Subject: Genetic Testing for Circulating Tumor DNA Tests for Management of Cancer

Medical Policy: 54.0 **Original Effective Date:** 03-22-2023

Status: Reviewed **Last Review Date:** 03-20-2024

Disclaimer

Refer to the member's specific benefit plan and Schedule of Benefits to determine coverage. This may not be a benefit on all plans or the plan may have broader or more limited benefits than those listed in this Medical Policy.

Description

Minimal Residual Disease (MRD) testing for cancer is rapidly becoming a sensitive and specific method for monitoring the relative amounts of tumor-derived genetic material circulating in the blood of cancer patients. These tests leverage new genomic technologies that allow detection of extremely dilute tumor material, yielding an extremely sensitive method for determining the continued presence of tumor material or, buy serially testing the same individual, tracking the relative increase or decrease of tumor material being deposited in the blood. Although it is a relatively new application of novel genomic technologies, it has rapidly demonstrated its ability to impact patient care in several ways in cancer diagnosis and treatment. MRD testing can be used to:

- diagnose cancer progression, recurrence, or relapse before there is clinical, biological, or radiographical evidence of progression, recurrence, or relapse
- detect tumor response to therapy by measuring the proportional changes in the amount of available tumor DNA

Both above uses may enable physicians to better assign risk stratification, deploy alternate treatment strategies, or preclude the use of unnecessary adjuvant therapies.

Coverage Determination

Prior Authorization is required. Logon to Pres Online to submit a request: https://ds.phs.org/preslogin/index.jsp

Presbyterian follows CMS, LCD MolDX: Minimal Residual Disease (MRD) Testing for Cancer (L38835). For MRD in solid tumor and MRD in Hematopoietic, for Medicare, Medicaid and Commercial.

See the related articles for types of tests:

- See LCA (A58468), MolDX: Minimal Residual Disease Testing for **Solid Tumor Cancers**.
- See LCA (A59004), MolDX Minimal Residual Disease Testing for **Hematologic Cancers.**

Coding

The coding listed in this medical policy is for reference only. Covered and non-covered codes are within this list.

Minimal Residual Disease (MRD) Testing for Solid Tumor Cancers, LCA (A58468)	
CPT Codes	**Description**
0340U	Oncology (pan-cancer), analysis of minimal residual disease (MRD) from plasma, with assays personalized to each patient based on prior next-generation sequencing of the patient's tumor and germline DNA, reported as absence or presence of MRD, with disease-burden correlation, if appropriate. Includes Signatera™, Natera, Inc
0356U	Oncology (oropharyngeal or anal), evaluation of 17 DNA biomarkers using droplet digital PCR (ddPCR), cell-free DNA, algorithm reported as a prognostic risk score for cancer recurrence Includes: NavDx®, Naveris, Inc, Naveris, Inc
0422U	Oncology (pan-solid tumor), analysis of DNA biomarker response to anti-cancer therapy using cell-free circulating DNA, biomarker comparison to a previous baseline pre-treatment cell-free circulating DNA analysis using next-generation sequencing, algorithm reported as a quantitative change from baseline, including specific alterations, if appropriate Includes: Guardant360 Response™

Minimal Residual Disease (MRD) Testing for Solid Tumor Cancers, LCA (A58468)	
CPT Codes	**Description**
81445	Solid organ neoplasm, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants and copy number variants or rearrangements, if performed; DNA analysis or combined DNA and RNA analysis
81479	Unlisted molecular pathology procedure.

