood group) genotyping (IN), gene analysis, CD44 (CD44 molecule [Indian blood group]) exons 2, 3, 6 (use to report: Navigator IN Sequencing)
0192U	Red cell antigen (Kidd blood group) genotyping (JK), gene analysis, SLC14A1 (solute carrier family 14 member 1 [Kidd blood group]) gene promoter, exon 9 (use to report: Navigator JK Sequencing)

Code	Description
0193U	Red cell antigen (JR blood group) genotyping (JR), gene analysis, ABCG2 (ATP binding cassette subfamily G member 2 [Junior blood group]) exons 2-26 (use to report: Navigator JR Sequencing)
0194U	Red cell antigen (Kell blood group) genotyping (KEL), gene analysis, KEL (Kell metallo-endopeptidase [Kell blood group]) exon 8 (use to report: Navigator KEL Sequencing)
0195U	KLF1 (Kruppel-like factor 1), targeted sequencing (i.e., exon 13) (use to report: Navigator KLF1 Sequencing)
0196U	Red cell antigen (Lutheran blood group) genotyping (LU), gene analysis, BCAM (basal cell adhesion molecule [Lutheran blood group]) exon 3 (use to report: Navigator LU Sequencing)
0197U	Red cell antigen (Landsteiner-Wiener blood group) genotyping (LW), gene analysis, ICAM4 (intercellular adhesion molecule 4 [Landsteiner-Wiener blood group]) exon 1(use to report: Navigator LW Sequencing)
0198U	Red cell antigen (RH blood group) genotyping (RHD and RHCE), gene analysis Sanger/chain termination/conventional sequencing, RHD (Rh blood group D antigen) exons 1-10 and RHCE (Rh blood group CcEe antigens) exon 5 (use to report: Navigator RHD/CE Sequencing)
0199U	Red cell antigen (Scianna blood group) genotyping (SC), gene analysis, ERMAP (erythroblast membrane associated protein [Scianna blood group]) exons 4, 12 (use to report: Navigator SC Sequencing)
0200U	Red cell antigen (Kx blood group) genotyping (XK), gene analysis, XK (X-linked Kx blood group) exons 1-3 (use to report: Navigator XK Sequencing)
0201U	Red cell antigen (Yt blood group) genotyping (YT), gene analysis, ACHE (acetylcholinesterase [Cartwright blood group]) exon 2 (use to report: Navigator YT Sequencing)
0210U	Syphilis test, non-treponemal antibody, immunoassay, quantitative (RPR) (BioPlex 2200 RPR Assay)
0219U	Infectious agent (human immunodeficiency virus), targeted viral next-generation sequence analysis (i.e., protease [PR], reverse transcriptase [RT], integrase [INT]), algorithm reported as prediction of antiviral drug susceptibility (use to report: Sentosa SQ HIV-1 Genotyping Assay)
0220U	Oncology (breast cancer), image analysis with artificial intelligence assessment of 12 histologic and immunohistochemical features, reported as a recurrence score (use to report: PreciseDx Breast Cancer Test)
0221U	Red cell antigen (ABO blood group) genotyping (ABO), gene analysis, next-generation sequencing, ABO (ABO, alpha 1-3-N-acetylgalactosaminyltransferase and alpha 1-3-galactosyltransferase) gene (use to report: Navigator ABO Blood Group NGS)

