PHP_2.04.159	Laboratory Testing Investigational Services		
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State Guidelines

Applicable Medi-Cal guidelines as of the publication of this policy (this guideline supersedes the criteria in the Policy Statement section below):

I. Department of Managed Health Care (DMHC) All Plan Letter (APL) Guideline:
- N/A

II. Department of Health Care Services (DHCS) Provider Manual Guideline:
- TAR and Non-Standard Benefits List: Codes 0001M thru 0999U (tar and non cd0)
- TAR and Non-Standard Benefits List: Codes 80000 thru 89999 (tar and non cd8)
- Pathology: Molecular Pathology (path molec)

Below is an excerpt of the Molecular Pathology guideline language. Please refer to the specific Provider Manual in the link above for the complete guideline.

Biomarker and Pharmacogenetic Testing
Medi-Cal covers medically necessary biomarker and pharmacogenomic testing, as described in the manual section Proprietary Laboratory Analyses (PLA). Medi-Cal may not cover all CPT and HCPCS codes associated with a particular biomarker or pharmacogenomic test. As such, the particular biomarker or pharmacogenomic test code may be covered with an approved Treatment Authorization Request (TAR) if medical necessity is established, as described in the TAR and Non-Benefit: Introduction to List section of the Provider Manual.

Biomarker Testing
Biomarker testing is used to diagnose, treat, manage, or monitor a Medi-Cal member's disease or condition to guide treatment decisions. As defined by Section 14132.09 of the Welfare and Institutions Code, biomarker testing is the analysis of an individual's tissue, blood or other biospecimen for the presence of a biomarker. Biomarker testing includes, but is not limited to, single-analyte tests, multiplex panel tests and whole genome sequencing. Biomarkers are a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacologic responses to a specific therapeutic intervention. A biomarker includes, but is not limited to, gene mutations or protein expression. Medically necessary biomarker testing is subject to utilization controls and evidence-based clinical practice guidelines.

When testing for biomarkers, all Medi-Cal providers must ensure that they are provided in a manner that limits disruptions to care. As with all Medi-Cal benefits, restricted or denied use of biomarker testing for the purpose of diagnosis, treatment or ongoing monitoring of any medical condition is subject to Medi-Cal's grievance, appeal and State Fair Hearing processes, as well as any additional processes established specifically for Medi-Cal managed care plans.

Pharmacogenomic Testing
Pharmacogenomic testing is defined as a laboratory genetic testing that includes, but is not limited to, a panel test to identify how a person's genetics may impact the efficacy, toxicity

and safety of medications. Medically necessary pharmacogenomic testing is covered subject to utilization controls and evidence-based clinical practice guidelines.

III. Department of Health Care Services (DHCS) All Plan Letter (APL) Guideline:
- APL 22-010 – Cancer Biomarker Testing

Below is an excerpt of the guideline language. Please refer to the specific All Plan Letter in the link above for the complete guideline.

For the purposes of this APL, "Biomarker test" is defined as a diagnostic test, single or multigene, of an individual's biospecimen, such as tissue, blood, or other bodily fluids, for DNA or RNA alterations, including phenotypic characteristics of a malignancy, to identify an individual with a subtype of cancer, in order to guide treatment. Biomarkers, also called tumor markers, are substances found in higher-than-normal levels in the cancer itself, or in blood, urine, or tissues of some individuals with cancer. Biomarkers can determine the likelihood some types of cancer will spread. They can also help doctors choose the best treatment.

Medi-Cal managed care health plans (MCPs) are required to cover medically necessary biomarker testing for members with:
- Advanced or metastatic stage 3 or 4 cancer.
- Cancer progression or recurrence in the member with advanced or metastatic stage 3 or 4 cancer.

MCPs are prohibited from imposing prior authorization requirements on biomarker testing that is associated with a federal Food and Drug Administration (FDA)-approved therapy for advanced or metastatic stage 3 or 4 cancer. If the biomarker test is not associated with an FDA-approved cancer therapy for advanced or metastatic stage 3 or 4 cancer, MCPs may still require prior authorization for such testing.

