MEDICAL POLICY	Genetic Testing: Gene Expression Profile Testing for Breast Cancer (Medicare Only)
Effective Date: 10/1/2022  10/1/2022 Medical Officer Date	Medical Policy Number: 48 Medical Policy Committee Approved Date: 6/17; 12/17; 1/18; 8/18; 12/18; 12/19; 05/2021; 9/2021; 11/2021; 2/2022; 7/2022; 9/2022

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:

Medicare only

MEDICARE POLICY CRITERIA

The following Centers for Medicare & Medicaid Service (CMS) guidelines should be utilized for medical necessity coverage determinations. Click the link provided in the table below to access applicable medical necessity criteria. All listed guidelines apply.

Service	Code(s)	Medicare Guidelines
BluePrint (Agendia®; California)	CPT 81479	Local Coverage Articles (LCA): MolDX: BluePrint® Coding and Billing Guidelines (A55115)
Breast Cancer Index (BCI) (bioTheranostics, Inc.; California)	CPT 81518	Local Coverage Determination (LCD): MolDX: Breast Cancer Index℠ Genetic Assay (L37822)
EndoPredict (Myriad®; Utah)	CPT 81522	LCD: MolDX: EndoPredict® Breast Cancer Gene Expression Test (L37311)
MammaPrint or MammaPrint – NGS (Agendia®; California)	CPT 81521, 81523	LCA: MolDX: MammaPrint Coding and Billing Guidelines (A54445)
Oncotype DX Breast (Genomic Health Inc.; California)	CPT 81519	LCA: MolDX: Oncotype DX® Breast Cancer Assay Billing and Coding Guidelines (A54480)
Oncotype DCIS (Genomic Health Inc.; California)	CPT 0045U	LCD: MolDX - Oncotype DX® Breast Cancer for DCIS (Genomic Health™) (L36941)

Prosigna (PAM50) (NanoString Technologies Inc.; Washington)	CPT 81520	LCD: MolDX: Breast Cancer Assay: Prosigna (L36386)
DCISionRT® (Prelude Corp., California) (0295U) *TargetPrint® (Agendia®; California)* *BreastOncPx™ (LabCorp; headquartered in North Carolina)* *BreastPRS™ (Signal Genetics; California)* *Mammostrat® (Clarient Diagnostic Services; California)*	Varies	These tests are considered **not medically necessary**, based on Medicare guidelines. *See "Policy Guidelines" below.*
Molecular Grade Index (AviaraDx, Inc.) *Theralink® Reverse Phase Protein Array (RPPA)* *(Theralink® Technologies, Inc.) (Code 0249U)*	Varies	Company medical policy for Genetic Testing: Gene Expression Profile Testing for Breast Cancer (All Lines of Business Except Medicare) I. These tests are considered **not medically necessary** for Medicare Plan members based on the Company medical policy. *"Investigational" services are considered not medically necessary for Medicare Plan members. See Policy Guidelines below.*

POLICY GUIDELINES

Medicare and Medical Necessity

General

In order for a laboratory test to be considered for coverage, Medicare requires the test in question meet all of the following:

- Not be excluded from coverage by statute, regulation, National Coverage Determination, (NCD), or Local Coverage Determination (LCD);

- Be ordered by a physician or practitioner who is treating the beneficiary;
- Provide data that will be directly used in the management of a beneficiary's specific medical problem;
- Be considered medically reasonable and necessary, as required per the Social Security Act, §1862(a)(1)(A).

In addition to the test being medically appropriate for the condition, this also includes performing the services at an appropriate frequency, in accordance with accepted standards of medical practice for the condition.

Medicare Molecular Diagnostics (MolDX) Program

Laboratories performing tests in service areas which have adopted guidelines or coverage determinations made by the Medicare Molecular Diagnostics (MolDX) Program contractor are required to submit a technology assessment (TA) to establish analytical and clinical validity (AV/CV) and clinical utility (CU). Supporting LCDs regarding TA reviews include, but are not limited to, the following:

- Laboratories in CA & NV: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L35160)
- Laboratories in NC, SC, GA, TN, AL, VA, & WV: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L35025)
- Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, & WY: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L36256)

Coverage or non-coverage determinations made by MolDX are maintained in the DEX™ Diagnostics Exchange registry catalog and are available for public viewing. If a test does not have a coverage determination by the MolDX Program, then AV/CV and CU have **not** been established and the test is considered not medically reasonable and necessary under *SSA §1862(a)(1)(A)* until a MolDX review is complete and coverage is indicated by MolDX or Noridian. Therefore, tests identified in this policy as not meeting this requirement are not medically reasonable or necessary for Medicare under *SSA §1862(a)(1)(A).*

Non-MolDX Service Areas and Coverage in the Absence of a Specific Medicare Policy Guideline

Services areas which have **not** adopted MolDX guidelines include testing performed in the following states: FL, CO, NM, OK, TX, AR, LA, MS, DE, MD, NJ, PA, IL, MN, WI, CT, NY, ME, MA, NH, RI, and VT.