Code	Description
0222U	Red cell antigen (RH blood group) genotyping (RHD and RHCE), gene analysis, next-generation sequencing, RH proximal promoter, exons 1-10, portions of introns 2-3 (use to report: Navigator Rh Blood Group NGS)
0295U	Oncology (breast ductal carcinoma in situ), protein expression profiling by immunohistochemistry of 7 proteins (COX2, FOXA1, HER2, Ki-67, p16, PR, SIAH2), with 4 clinicopathologic factors (size, age, margin status, palpability), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a recurrence risk score (use to report: DCISionRT, PreludeDX)
0337U	Oncology (plasma cell disorders and myeloma), circulating plasma cell immunologic selection, identification, morphological characterization, and enumeration of plasma cells based on differential CD138, CD38, CD19, and CD45 protein biomarker expression, peripheral blood (use to report: CELLSEARCH Circulating Multiple Myeloma Cell (CMMC) Test)
0338U	Oncology (solid tumor), circulating tumor cell selection, identification, morphological characterization, detection and enumeration based on differential EpCAM, cytokeratins 8, 18, and 19, and CD45 protein biomarkers, and quantification of HER2 protein biomarker-expressing cells, peripheral blood (CELLSEARCH HER2 Circulating Tumor Cell (use to report: CTC-HER2) Test)
0342U	Oncology (pancreatic cancer), multiplex immunoassay of C5, C4, cystatin C, factor B, osteoprotegerin (OPG), gelsolin, IGFBP3, CA125 and multiplex electrochemiluminescent immunoassay (ECLIA) for CA19-9, serum, diagnostic algorithm reported qualitatively as positive, negative, or borderline (use to report: IMMray PanCan-d)
0344U	Hepatology (nonalcoholic fatty liver disease [NAFLD]), semiquantitative evaluation of 28 lipid markers by liquid chromatography with tandem mass spectrometry (LC-MS/MS), serum, reported as at-risk for nonalcoholic steatohepatitis (NASH) or not NASH (use to report: OWLiver)
0357U	Oncology (melanoma), artificial intelligence (AI)-enabled quantitative mass spectrometry analysis of 142 unique pairs of glycopeptide and product fragments, plasma, prognostic, and predictive algorithm reported as likely, unlikely, or uncertain benefit from immunotherapy agents (use to report: DAWN IO)
0365U	Oncology (bladder), analysis of 10 protein biomarkers (A1AT, ANG, APOE, CA9, IL8, MMP9, MMP10, PAI1, SDC1 and VEGFA) by immunoassays, urine, algorithm reported as a probability of bladder cancer (use to report: Oncuria Detect)
0366U	Oncology (bladder), analysis of 10 protein biomarkers (A1AT, ANG, APOE, CA9, IL8, MMP9, MMP10, PAI1, SDC1 and VEGFA) by immunoassays, urine, algorithm reported as a probability of recurrent bladder cancer (use to report: Oncuria Monitor)
0367U	Oncology (bladder), analysis of 10 protein biomarkers (A1AT, ANG, APOE, CA9, IL8, MMP9, MMP10, PAI1, SDC1 and VEGFA) by immunoassays, urine, diagnostic algorithm

Code	Description
	reported as a risk score for probability of rapid recurrence of recurrent or persistent cancer following transurethral resection (use to report: Oncuria Predict)
0371U	Infectious agent detection by nucleic acid (DNA or RNA), genitourinary pathogen, semiquantitative identification, DNA from 16 bacterial organisms and 1 fungal organism, multiplex amplified probe technique via quantitative polymerase chain reaction (qPCR), urine (use to report: Qlear UTI)
0372U	Infectious disease (genitourinary pathogens), antibiotic-resistance gene detection, multiplex amplified probe technique, urine, reported as an antimicrobial stewardship risk score (use to report: Qclear UTI-Reflex ABR)
0373U	Infectious agent detection by nucleic acid (DNA and RNA), respiratory tract infection, 17 bacteria, 8 fungus, 13 virus, and 16 antibiotic-resistance genes, multiplex amplified probe technique, upper or lower respiratory specimen (use to report: Respiratory Pathogen with ABR [RPX])
0374U	Infectious agent detection by nucleic acid (DNA or RNA), genitourinary pathogens, identification of 21 bacterial and fungal organisms and identification of 21 associated antibiotic-resistance genes, multiplex amplified probe technique, urine (use to report: Urogenital Pathogen with Rx Panel [UPX])
0375U	Oncology (ovarian), biochemical assays of 7 proteins (follicle stimulating hormone, human epididymis protein 4, apolipoprotein A-1, transferrin, beta-2 macroglobulin, prealbumin [i.e., transthyretin], and cancer antigen 125), algorithm reported as ovarian cancer risk score (use to report: OvaWatch)
0376U	Oncology (prostate cancer), image analysis of at least 128 histologic features and clinical factors, prognostic algorithm determining the risk of distant metastases, and prostate cancer-specific mortality, includes predictive algorithm to androgen deprivation-therapy response, if appropriate. (use to report: ArteraAI Prostate Test)
0377U	Cardiovascular disease, quantification of advanced serum or plasma lipoprotein profile, by nuclear magnetic resonance (NMR) spectrometry with report of a lipoprotein profile (including 23 variables) (use to report: Liposcale)
0384U	Nephrology (chronic kidney disease), carboxymethyllysine, methylglyoxal hydroimidazolone, and carboxyethyl lysine by liquid chromatography with tandem mass spectrometry (LC-MS/MS) and HbA1c and estimated glomerular filtration rate (GFR), with risk score reported for predictive progression to high-stage kidney disease (use to report: NaviDKD Predictive Diagnostic Screening for Kidney Health)
0385U	Nephrology (chronic kidney disease), apolipoprotein A4 (ApoA4), CD5 antigen-like (CD5L), and insulin-like growth factor binding protein 3 (IGFBP3) by enzyme-linked immunoassay (ELISA), plasma, algorithm combining results with HDL, estimated glomerular filtration rate (GFR) and clinical data reported as a risk score for developing diabetic kidney disease (use to report: PromarkerD)