Policy Statement

Any criteria that are not specifically addressed in the above APL and Provider Manuals, please refer to the criteria below.

I. 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 (see Policy Guidelines).

Policy Guidelines

Genetic testing is considered **investigational** when Blue Shield of California criteria are not met, including when there is insufficient evidence to determine that the technology results in an improvement in the net health outcome. The following tests listed in the table below and within the table in the "*Codes*" section are considered investigational.

Test Name	Laboratory	PLA/CPT code
Polygenic Risk Score	Many	N/A
Prometheus® Celiac PLUS	Prometheus Laboratories	No specific code
Prometheus® Crohn's Prognostic	Prometheus Laboratories	No specific code
DNA Methylation Pathway Profile	Mosaic Diagnostics (formerly Great Plains Laboratory)	No specific code
Prometheus® IBD sgi Diagnostic®	Prometheus Laboratories	No specific code

Test Name	Laboratory	PLA/CPT code
ToxProtect	Genotox Laboratories LTD	0007U
Cytochrome P450 1A2 Genotype	Mayo Clinic	0031U
Onco4D™	Animated Dynamics, Inc	0083U
Vita Risk®	Arctic Medical Laboratories	0205U
Colvera®	Clinical Genomics Pathology Inc	0229U
PancreaSeq® Genomic Classifier	Molecular and Genomic Pathology Laboratory, University of Pittsburgh Medical Center	0313U
AMBLor® melanoma prognostic test	Avero® Diagnostics	0387U
LungOI	Imagene	0414U
RightMed® Oncology Gene Report	OneOme® LLC	0460U
RightMed® Oncology Medication Report	OneOme® LLC	0461U
Shield™	Guardant Health, Inc	0537U
ClarityDx Prostate	Protean BioDiagnostics	0550U
ChemoFx	Helomics Corporation	81535, 81536
Octave® Multiple Sclerosis Disease Activity (MSDA)	Octave Biosciences	No specific code
know error®	Strand Diagnostics	No specific code

Please refer to the list of related evidence reviews for an assessment of other molecular and genetic tests not listed in this policy.

Genetics Nomenclature Update

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the Human Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Disease-associated variant	Disease-associated change in the DNA sequence
	Variant	Change in the DNA sequence
	Familial variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives

Table PG2. American College of Medical Genetics and Genomics and the Association for Molecular Pathology Standards and Guidelines for Variant Classification

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

Genetic Counseling

Experts recommend formal genetic counseling for patients who are at-risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding

risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Coding
See the Codes table for details.

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 review relates to genetic and molecular diagnostic tests not addressed in a separate review and have not received clearance/approval/de novo classification from the Food and Drug Administration (FDA). If a separate evidence review exists, then conclusions reached there supersede conclusions here. The main criterion for inclusion in this review 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 and will not be subjected to a full evidence review.

Summary of Evidence
For individuals with various indications for diagnostic, prognostic, therapeutic, or future risk assessment testing who receive the genetic and molecular tests addressed in this review, 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 review 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.

Related Policies

- Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer
- Gene Expression Profiling for Cutaneous Melanoma
- General Approach to Evaluating the Utility of Genetic Panels
- General Approach to Genetic Testing
- Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
- Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
- Genetic Testing for Alzheimer Disease
- Identification of Microorganisms Using Nucleic Acid Probes
- Molecular Genomic Profiling for Cancers of Unknown Primary
- Multimarker Serum Testing Related to Ovarian Cancer

- Use of Common Genetic Variants (Single Nucleotide Variants) to Predict Risk of Nonfamilial Breast Cancer

Benefit Application

Blue Shield of California Promise Health Plan is contracted with L.A. Care Health Plan for Los Angeles County and the Department of Health Care Services for San Diego County to provide Medi-Cal health benefits to its Medi-Cal recipients. In order to provide the best health care services and practices, Blue Shield of California Promise Health Plan has an extensive network of Medi-Cal primary care providers and specialists. Recognizing the rich diversity of its membership, our providers are given training and educational materials to assist in understanding the health needs of their patients as it could be affected by a member's cultural heritage.

