

| CLINICAL MEDICAL POLICY | | |
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| Policy Name: | Experimental/Investigational Laboratory Services | |
| Policy Number: | MP-121-MD-PA | |
| Responsible Department(s): | Medical Management | |
| Provider Notice/Issue Date: | 08/01/2024; 11/01/2023 | |
| Effective Date: | 09/01/2024; 12/01/2023 | |
| Next Annual Review: | 06/2025 | |
| Revision Date: | 06/19/2024; 06/21/2023 | |
| Products: | Highmark Wholecare [™] Medicaid | |
| Application: | All participating hospitals and providers | |
| Page Number(s): | 1 of 7 | |

Policy History

| Date | Action |
|------------|---|
| 09/01/2024 | Provider Effective date |
| 07/22/2024 | PARP Approval |
| 06/19/2024 | QI/UM Committee review |
| 06/19/2024 | Annual Review: No changes to criteria. Updated 'Reference Sources' section. |
| 12/01/2023 | Provider Effective date |
| 07/18/2023 | PARP Approval |
| 06/21/2023 | QI/UM Committee review |
| 06/21/2023 | Policy initially developed |

Disclaimer

Highmark Wholecare[™] medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

Policy Statement

Highmark Wholecare[™] does not provide coverage under the medical-surgical benefits of the Company's Medicaid products for services considered to be services considered to be experimental or investigational laboratory services.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

Definitions

Prior Authorization Review Panel (PARP) – A panel of representatives from within the PA Department of Human Services who have been assigned organizational responsibility for the review, approval and denial of all PH-MCO Prior Authorization policies and procedures.

Experimental/investigational procedure - the use of a service, supply, drug or device that is not recognized as standard medical care for the condition, disease, illness or injury being treated. All laboratory services identified within this policy are considered experimental/investigational, and therefore, non-covered because the safety and/or effectiveness of the services cannot be established by the available published peer-reviewed literature.

Procedures

- This policy addresses laboratory services that are considered to be experimental/investigational and, therefore, are considered not medically necessary. These tests are often available on a clinical basis long before the required and necessary evidence base to support clinical validity 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.
- 2. Post-payment Audit Statement

The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Wholecare^{s™} at any time pursuant to the terms of your provider agreement.

3. Place of Service

Experimental/Investigational (E/I) services are not medically necessary regardless of place of service. An E/I laboratory service is typically an outpatient procedure which is only eligible for coverage as an inpatient procedure in special circumstances, including, but not limited to, the presence of a comorbid condition that would require monitoring in a more controlled environment such as the inpatient setting.

- 4. Related Policies
 - MP-108-MD-PA Multimarker Serum Testing Related to Ovarian Cancer
 - MP-118-MD-PA Experimental/Investigational Services

Coding Requirements

Experimental/Investigational Procedure Codes

These procedure codes will not be reimbursed without Medical Director approval.