Code	Description
0390U	Obstetrics (preeclampsia), kinase insert domain receptor (KDR), Endoglin (ENG), and retinol-binding protein 4 (RBP4), by immunoassay, serum, algorithum reported as risk score (use to report: PEPredictDx by OncoOmicsDx Laboratory mProbe)
0395U	Oncology (lung), multi-omics (microbial DNA by shotgun nextgeneration sequencing and carcinoembryonic antigen and osteopontin by immunoassay), plasma, algorithm reported as malignancy risk for lung nodules in early-stage disease (use to report: OncobiotaLUNG)
0404U	Oncology (breast), semiquantitative measurement of thymidine kinase activity by immunoassay, serum, results reported as risk of disease progression
0406U	Oncology (lung), flow cytometry, sputum, 5 markers (meso-tetra [4-carboxyphenyl] porphyrin [TCPP], CD206, CD66b, CD3, CD19), algorithm reported as likelihood of lung cancer
0415U	Cardiovascular disease (acute coronary syndrome [ACS]), IL-16, FAS, FASLigand, HGF, CTACK, EOTAXIN, and MCP-3 by immunoassay combined with age, sex, family history, and personal history of diabetes, blood, algorithm reported as a 5-year (deleted risk) score for ACS
0418U	Oncology (breast), augmentative algorithmic analysis of digitized whole slide imaging of 8 histologic and immunohistochemical features, reported as a recurrence score
0421U	Oncology (colorectal) screening, quantitative real-time target and signal amplification of 8 RNA markers (GAPDH, SMAD4, ACY1, AREG, CDH1, KRAS, TNFRSF10B, EGLN2) and fecal hemoglobin, algorithm reported as a positive or negative for colorectal cancer risk
0435U	Oncology, chemotherapeutic drug cytotoxicity assay of cancer stem cells (CSCs), from cultured CSCs and primary tumor cells, categorical drug response reported based on cytotoxicity percentage observed, minimum of 14 drugs or drug combinations
0436U	Oncology (lung), plasma analysis of 388 proteins, using aptamer-based proteomics technology, predictive algorithm reported as clinical benefit from immune checkpoint inhibitor therapy
0441U	Infectious disease (bacterial, fungal, or viral infection), semiquantitative biomechanical assessment (via deformability cytometry), whole blood, with algorithmic analysis and result reported as an index
0442U	Infectious disease (respiratory infection), Myxovirus resistance protein A (MxA) and C-reactive protein (CRP), fingerstick whole blood specimen, each biomarker reported as present or absent
0450U	Oncology (multiple myeloma), liquid chromatography with tandem mass spectrometry (LC-MS/MS), monoclonal paraprotein sequencing analysis, serum, results reported as baseline presence or absence of detectable clonotypic peptides
0451U	Oncology (multiple myeloma), LC-MS/MS, peptide ion quantification, serum, results compared with baseline to determine monoclonal paraprotein abundance