The benefit designs associated with the Blue Shield of California Promise Medi-Cal plans are described in the Member Handbook (also called Evidence of Coverage).

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. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

Health Equity Statement

Blue Shield of California Promise Health Plan's mission is to transform its health care delivery system into one that is worthy of families and friends. Blue Shield of California Promise Health Plan seeks to advance health equity in support of achieving Blue Shield of California Promise Health Plan's mission.

Blue Shield of California Promise Health Plan ensures all Covered Services are available and accessible to all members regardless of sex, race, color, religion, ancestry, national origin, ethnic group identification, age, mental disability, physical disability, medical condition, genetic information, marital status, gender, gender identity, or sexual orientation, or identification with any other persons or groups defined in Penal Code section 422.56, and that all Covered Services are provided in a culturally and linguistically appropriate manner.

Rationale

Background
This policy applies if there is not a separate evidence review that outlines specific criteria for testing. If a separate evidence review 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.

Literature Review

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Laboratory Testing Investigational Services

Clinical Context and Test Purpose

The purpose of various commercially available genetic and molecular diagnostic, prognostic, and therapeutic tests for individuals with relevant indications is to inform a clinical management decision that improves the net health outcome.

No formal evidence review was conducted.

Supplemental Information

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

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a U.S. professional society, an international society with U.S. 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.[1] 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.[2]

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.[3] 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 2022, the guideline was reviewed and validated. In 2025, this guideline was amended but the association still holds the position 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.[4] 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 NMIBC, a clinician may use biomarkers to assess response to intravesical BCG (UroVysion FISH) and adjudicate equivocal cytology (UroVysion FISH and ImmunoCyt) (Expert Opinion)."

National Comprehensive Cancer Network

National Comprehensive Cancer Network clinical practice guidelines on bladder cancer (v.4.2024) state the following regarding urine molecular tests for urothelial tumor markers:[5] "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 non-muscle invasive bladder tumors. 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."[6]

National Human Genome Research Institute et al

In 2021, the National Human Genome Research Institute's ClinGen Complex Disease Working Group updated the Genetic Risk Prediction (GRIPS) Reporting Statement in collaboration with the Polygenic Score (PGS) Catalog.[7] The 22-item reporting framework developed to define the minimal information needed to interpret and evaluate polygenic risk scores is summarized in Table 1.

Table 1. Polygenic Risk Score Reporting Statement

Reporting Standard	
Background	Study Type
	Risk Model Purpose & Predicted Outcome
Study Population and Data	Study Design & Recruitment
	Participant Demographic and Clinical Characteristics
	Ancestry
	Genetic Data
	Non-Genetic Variables
	Outcome of Interest
	Missing Data
Risk Model Development & Application	Polygenic Risk Score Construction & Estimation
	Risk Model Type
	Integrated Risk Model(s) Description & Fitting
Risk Model Evaluation	PRS Distribution
	Risk Model Predictive Ability
	Risk Model Discrimination
	Risk Model Calibration
	Subgroup Analyses
Limitations & Clinical Implications	Risk Model Interpretation
	Limitations
	Generalizability
	Risk Model Intended Uses
Data Transparency & Availability	

PRS: polygenic risk score.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. 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 (unknown status)
NCT05287438[a]	Next Generation Sequencing Versus Traditional Cultures for Clinically Infected Penile Implants: Impact of Culture Identification on Outcomes	40	Oct 2024 (unknown status)
NCT06417190	IIT2023-13-BALLAS-VHTMT: Bladder Preservation for Patients With Muscle Invasive Bladder Cancer (MIBC) With Variant Histology	20	Oct 2030