LCDs and LCAs for each of the above service areas require clinical utility and analytical validity to be established, but most tests are not called out by name specifically. Additionally, for multi-biomarker panel test, each requested biomarker needs to be individually contributory to the member's treatment. In the absence of specific guidance in these LCDs, the PHP Company policies for genetic tests provide a peer review of medical literature to evaluate clinical utility/analytical validity. When the biomarkers included in a test do not have proven clinical validity/utility, the test is not medically reasonable or necessary under Social Security Act, §1862(a)(1)(A) for Medicare members.

The Company policy for *PHA Medicare Medical Policy Development and Application* (MP50) provides details regarding Medicare's definition of medical necessity and the hierarchy of Medicare references and resources during the development of medical policies, as well as the Plan's use of evidence-based processes for policy development. In the absence of Medicare coverage policies (e.g., manual, national coverage determination [NCD], local coverage determination [LCD], article [LCA], etc.), Medicare regulatory guidelines do allow Medicare Advantage Organizations (MAOs) to make their own coverage determinations, as long as the MAO applies an objective, evidence-based process, based on authoritative evidence. *(Medicare Managed Care Manual, Ch. 4, §90.5)*

Following an evidence-based assessment of current peer-reviewed medical literature, the Company may consider certain medical services or technologies to be "investigational." The term "investigational" is not limited to devices or technologies which have not received the appropriate governmental regulatory approval (e.g., U.S. Food and Drug Administration [FDA]), but rather may also mean the procedure, device, or technology does not meet all of the Company's technology assessment criteria, as detailed within the Company policy for *Definition: Experimental/Investigational* (MP5).

For Medicare, only medically reasonable and necessary services or items which treat illness or injury are eligible for Medicare coverage, as outlined in *Title XVIII of the Social Security Act, §1862(a)(1)(A)*. Thus, services which lack scientific evidence regarding safety and efficacy because they are investigational are "not medically reasonable or necessary" for Medicare Plan members. *(Medicare Claims Processing Manual, Ch. 23, §30 A)*

BILLING GUIDELINES

General

See associated local coverage articles (LCAs) for additional coding and billing guidance:

- LCA for Coding Article for MolDX: Breast Cancer Index™ (BCI) Gene Expression Test (A56335)
- LCA for Billing and Coding: MolDX: Oncotype DX® Breast Cancer for DCIS (Genomic Health™) (A57620)
- LCA for Billing and Coding: MolDX: Breast Cancer Assay: Prosigna (A57364)
- LCA for Billing and Coding: MolDX: EndoPredict® Breast Cancer Gene Expression Test (A57608)

Frequency

Testing must be performed at an appropriate frequency, as determined by the above Medicare references, as well as established clinical edits (e.g., National Correct Coding Initiative [NCCI] edits) which may be in place.

CPT/HCPCS CODES

Medicare Only	
No Prior Authorization Required The following codes do not require routine review for medical necessity, but they may be subject to audit.	
0045U	Oncology (breast ductal carcinoma in situ), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score *(Used to report the Oncotype DCIS test)*
81518	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 11 genes (7 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithms reported as percentage risk for metastatic recurrence and likelihood of benefit from extended endocrine therapy *(Used to report the Breast Cancer Index (BCI) test)*
81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score *(Used to report the Oncotype DX Breast test)*
81520	Oncology (breast), mRNA gene expression profiling by hybrid capture of 58 genes (50 content and 8 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence risk score *(Used to report the Prosigna (PAM50) test)*
81521	Oncology (breast), mRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis *(Used to report the MammaPrint test)*
81522	Oncology (breast), mRNA, gene expression profiling by RT-PCR of 12 genes (8 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk score *(Used to report the EndoPredict test)*
81523	Oncology (breast), mRNA, next-generation sequencing gene expression profiling of 70 content genes and 31 housekeeping genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk to distant metastasis *(Used to report the MammaPrint test if performed by next generation sequencing [NGS])*
Not Covered	
0249U	Oncology (breast), semiquantitative analysis of 32 phosphoproteins and protein analytes, includes laser capture microdissection, with algorithmic analysis and interpretative report *(Used to report the Theralink® Reverse Phase Protein Array (RPPA) test)*
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 *(Used to report the DCISionRT® test)*

Unlisted Codes All unlisted codes will be reviewed for medical necessity, correct coding, and pricing. If an unlisted code is billed related to services addressed in this policy then **prior-authorization is required.**	
81479	Unlisted molecular pathology procedure
81599	Unlisted multi-analyte with algorithmic analysis
84999	Unlisted chemistry procedure

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.