Code	Description
0457U	Perfluoroalkyl substances (PFAS) (e.g., perfluorooctanoic acid, perfluorooctane sulfonic acid), 9 PFAS compounds by LC-MS/MS, plasma or serum, quantitative
0458U	Oncology (breast cancer), S100A8 and S100A9, by enzyme-linked immunosorbent assay (ELISA), tear fluid with age, algorithm reported as a risk score
0462U	Melatonin levels test, sleep study, 7 or 9 sample melatonin profile (cortisol optional), enzyme-linked immunosorbent assay (ELISA), saliva, screening/preliminary
0463U	Oncology (cervix), mRNA gene expression profiling of 14 biomarkers (E6 and E7 of the highest-risk human papillomavirus [HPV] types 16, 18, 31, 33, 45, 52, 58), by real-time nucleic acid sequence-based amplification (NASBA), exo- or endocervical epithelial cells, algorithm reported as positive or negative for increased risk of cervical dysplasia or cancer for each biomarker
0468U	Hepatology (nonalcoholic steatohepatitis [NASH]), miR-34a-5p, alpha 2-macroglobulin, YKL40, HbA1c, serum and whole blood, algorithm reported as a single score for NASH activity and fibrosis
0470U	Oncology (oropharyngeal), detection of minimal residual disease by next-generation sequencing (NGS) based quantitative evaluation of 8 DNA targets, cell-free HPV 16 and 18 DNA from plasma
0472U	Carbonic anhydrase VI (CA VI), parotid specific/secretory protein (PSP) and salivary protein (SP1) IgG, IgM, and IgA antibodies, enzyme-linked immunosorbent assay (ELISA), semiqualitative, blood, reported as predictive evidence of early Sjogren syndrome
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 (new code effective 10/01/24)
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 (new code effective 10/01/24)
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 (new code effective 10/01/24)
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 (new code effective 10/01/24)

Code	Description
0501U	Oncology (colorectal), blood, quantitative measurement of cell-free DNA (cfDNA) (new code effective 10/01/24)
0505U	Infectious disease (vaginal infection), identification of 32 pathogenic organisms, swab, real-time PCR, reported as positive or negative for each organism (new code effective 10/01/2024)
0510U	Oncology (pancreatic cancer), augmentative algorithmic analysis of 16 genes from previously sequenced RNA whole-transcriptome data, reported as probability of predicted molecular subtype (new code effective 10/01/24)
0511U	Oncology (solid tumor), tumor cell culture in 3D microenvironment, 36 or more drug panel, reported as tumor-response prediction for each drug (new code effective 10/01/24)
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) (new code effective 10/01/24)
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 (new code effective 10/01/24)
0521U	Rheumatoid factor IgA and IgM, cyclic citrullinated peptide (CCP) antibodies, and scavenger receptor A (SR-A) by immunoassay, blood (new code effective 01/01/25)
0522U	Carbonic anhydrase VI, parotid specific/secretory protein and salivary protein 1 (SP1), IgG, IgM, and IgA antibodies, chemiluminescence, semiqualitative, blood (new code effective 01/01/25)
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 (new code effective 01/01/25)
0526U	Nephrology (renal transplant), quantification of CXCL10 chemokines, flow cytometry, urine, reported as pg/mL creatinine baseline and monitoring over time (new code effective 01/01/25)
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 (new code effective 01/01/25)
0531U	Infectious disease (acid-fast bacteria and invasive fungi), DNA (673 organisms), next-generation sequencing, plasma (new code effective 04/01/25)