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

References

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3. Anger J, Lee U, Ackerman AL, et al. Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline. J Urol. Aug 2019; 202(2): 282-289. PMID 31042112
4. Chang SS, Boorjian SA, Chou R, et al. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. J Urol. Oct 2016; 196(4): 1021-9. PMID 27317986
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6. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Colon Cancer [Version 5.2024]. August 22, 2024; https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed September 24, 2024.
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11. Department of Healthcare Services All Plan Letter. All Plan Letter APL 22-010: Cancer Biomarker Testing. Accessed February 6, 2026, from https://www.dhcs.ca.gov/formsandpubs/Documents/MMCDAPLsandPolicyLetters/APL2022/APL22-010.pdf

Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
  - Family history if applicable
  - How test result will impact clinical decision making
  - Reason for performing test
  - Signs/symptoms/test results related to reason for testing (e.g., Cancer description, location and tumor staging, if applicable)
- Provider order for test
- Name and description of test
- Name of laboratory performing the test
- Any available evidence supporting the analytic validity and clinical validity/utility of the specific test
- CPT codes to be billed for the particular test

Post Service (in addition to the above, please include the following):

- Results/reports of tests performed

Coding

The list of codes in this Medical Policy is intended as a general reference and may not cover all codes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy.

Type	Code	Description
CPT®	0007U	Drug test(s), presumptive, with definitive confirmation of positive results, any number of drug classes, urine, includes specimen verification including DNA authentication in comparison to buccal DNA, per date of service ***(Includes ToxProtect, Genotox Laboratories LTD)***
	0017M	Oncology (diffuse large B-cell lymphoma [DLBCL]), mRNA, gene expression profiling by fluorescent probe hybridization of 20 genes, formalin-fixed paraffin-embedded tissue, algorithm reported as cell of origin
	0031U	CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(e.g., drug metabolism) gene analysis, common variants (i.e., *1F, *1K, *6, *7) ***(Includes Cytochrome P450 1A2 Genotype, Mayo Clinic)***
	0083U	Oncology, response to chemotherapy drugs using motility contrast tomography, fresh or frozen tissue, reported as likelihood of sensitivity or resistance to drugs or drug combinations

Type	Code	Description
		(Includes Onco4D™, Animated Dynamics, Inc)
	0112U	Infectious agent detection and identification, targeted sequence analysis (16S and 18S rRNA genes) with drug-resistance gene ***(Includes MicroGenDX qPCR & NGS For Infection, MicroGenDX)***
	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 ***(Includes LC-MS/MS Targeted Proteomic Assay, OncoOmicDx Laboratory, LDT)***
	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 age-related macular-degeneration risk associated with zinc supplements ***(Includes Vita Risk®, Arctic Medical Laboratories)***
	0229U	BCAT1 (Branched chain amino acid transaminase 1) and IKZF1 (IKAROS family zinc finger 1) (e.g., colorectal cancer) promoter methylation analysis ***(Includes Colvera®, Clinical Genomics Pathology Inc)***
	0313U	Oncology (pancreas), DNA and mRNA next-generation sequencing analysis of 74 genes and analysis of CEA (CEACAM5) gene expression, pancreatic cyst fluid, algorithm reported as a categorical result (i.e., negative, low probability of neoplasia or positive, high probability of neoplasia) ***(Includes PancreaSeq® Genomic Classifier, Molecular and Genomic Pathology Laboratory, University of Pittsburgh Medical Center)***
	0355U	APOL1 (apolipoprotein L1) (e.g., chronic kidney disease), risk variants (G1, G2) ***(Includes Apolipoprotein L1 (APOL1) Renal Risk Variant Genotyping, Quest Diagnostics®)***
	0362U	Oncology (papillary thyroid cancer), gene-expression profiling via targeted hybrid capture-enrichment RNA sequencing of 82 content genes and 10 housekeeping genes, fine needle aspirate or formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as one of three molecular subtypes ***(Includes Thyroid GuidePx®, Protean BioDiagnostics, Qualisure Diagnotics)***
	0365U	Oncology (bladder), 10 protein biomarkers (A1AT, ANG, APOE, CA9, IL8, MMP9, MMP10, PAI1, SDC1, and VEGFA), by immunoassays, urine, diagnostic algorithm, including patient's age, race, and gender, reported as a probability of harboring urothelial cancer ***(Includes Oncuria® Detect, DiaCarta Clinical Lab, DiaCarta, Inc)***
	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 ***(Includes Oncuria® Monitor, DiaCarta Clinical Lab, DiaCarta, Inc)***
	0367U	Oncology (bladder), analysis of 10 protein biomarkers (A1AT, ANG, APOE, CA9, IL8, MMP9, MMP10, PAI1, SDC1 and VEGFA) by immunoassays, urine, diagnostic algorithm reported as a risk score for probability of rapid recurrence of recurrent or persistent cancer following transurethral resection ***(Includes Oncuria® Predict, DiaCarta Clinical Lab, DiaCarta, Inc)***