| CPT Code | Description |
|----------|---|
| 81328 | SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (eg, adverse |
| | drug reaction), gene analysis, common variant(s) (eg, *5) |
| 81346 | TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene |
| | analysis, common variant(s) (eg, tandem repeat variant) |
| 81490 | Autoimmune (rheumatoid arthritis), analysis of 12 biomarkers using immunoassays, |
| | utilizing serum, prognostic algorithm reported as a disease activity score |
| 81500* | Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing |
| | serum, with menopausal status, algorithm reported as a risk score |
| 81529 | Oncology (cutaneous melanoma), mRNA, gene expression profiling by real-time RT-PCR |
| | of 31 genes (28 content and 3 housekeeping), utilizing formalin-fixed paraffin- |
| | embedded tissue, algorithm reported as recurrence risk, including likelihood of sentinel |
| | lymph node metastasis |
| 81554 | Pulmonary disease (idiopathic pulmonary fibrosis [IPF]), mRNA, gene expression analysis |
| | of 190 genes, utilizing transbronchial biopsies, diagnostic algorithm reported as |
| | categorical result (eg, positive or negative for high probability of usual interstitial |
| 001014 | |
| 0018M | Iransplantation medicine (allograft rejection, renal), measurement of donor and third- |
| | party-induced CD154+1-cytotoxic memory cells, utilizing whole peripheral blood, |
| 000511 | algorithm reported as a rejection risk score |
| 00050 | oncology (prostate) gene expression prome by real-time RT-PCR of 3 genes (ERG, PCA3, |
| 000811 | Helicobacter pylori detection and antibiotic resistance. DNA 165 and 235 rPNA gyrA |
| 00080 | nbn1 rdvA and rnoB nevt-generation sequencing formalin-fixed paraffin-embedded or |
| | fresh tissue or fecal sample, predictive, reported as positive or negative for resistance |
| | to clarithromycin fluoroquinolones metronidazole amoxicillin tetracycline and |
| | rifabutin |
| 0009U | Oncology (breast cancer), ERBB2 (HER2) copy number by FISH, tumor cells from formalin |
| | fixed paraffin embedded tissue isolated using image-based dielectrophoresis (DEP) |
| | sorting, reported as ERBB2 gene amplified or non-amplified |
| 0019U | Oncology, RNA, gene expression by whole transcriptome sequencing, formalin-fixed |
| | paraffin embedded tissue or fresh frozen tissue, predictive algorithm reported as |
| | potential targets for therapeutic agents |
| 0029U | Drug metabolism (adverse drug reactions and drug response), targeted sequence |
| | analysis (ie, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, |
| | VKORC1 and rs12777823) |
| 0030U* | Drug metabolism (warfarin drug response), targeted sequence analysis (ie, CYP2C9, |
| | CYP4F2, VKORC1, rs12777823) |
| 0031U | CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(eg, drug metabolism) gene |
| | analysis, common variants (ie, *1F, *1K, *6, *7) |
| 0032U | COMT (catechol-O-methyltransferase)(drug metabolism) gene analysis, c.472G>A |
| | (rs4680) variant |

| 0033U | HTR2A (5-hydroxytryptamine receptor 2A), HTR2C (5-hydroxytryptamine receptor 2C) |
|--------|---|
| | (eg, citalopram metabolism) gene analysis, common variants (ie, HTR2A rs7997012 |
| | [c.614-2211T>C], HTR2C rs3813929 [c759C>T] and rs1414334 [c.551-3008C>G]) |
| 0034U | TPMT (thiopurine S-methyltransferase), NUDT15 (nudix hydroxylase 15)(eg, thiopurine |
| | metabolism) gene analysis, common variants (ie, TPMT *2, *3A, *3B, *3C, *4, *5, *6, *8, |
| 004511 | *12; NUD115 *3, *4, *5) |
| 00450 | Dr. DCD of 12 games (7 content and 5 housekeeping) utilizing formalin fixed parefin |
| | RI-PCR of 12 genes (7 content and 5 nousekeeping), utilizing formalin-lixed paramin- |
| 004711 | Oncology (prostate), mPNA, gono expression profiling by real time BT DCP of 17 gonos |
| 00470 | (12 content and 5 housekeeping) utilizing formalin-fixed paraffin-embedded tissue |
| | algorithm reported as a risk score |
| 005311 | Oncology (prostate cancer) FISH analysis of 4 genes (ASAP1_HDAC9_CHD1 and PTEN) |
| 00550 | needle biopsy specimen, algorithm reported as probability of higher tumor grade |
| 0055U | Cardiology (heart transplant), cell-free DNA, PCR assay of 96 DNA target sequences (94 |
| | single nucleotide polymorphism targets and two control targets), plasma |
| 0060U | Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating |
| | cell-free fetal DNA in maternal blood |
| 0067U | Oncology (breast), immunohistochemistry, protein expression profiling of 4 biomarkers |
| | (matrix metalloproteinase-1 [MMP-1], carcinoembryonic antigen-related cell adhesion |
| | molecule 6 [CEACAM6], hyaluronoglucosaminidase [HYAL1], highly expressed in cancer |
| | protein [HEC1]), formalin-fixed paraffin-embedded precancerous breast tissue, |
| 000011 | algorithm reported as carcinoma risk score |
| 00690 | fixed paraffin embedded ticsue, algorithm reported as an expression score |
| 007811 | Pain management (onioid-use disorder) genetyping papel 16 common variants (in |
| 00780 | ABCB1 COMT DAT1 DBH DOR DRD1 DRD2 DRD4 GABA GAL HTR2A HTTIPR |
| | MTHER MIJOR OPRK1 OPRM1) buccal swab or other germline tissue sample |
| | algorithm reported as positive or negative risk of opioid-use disorder |
| 0079U | Comparative DNA analysis using multiple selected single-nucleotide polymorphisms |
| | (SNPs), urine and buccal DNA, for specimen identity verification |
| 0086U | Infectious disease (bacterial and fungal), organism identification, blood culture, using |
| | rRNA FISH, 6 or more organism targets, reported as positive or negative with phenotypic |
| | minimum inhibitory concentration (MIC)-based antimicrobial susceptibility |
| 0087U | Cardiology (heart transplant), mRNA gene expression profiling by microarray of 1283 |
| | genes, transplant biopsy tissue, allograft rejection and injury algorithm reported as a |
| | probability score |
| 0088U | Transplantation medicine (kidney allograft rejection), microarray gene expression |
| | profiling of 1494 genes, utilizing transplant biopsy tissue, algorithm reported as a |
| | probability score for rejection |
| 00900 | Oncology (cutaneous melanoma), mRNA gene expression protiling by RT-PCR of 23 |
| | genes (14 content and 9 housekeeping), utilizing formalin-fixed paraffin-embedded |
| | (FFE) ussue, algorithm reported as a categorical result (le, benign, intermediate, malignant) |
| 01001 | Informations disease (Aspergillus species) real time DCP for detection of DNA from 4 |
| 01090 | species (A fumigatus A terreus A niger and A flavus) blood lavage fluid or tissue |
| | qualitative reporting of presence or absence of each species |
| | quantative reporting or presence of absence of each species |