Code	Description
0535U	Perfluoroalkyl substances (PFAS) (eg, perfluorooctanoic acid, perfluorooctane sulfonic acid), by liquid chromatography with tandem mass spectrometry (LC-MS/MS), plasma or serum, quantitative (new code effective 04/01/25)
0541U	Cardiovascular disease (HDL reverse cholesterol transport), cholesterol efflux capacity, LC-MS/MS, quantitative measurement of 5 distinct HDL-bound apolipoproteins (apolipoproteins A1, C1, C2, C3, and C4), serum, algorithm reported as prediction of coronary artery disease (pCAD) score (new code effective 04/01/25)
0542U	Nephrology (renal transplant), urine, nuclear magnetic resonance (NMR) spectroscopy measurement of 84 urinary metabolites, combined with patient data, quantification of BK virus (human polyomavirus 1) using real-time PCR and serum creatinine, algorithm reported as a probability score for allograft injury status (new code effective 04/01/25)
0545U	Acetylcholine receptor (AChR), antibody identification by immunofluorescence, using live cells, reported as positive or negative (new code effective 04/01/25)
0546U	Low-density lipoprotein receptor-related protein 4 (LRP4), antibody identification by immunofluorescence, using live cells, reported as positive or negative (new code effective 04/01/25)
0548U	Glial fibrillary acidic protein (GFAP), chemiluminescent enzyme immunoassay, using plasma (new code effective 04/01/25)
0550U	Oncology (prostate), enzyme-linked immunosorbent assays (ELISA) for total prostate-specific antigen (PSA) and free PSA, serum, combined with age, previous negative prostate biopsy status, digital rectal examination findings, prostate volume, and image and data reporting of the prostate, algorithm reported as a risk score for the presence of high-grade prostate cancer (new code effective 04/01/25)
0558U	Oncology (colorectal), quantitative enzyme-linked immunosorbent assay (ELISA) for secreted colorectal cancer protein marker (BF7 antigen), using serum, result reported as indicative of response/no response to therapy or disease progression/regression (new code effective 07/01/25)
0559U	Oncology (breast), quantitative enzyme-linked immunosorbent assay (ELISA) for secreted breast cancer protein marker (BF9 antigen), serum, result reported as indicative of response/no response to therapy or disease progression/regression (new code effective 07/01/25)
0563U	Infectious disease (bacterial and/or viral respiratory tract infection), pathogen-specific nucleic acid (DNA or RNA), 11 viral targets and 4 bacterial targets, qualitative RT-PCR, upper respiratory specimen, each pathogen reported as positive or negative (new code effective 07/01/25)
0564U	Infectious disease (bacterial and/or viral respiratory tract infection), pathogen-specific nucleic acid (DNA or RNA), 10 viral targets and 4 bacterial targets, qualitative RT-PCR, upper respiratory specimen, each pathogen reported as positive or negative (new code effective 07/01/25)

Code	Description
0570U	Neurology (traumatic brain injury), analysis of glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1), immunoassay, whole blood or plasma, individual components reported with the overall result of elevated or non-elevated based on threshold comparison (new code effective 07/01/25)
0571U	Oncology (solid tumor), DNA (80 genes) and RNA (10 genes), by next-generation sequencing, plasma, including single-nucleotide variants, insertions/deletions, copy-number alterations, microsatellite instability, and fusions, reported as clinically actionable variants (new code effective 07/01/25)
0572U	Oncology (prostate), high-throughput telomere length quantification by FISH, whole blood, diagnostic algorithm reported as risk of prostate cancer (new code effective 07/01/25)
0573U	Oncology (pancreas), 3 biomarkers (glucose, carcinoembryonic antigen, and gastricsin), pancreatic cyst lesion fluid, algorithm reported as categorical mucinous or non-mucinous (new code effective 07/01/25)
0574U	Mycobacterium tuberculosis, culture filtrate protein-10-kDa (CFP-10), serum or plasma, liquid chromatography mass spectrometry (LC-MS) (new code effective 07/01/25)
84999	Unlisted chemistry procedure (use to report: known error test, Prometheus precision-guided dosing PredictrPK test).

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

N/A

Evidence Review

Description

There are numerous commercially available genetic and molecular diagnostic, prognostic, and therapeutic tests for individuals with certain diseases or asymptomatic individuals with future risk. This policy relates to diagnostic tests not addressed in a separate policy. If a separate policy exists, then conclusions reached there supersede conclusions here. The main criterion for

inclusion in this policy is the limited evidence on the clinical utility for the test. As these tests do not have clinical utility, the evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Background

This policy applies if there is not a separate policy that outlines specific criteria for testing. If a separate policy does exist, then the criteria for medical necessity therein supersede the guidelines herein.