Type	Code	Description
	0368U	Oncology (colorectal cancer), evaluation for mutations of APC, BRAF, CTNNB1, KRAS, NRAS, PIK3CA, SMAD4, and TP53, and methylation markers (MYO1G, KCNQ5, C9ORF50, FLI1, CLIP4, ZNF132 and TWIST1), multiplex quantitative polymerase chain reaction (qPCR), circulating cell-free DNA (cfDNA), plasma, report of risk score for advanced adenoma or colorectal cancer ***(Includes ColoScape™ Colorectal Cancer Detection, DiaCarta Clinical Lab, DiaCarta, Inc)***
	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 ***(Includes Qlear UTI, Lifescan Labs of Illinois, Thermo Fisher Scientific)***
	0372U	Infectious disease (genitourinary pathogens), antibiotic-resistance gene detection, multiplex amplified probe technique, urine, reported as an antimicrobial stewardship risk score ***(Includes Qlear UTI - Reflex ABR, Lifescan Labs of Illinois, Thermo Fisher Scientific)***
	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 ***(Deleted code effective 7/1/2025)***
	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 ***(Deleted code effective 7/1/2025)***
	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 ***(Includes ArteraAI Prostate Test, Artera Inc®)***
	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) ***(Includes Liposcale®, CIMA Sciences, LLC)***
	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 ***(Includes NaviDKD™ Predictive Diagnostic Screening for Kidney Health, Journey Biosciences, Inc)***
	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 ***(Includes PromarkerD, Sonic Reference Laboratory, Proteomics International Pty Ltd)***

Type	Code	Description
	0387U	Oncology (melanoma), autophagy and beclin 1 regulator 1 (AMBRA1) and loricrin (AMLo) by immunohistochemistry, formalin-fixed paraffin-embedded (FFPE) tissue, report for risk of progression ***(Includes AMBLor® melanoma prognostic test, Avero® Diagnostics)***
	0390U	Obstetrics (preeclampsia), kinase insert domain receptor (KDR), Endoglin (ENG), and retinol-binding protein 4 (RBP4), by immunoassay, serum, algorithm reported as a risk score ***(Includes PEPredictDx, OncoOmicsDx Laboratory, mProbe)***
	0394U	Perfluoroalkyl substances (PFAS) (e.g., perfluorooctanoic acid, perfluorooctane sulfonic acid), 16 PFAS compounds by liquid chromatography with tandem mass spectrometry (LC-MS/MS), plasma or serum, quantitative ***(Includes PFAS Testing & PFASure™, National Medical Services, NMS Labs, Inc) (Code effective 10/01/2025)***
	0405U	Oncology (pancreatic), 59 methylation haplotype block markers, next-generation sequencing, plasma, reported as cancer signal detected or not detected ***(Includes BTG Early Detection of Pancreatic Cancer, Breakthrough Genomics)***
	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 ***(Includes CyPath® Lung, Precision Pathology Services, bioAffinity Technologies, Inc)***
	0410U	Oncology (pancreatic), DNA, whole genome sequencing with 5-hydroxymethylcytosine enrichment, whole blood or plasma, algorithm reported as cancer detected or not detected ***(Includes Avantect™ Pancreatic Cancer Test, ClearNote™ Health)***
	0414U	Oncology (lung), augmentative algorithmic analysis of digitized whole slide imaging for 8 genes (ALK, BRAF, EGFR, ERBB2, MET, NTRK1-3, RET, ROS1), and KRAS G12C and PD-L1, if performed, formalin-fixed paraffin-embedded (FFPE) tissue, reported as positive or negative for each biomarker ***(Includes LungOI, Imagene)***
	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 ***(Includes SmartHealth Vascular Dx™, Morningstar Laboratories, LLC, SmartHealth DX)***
	0457U	Perfluoroalkyl substances (PFAS) (e.g., perfluorooctanoic acid, perfluorooctane sulfonic acid), 9 PFAS compounds by LC-MS/MS, plasma or serum, quantitative ***(Includes PFAS (Forever Chemicals) 9 Panel, Quest Diagnostics®) (Code effective 10/01/2025)***
	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 ***(Includes RightMed® Oncology Gene Report, OneOme® LLC)***
	0461U	Oncology, pharmacogenomic analysis of single-nucleotide polymorphism (SNP) genotyping by real-time PCR of 24 genes, whole