| 0112U | Infectious agent detection and identification, targeted sequence analysis (16S and 18S |
|--------|--|
| | rRNA genes) with drug-resistance gene |
| 0113U | Oncology (prostate), measurement of PCA3 and TMPRSS2-ERG in urine and PSA in serum |
| | following prostatic massage, by RNA amplification and fluorescence-based detection, |
| | algorithm reported as risk score |
| 0114U | Gastroenterology (Barrett's esophagus), VIM and CCNA1 methylation analysis, |
| | esophageal cells, algorithm reported as likelihood for Barrett's esophagus |
| 0118U | Transplantation medicine, quantification of donor-derived cell-free DNA using whole |
| | genome next-generation sequencing, plasma, reported as percentage of donor-derived |
| | cell-free DNA in the total cell-free DNA |
| 0120U | Oncology (B-cell lymphoma classification), mRNA, gene expression profiling by |
| | fluorescent probe hybridization of 58 genes (45 content and 13 housekeeping genes), |
| | formalin-fixed paraffin-embedded tissue, algorithm reported as likelihood for primary |
| | mediastinal B-cell lymphoma (PMBCL) and diffuse large B-cell lymphoma (DLBCL) with |
| | cell of origin subtyping in the latter |
| 01310 | Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary |
| | (12 genes) (List separately in addition to endo for primary presedure) |
| 012211 | (13 genes) (List separately in addition to code for primary procedure) |
| 01520 | evering concer bereditary endometrial cancer) targeted mPNA sequence analysis panel |
| | (17 genes) (List separately in addition to code for primary procedure) |
| 012211 | Hereditary prostate cancer-related disorders, targeted mPNA sequence analysis nanel |
| 01330 | (11 genes) (List separately in addition to code for primary procedure) |
| 013/11 | Hereditary pan cancer (eg. bereditary breast and ovarian cancer, bereditary endometrial |
| 01340 | cancer bereditary colorectal cancer) targeted mRNA sequence analysis nanel (18 |
| | genes) (List separately in addition to code for primary procedure) |
| 013511 | Hereditary gynecological cancer (eg. hereditary breast and ovarian cancer, hereditary |
| 01000 | endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis |
| | panel (12 genes) (List separately in addition to code for primary procedure) |
| 0136U | ATM (ataxia telangiectasia mutated) (eg. ataxia telangiectasia) mRNA sequence analysis |
| | (List separately in addition to code for primary procedure) |
| 0137U | PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) mRNA |
| | sequence analysis (List separately in addition to code for primary procedure) |
| 0138U | BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, |
| | hereditary breast and ovarian cancer) mRNA sequence analysis (List separately in |
| | addition to code for primary procedure) |
| 0150U | Drug assay, definitive, 120 or more drugs or metabolites, urine, quantitative liquid |
| | chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction |
| | monitoring (MRM), with drug or metabolite description, comments including sample |
| | validation, per date of service |
| 0152U | Infectious disease (bacteria, fungi, parasites, and DNA viruses), microbial cell-free DNA, |
| | plasma, untargeted next-generation sequencing, report for significant positive |
| | pathogens |
| 0153U | Oncology (breast), mRNA, gene expression profiling by next-generation sequencing of |
| | 101 genes, utilizing formalin-fixed parattin-embedded tissue, algorithm reported as a |
| | triple negative preast cancer clinical subtype(s) with information on immune cell |
| 01561 | INVOIVEMENT |
| U156U | Copy number (eg, intellectual disability, dysmorphology), sequence analysis |