This policy addresses laboratory services considered to be investigational. These tests are often available on a clinical basis before the required and necessary evidence base to support clinical validity and utility is established. Because these tests are often proprietary, there may be no independent test evaluation data available in the early stages to support the laboratory's claims regarding test performance and utility. While studies using these tests may generate information that may help elucidate the biologic mechanisms of disease and eventually help design treatments, the tests listed in this policy are currently in a developmental phase, with limited evidence of clinical utility for diagnosis, prognosis, or risk assessment.

Summary of Evidence

For individuals with various indications for diagnostic, prognostic, therapeutic, or future risk assessment testing who receive the tests addressed in this policy, the evidence on clinical utility is insufficient or non-evaluable. For each test addressed, a brief description is provided for informational purposes. No formal evidence review was conducted. To sufficiently evaluate clinical utility, features of well-defined test, intended use, and clinical management pathway characteristics are summarized. If it is determined that enough evidence has accumulated to reevaluate its potential clinical utility, the test will be removed from this policy and addressed separately. The lack of demonstrated clinical utility of these tests is based on the following factors: (1) there is no or extremely limited published data addressing the test; and/or (2) it is unclear where in the clinical pathway the test fits (replacement, triage, add-on); and/or (3) it is unclear how the test leads to changes in management that would improve health outcomes and/or avoiding existing burdensome and invasive testing; and/or (4) thresholds for decision making have not been established; (5) and/or the outcome from the test result does not result in a clinically meaningful improvement relative to the outcomes(s) obtained without the test.

Ongoing and Unpublished Clinical Trials

Some currently ongoing trials that might influence this review are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05276466[a]	Assessment of Urinary Polymerase Chain Reaction (PCR) and Next Generation Sequencing (NGS) Technology in the Evaluation and Management of Females With Chronic Bladder Pain and Cystitis-like Symptoms	100	Dec 2023
NCT05287438[a]	Next Generation Sequencing Versus Traditional Cultures for Clinically Infected Penile Implants: Impact of Culture Identification on Outcomes	40	Oct 2024

NCT: National Clinical Trial.

[a] Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Gastroenterology

In 2023, the American College of Gastroenterology published a clinical practice update for the diagnosis and management of celiac disease.[27] A recommendation for genetic testing using a multigene panel test (e.g., Celiac PLUS) was not included.

In 2018, the American College of Gastroenterology practice guidelines on Crohn disease state that genetic and routine serologic testing is not indicated to establish the diagnosis of Crohn's disease.[28]

American Urological Association et al

In 2019, the American Urological Association (AUA) published joint guidelines with the Canadian Urological Association (CUA) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) on the management of recurrent uncomplicated urinary tract infections in women.[29] Regarding the use of polymerase chain reaction (PCR) and next-generation sequencing (NGS) techniques for the identification of bacterial species, the guideline states that "more evidence is needed before these technologies become incorporated into the guideline, as there is concern that adoption of this technology in the evaluation of lower urinary tract symptoms may lead to over treatment with antibiotics."

In 2016, the AUA published joint guidelines with the Society of Urologic Oncology on the diagnosis and treatment of non-muscle invasive bladder cancer.[30] For use of urinary biomarkers after diagnosis, the guidelines state: "a clinician should not use urinary biomarkers in place of cystoscopic evaluation" (Strong Recommendation; Evidence Strength: Grade B); that "in a patient with a history of low-risk cancer and a normal cystoscopy, a clinician should not routinely use a urinary biomarker or cytology during surveillance (Expert Opinion); and that "in a patient with non-muscle invasive bladder cancer (NMIBC), a clinician may use biomarkers to assess response to intravesical Bacillus Calmette-Guerin (BCG) (UroVysion FISH) and adjudicate equivocal cytology (UroVysion FISH and ImmunoCyt) (Expert Opinion)."

National Comprehensive Cancer Network

NCCN clinical practice guidelines on bladder cancer v.4.2024 state the following regarding urine molecular tests for urothelial tumor markers.[31] Many of these tests have a better sensitivity for detecting bladder cancer than urinary cytology, but specificity is lower. Considering this, evaluation of urinary urothelial tumor markers may be considered during surveillance of high-

risk non-muscle invasive bladder cancer (NMIBC). However, it remains unclear whether these tests offer additional useful information for detection and management of NMIBC. Therefore, the panel considers this to be a category 2B recommendation.