Type	Code	Description
		blood or buccal swab, with variant analysis, including impacted gene-drug interactions and reported phenotypes ***(Includes RightMed® Oncology Medication Report, OneOme® LLC)***
	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) ***(Includes Tempus p-MSI, Tempus AI, Inc)***
	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 ***(Includes Tempus p-Prostate, Tempus AI, Inc)***
	0535U	Perfluoroalkyl substances (PFAS) (e.g., perfluorooctanoic acid, perfluorooctane sulfonic acid), by liquid chromatography with tandem mass spectrometry (LC-MS/MS), plasma or serum, quantitative ***(Includes PFAS Testing & PFASure®FT, National Medical Services (NMS Labs), Laboratory Developed Test) (Code effective 10/01/2025)***
	0537U	Oncology (colorectal cancer), analysis of cell-free DNA for epigenomic patterns, next-generation sequencing, >2500 differentially methylated regions (DMRs), plasma, algorithm reported as positive or negative ***(Includes Shield™, Guardant Health, Inc)***
	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 ***(Includes ClarityDx Prostate, Protean BioDiagnostics)***
	0573U	Oncology (pancreas), 3 biomarkers (glucose, carcinoembryonic antigen, and gastricsin), pancreatic cyst lesion fluid, algorithm reported as categorical mucinous or non-mucinous ***(Includes Amplified Sciences PanCystPro™, Amplified Sciences, Inc)***
	0577U	Oncology (ovarian), serum, analysis of 39 glycoproteins by liquid chromatography with tandem mass spectrometry (LC-MS/MS) in multiple reaction monitoring mode, reported as likelihood of malignancy ***(Includes: GlycoKnow™ Ovarian, InterVenn Biosciences) (Code effective 10/01/2025)***
	0579U	Nephrology (diabetic chronic kidney disease), enzyme-linked immunosorbent assay (ELISA) of apolipoprotein A4 (APOA4), CD5 antigen-like (CD5L) combined with estimated glomerular filtration rate (GFR), age, plasma, algorithm reported as a risk score for kidney function decline ***(Code effective 10/01/2025)***
	0589U	Perfluoroalkyl substances (PFAS) (eg, perfluorooctanoic acid, perfluorooctane sulfonic acid), 24 PFAS compounds by high-performance liquid chromatography with tandem mass spectrometry (LC-MS/MS), plasma or serum, quantitative ***(Code effective 10/01/2025)***
	0594U	Infectious disease (sepsis), semiquantitative measurement of pancreatic stone protein concentration, whole blood, reported as risk of sepsis