| 0157U | APC (APC regulator of WNT signaling pathway) (eg, familial adenomatosis polyposis [FAP]) mRNA sequence analysis (List separately in addition to code for primary |
|-------|---|
| 0158U | MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary |
| 0159U | procedure) MSH2 (mutS homolog 2) (eg. hereditary colon cancer, Lynch syndrome) mRNA sequence |
| | analysis (List separately in addition to code for primary procedure) |
| 0160U | MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) |
| 0161U | PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non- polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) |
| 0162U | Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure) |
| 0169U | NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants |
| 0170U | Neurology (autism spectrum disorder [ASD]), RNA, next-generation sequencing, saliva, algorithmic analysis, and results reported as predictive probability of ASD diagnosis |
| 0203U | Autoimmune (inflammatory bowel disease), mRNA, gene expression profiling by quantitative RT-PCR, 17 genes (15 target and 2 reference genes), whole blood, reported as a continuous risk score and classification of inflammatory bowel disease aggressiveness |
| 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 |
| 0209U | Neurology (Alzheimer disease); cell aggregation using morphometric imaging and protein kinase C-epsilon (PKCe) concentration in response to amylospheroid treatment by ELISA, cultured skin fibroblasts, each reported as positive or negative for Alzheimer disease |
| 0220U | Oncology (breast cancer), image analysis with artificial intelligence assessment of 12 histologic and immunohistochemical features, reported as a recurrence score |
| 0228U | Oncology (prostate), multianalyte molecular profile by photometric detection of macromolecules adsorbed on nanosponge array slides with machine learning, utilizing first morning voided urine, algorithm reported as likelihood of prostate cancer |
| 0229U | BCAT1 (Branched chain amino acid transaminase 1) and IKZF1 (IKAROS family zinc finger 1) (eg, colorectal cancer) promoter methylation analysis |
| 0243U | Obstetrics (preeclampsia), biochemical assay of placental-growth factor, time-resolved fluorescence immunoassay, maternal serum, predictive algorithm reported as a risk score for preeclampsia |
| 0247U | Obstetrics (preterm birth), insulin-like growth factor-binding protein 4 (IBP4), sex hormone-binding globulin (SHBG), quantitative measurement by LC-MS/MS, utilizing maternal serum, combined with clinical data, reported as predictive-risk stratification for spontaneous preterm birth |
| 0248U | Oncology (brain), spheroid cell culture in a 3D microenvironment, 12 drug panel, tumor- response prediction for each drug |

| 0249U | Oncology (breast), semiquantitative analysis of 32 phosphoproteins and protein analytes, includes laser capture microdissection, with algorithmic analysis and interpretative report |
|-------|--|
| 0328U | Drug assay, definitive, 120 or more drugs and metabolites, urine, quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS), includes specimen validity and algorithmic analysis describing drug or metabolite and presence or absence of risks for a significant patient-adverse event, per date of service |

* Codes are listed under medical policy MP-108-MD-PA *Multimarker Serum Testing Related to Ovarian Cancer*

Reimbursement

Participating facilities will be reimbursed per their Highmark Wholecare[™] contract.