NCCN clinical practice guidelines on colon cancer (v.5.2024) state that "it has not been established if molecular markers (other than MSI-H/dMMR) are useful in treatment determination (predictive markers) and prognosis.[32]

NCCN clinical practice guidelines on prostate cancer (v.4.2024) state that "there are advanced risk stratification tools (i.e., gene expression biomarkers, AI digital pathology) that have been variably demonstrated to independently improve risk stratification beyond NCCN or CAPRA risk stratification" and that "these tools are recommended to be used when they have the potential ability to change disease management. These tools should not be ordered reflexively. The most common treatment decisions in localized prostate cancer to use these tests include the use and/or intensity of active surveillance versus radical therapy, [radiotherapy](RT) versus RT + short-term (ST)-[androgen deprivation therapy](ADT), and RT + ST-ADT versus long-term (LT)-ADT. The most common treatment decisions in biochemically recurrent prostate cancer post-RP to use these tests include secondary RT versus secondary RT + ADT. These tools are not recommended for patients with very-low-risk prostate cancer. There are an extensive number of these tools created with substantial variability in quality of reporting and model design, endpoint selection, and quality and caliber of validation. It is recommended to use models that have high-quality and robust validation, ideally with high-quality, long-term clinical trial data, which usually comes from randomized trials and across multiple clinical trials."[33] For the ArteraAI Prostate test 2A recommendation, continuous scores may be used to provide more accurate risk stratification to inform shared decision-making; however, NCCN notes that "specific score cut points have not been published to date for specific treatment decisions." Predictive biomarker testing with ArteraAI in individuals with intermediate-risk prostate cancer can help to identify patients with a more favorable prognostic risk who "may consider the use of RT alone" without ST-ADT.

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Laboratories that offer laboratory-developed tests must be licensed by the CLIA for high-complexity testing. To date, the US Food and Drug Administration has chosen not to require any regulatory review of these tests.

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History

Date	Comments
09/01/23	New policy, approved August 8, 2023. Policy created with literature review through May 12, 2023. All tests listed in this policy are considered investigational. Added CPT codes 0112U, and 0365U-0367U.
10/01/23	Coding update. Added new CPT codes 0406U, 0415U and 0418U.
01/01/24	Interim Review, approved December 11, 2023. Policy updated with literature review through September 25, 2023. Added CPT codes 0371U, 0372U, 0373U, 0374U, 0377U, 0384U, 0385U, and 84999. Added CPT code 81382, effective April 4, 2024, following a 90-day notification. Added CPT code 0390U.
04/01/24	Coding update. Added CPT codes 0390U and 81382.
05/01/24	Minor update to related policies. 2.04.100 was replaced with 2.04.509 Cardiovascular Risk Panels.
07/01/24	Coding update. Removed CPT code 81382. Added new CPT codes 0450U, 0451U, 0457U, 0458U, 0462U, 0463U, 0468U, 0470U and 0472U.
10/01/24	Coding update. Added new CPT codes 0490U, 0491U, 0492U, 0495U, 0501U, 0505U, 0510U, 0511U, 0512U and 0513U.
01/01/25	Annual Review, approved December 9, 2024. Policy updated with literature review through September 30, 2024; references added. Policy statement unchanged. Added CPT code 0376U. Added new CPT codes 0521U, 0522U, 0525U, 0526U, 0528U, 81515. The following codes were moved from policy 10.01.533: 0002U, 0016M, 0019M, 0163U, 0174U. 0176U, 0180U-0201U, 0210U, 0219U-0222U, 0295U, 0337U, 0338U, 0342U, 0344U, 0357U, 0375U, 0376U, 0395U, 0404U, 0435U, 0436U, 0441U and 0442U.
04/01/25	Coding update. Added new CPT codes: 0531U, 0535U, 0541U, 0542U, 0545U, 0546U, 0548U and 0550U.
06/06/25	Coding update. Removed CPT code 81515.
07/01/25	Coding update. Added new CPT codes: 0558U, 0559U, 0563U, 0564U, 0570U, 0571U, 0572U, 0573U, 0574U following Q3 coding updates.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2025 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to

the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.