Type	Code	Description
		(Includes: IVD CAPSULE PSP – Rapid Sepsis Test, Abionic SA) (Code effective 10/01/2025)
	0598U	Gastroenterology (irritable bowel syndrome), IgG antibodies to 18 food items by microarray-based immunoassay, whole blood or serum, report as elevated (positive) or normal (negative) antibody levels ***(Code effective 10/01/2025)***
	0599U	Oncology (pancreatic cancer), multiplex immunoassay of ICAM1, TIMP1, CTSD, THBS1, and CA 19-9, serum, diagnostic algorithm reported as positive or negative ***(Code effective 10/01/2025)***
	0607U	Reproductive medicine (endometrial microbiome assessment), real-time PCR analysis for 31 bacterial DNA targets from endometrial biopsy, reported with quantified levels of bacterial presence and targeted treatment recommendations ***(Includes EMMA (Endometrial Microbiome Metagenomic Analysis), Igenomix®, Igenomix® USA) (Code effective 01/01/2026)***
	0608U	Reproductive medicine (endometrial microbiome assessment), real-time PCR analysis for 10 bacterial DNA targets from endometrial biopsy, reported with quantified levels of bacterial presence and targeted treatment recommendations ***(Includes ALICE (Analysis of Infectious Chronic Endometritis), Igenomix®, Igenomix® USA) (Code effective 01/01/2026)***
	81535	Oncology (gynecologic), live tumor cell culture and chemotherapeutic response by DAPI stain and morphology, predictive algorithm reported as a drug response score; first single drug or drug combination
	81536	Oncology (gynecologic), live tumor cell culture and chemotherapeutic response by DAPI stain and morphology, predictive algorithm reported as a drug response score; each additional single drug or drug combination (List separately in addition to code for primary procedure)
	81599	Unlisted multianalyte assay with algorithmic analysis ***[when specified as a biomarker MAAA test for MS, e.g., Octave® (MSDA)]***
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
04/01/2026	New policy.

Definitions of Decision Determinations

Healthcare Services: For the purpose of this Medical Policy, Healthcare Services means procedures, treatments, supplies, devices, and equipment.

Medically Necessary or **Medical Necessity** means reasonable and necessary services to protect life, to prevent significant illness or significant disability, or alleviate severe pain through the diagnosis or treatment of disease, illness, or injury, as required under W&I section 14059.5(a) and 22 CCR section 51303(a). Medically Necessary services must include services necessary to achieve age-appropriate growth and development, and attain, maintain, or regain functional capacity.

For Members less than 21 years of age, a service is Medically Necessary if it meets the Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) standard of Medical Necessity set forth in 42 USC section 1396d(r)(5), as required by W&I sections 14059.5(b) and 14132(v). Without limitation, Medically Necessary services for Members less than 21 years of age include all services necessary to achieve or maintain age-appropriate growth and development, attain, regain or maintain functional capacity, or improve, support, or maintain the Member's current health condition. Contractor must determine Medical Necessity on a case-by-case basis, taking into account the individual needs of the Child.

Criteria Determining Experimental/Investigational Status

In making a determination that any procedure, treatment, therapy, drug, biological product, facility, equipment, device, or supply is "experimental or investigational" by the Plan, the Plan shall refer to evidence from the national medical community, which may include one or more of the following sources:

1. Evidence from national medical organizations, such as the National Centers of Health Service Research.
2. Peer-reviewed medical and scientific literature.
3. Publications from organizations, such as the American Medical Association (AMA).
4. Professionals, specialists, and experts.
5. Written protocols and consent forms used by the proposed treating facility or other facility administering substantially the same drug, device, or medical treatment.
6. An expert physician panel selected by one of two organizations, the Managed Care Ombudsman Program of the Medical Care Management Corporation or the Department of Managed Health Care.

Feedback

Blue Shield of California Promise Health Plan is interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration. Our medical policies are available to view or download at www.blueshieldca.com/en/bsp/providers.

For medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Questions regarding the applicability of this policy should be directed to the Blue Shield of California Promise Health Plan Prior Authorization Department at (800) 468-9935, or the Complex Case Management Department at (855) 699-5557 (TTY 711) for San Diego County and (800) 605-2556 (TTY 711) for Los Angeles County or visit the provider portal at www.blueshieldca.com/en/bsp/providers.

Disclaimer: Blue Shield of California Promise Health Plan may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as member health services contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member health services contracts may differ in their benefits. Blue Shield of California Promise Health Plan reserves the right to review and update policies as appropriate.