Minimal Residual Disease (MRD) Testing for Hematologic Cancers, LCA (A59004)	
CPT Codes	**Description**
81450	HEMATOLYMPHOID NEOPLASM OR DISORDER, GENOMIC SEQUENCE ANALYSIS PANEL, 5-50 GENES, INTERROGATION FOR SEQUENCE VARIANTS, AND COPY NUMBER VARIANTS OR REARRANGEMENTS, OR ISOFORM EXPRESSION OR MRNA EXPRESSION LEVELS, IF PERFORMED; DNA ANALYSIS OR COMBINED DNA AND RNA ANALYSIS
81479	Unlisted molecular pathology procedure For CLONOSEQ®
81206	BCR/ABL1 (T(9;22)) (EG, CHRONIC MYELOGENOUS LEUKEMIA) TRANSLOCATIONANALYSIS; MAJOR BREAKPOINT, QUALITATIVE OR QUANTITATIVE
81207	BCR/ABL1 (T(9;22)) (EG, CHRONIC MYELOGENOUS LEUKEMIA) TRANSLOCATIONANALYSIS; MINOR BREAKPOINT, QUALITATIVE OR QUANTITATIVE
81208	BCR/ABL1 (T(9;22)) (EG, CHRONIC MYELOGENOUS LEUKEMIA) TRANSLOCATIONANALYSIS; OTHER BREAKPOINT, QUALITATIVE OR QUANTITATIVE
81310	NPM1 (NUCLEOPHOSMIN) (EG, ACUTE MYELOID LEUKEMIA) GENE ANALYSIS, EXON12 VARIANTS
81315	PML/RARALPHA, (T(15;17)), (PROMYELOCYTIC LEUKEMIA/RETINOIC ACID RECEPTOR ALPHA) (EG, PROMYELOCYTIC LEUKEMIA) TRANSLOCATION ANALYSIS;COMMON BREAKPOINTS (EG, INTRON 3 AND INTRON 6), QUALITATIVE OR QUANTITATIVE
81316	PML/RARALPHA, (T(15;17)), (PROMYELOCYTIC LEUKEMIA/RETINOIC ACID RECEPTOR ALPHA) (EG, PROMYELOCYTIC LEUKEMIA) TRANSLOCATION ANALYSIS;SINGLE BREAKPOINT (EG, INTRON 3, INTRON 6 OR EXON 6), QUALITATIVE OR QUANTITATIVE
81334	RUNX1 (RUNT RELATED TRANSCRIPTION FACTOR 1) (EG, ACUTE MYELOIDLEUKEMIA, FAMILIAL PLATELET DISORDER WITH ASSOCIATED MYELOID MALIGNANCY) GENE ANALYSIS, TARGETED SEQUENCE ANALYSIS (EG, EXONS 3-8)
81401	MOLECULAR PATHOLOGY PROCEDURE, LEVEL 2 (EG, 2-10 SNPS, 1 METHYLATED VARIANT, OR 1 SOMATIC VARIANT [TYPICALLY USING NONSEQUENCING TARGETVARIANT ANALYSIS], OR DETECTION OF A DYNAMIC MUTATION DISORDER/TRIPLET REPEAT)
0040U	BCR/ABL1 (T(9;22)) (EG, CHRONIC MYELOGENOUS LEUKEMIA) TRANSLOCATIONANALYSIS, MAJOR BREAKPOINT, QUANTITATIVE
81261	IGH@ (IMMUNOGLOBULIN HEAVY CHAIN LOCUS) (EG, LEUKEMIAS AND LYMPHOMAS, B-CELL), GENE REARRANGEMENT ANALYSIS TO DETECT ABNORMALCLONAL POPULATION(S); AMPLIFIED METHODOLOGY (EG, POLYMERASE CHAIN REACTION)
81263	IGH@ (IMMUNOGLOBULIN HEAVY CHAIN LOCUS) (EG, LEUKEMIA AND LYMPHOMA,B-CELL), VARIABLE REGION SOMATIC MUTATION ANALYSIS
81264	IGK@ (IMMUNOGLOBULIN KAPPA LIGHT CHAIN LOCUS) (EG, LEUKEMIA AND LYMPHOMA, B-CELL), GENE REARRANGEMENT ANALYSIS, EVALUATION TO DETECTABNORMAL CLONAL POPULATION(S)
81340	TRB@ (T CELL ANTIGEN RECEPTOR, BETA) (EG, LEUKEMIA AND LYMPHOMA), GENE REARRANGEMENT ANALYSIS TO DETECT ABNORMAL CLONAL POPULATION(S); USING AMPLIFICATION METHODOLOGY (EG, POLYMERASE CHAIN REACTION)
81342	TRG@ (T CELL ANTIGEN RECEPTOR, GAMMA) (EG, LEUKEMIA AND LYMPHOMA), GENE REARRANGEMENT ANALYSIS, EVALUATION TO DETECT ABNORMAL CLONALPOPULATION(S)

Reviewed by / Approval Signatures

Population Health & Clinical Quality Committee (PHCQC): Gray Clarke MD
Medical Director: Ana Maria Rael MD
Date Approved: 03-20-2024

References

1. CMS, LCD MolDX: Minimal Residual Disease Testing for Cancer (L38835), revision date 10/26/2023, R2; [Cited 02/23/2024]
   Related Articles:
   a. A59004 - Billing and Coding: MolDX: Minimal Residual Disease Testing for Hematologic Cancers, revision date: 01/01/2024, R4
   b. A58468 - Billing and Coding: MolDX: Minimal Residual Disease Testing for Solid Tumor Cancers, revision date: 01/01/2024, R6
2. Hayes, Signatera (Natera Inc.), Molecular Test assessment, Jan 18, 2023 [Cited 0/23/2024]
3. Hayes, Signatera (Natera Inc.), Precision Medicine Research Brief, May 04, 2021 [Cited 02/23/2024]
4. Hayes, clonoSEQ (Adaptive Biotechnologies), Molecular Test Assessment, May 10, 2023 [Cited 01/16/2024]
5. AMA, CPT® Proprietary Laboratory Analyses (PLA) Codes: Long Descriptors, Updated December 29, 2022 [Cited 02/01/2023]
6. Hayes, Guardant Reveal (Guardant Health), Precision Medicine research Brief, Mar 20, 2023, Somatic [Cited 02/23/2024]

Publication History

03-22-2023 Original effective date. New policy. Reviewed by PHP Medical Policy Committee on 02-01-2023. Coverage will follow WPS, MolDX: Minimal Residual Disease Testing for Cancer LCD (L38835) for molecular residual disease assay (MRD) using ctDNA for management of Cancer for ALOB. Test includes:

- Signatera™ by Natera. Code 0340U effective 10/01/2022. Related article LCA (A58468). Code will require PA.
- ClonoSEQ® by Adaptive Biotechnologies. Code 81479. Related article LCA (A59004). Code will require PA. *AMA future PLA Code (0364U) to be published in 2024.

03-20-2024 Annual review. Reviewed by PHP Medical Policy Committee on 02-28-2024. No change in coverage only the names of test, such as Signatera and ClonoSEQ were removed throughout policy. Continue to follow LCD (L38835) MolDX: Minimal Residual Disease Testing for Cancer for ALOB.
The related LCAs are as follow:

- LCA (A58468) for Solid Tumor has added four additional tests in Table 1. Added codes 81445, 0422U and 0356U to policy and code 0422U will be set to require PA for ALOB. Codes 81445 and 0356U will continue to require PA.
- LCA (A59004) for Hematologic Cancer has no change. Added codes (81450, 81479, 81206, 81207, 81208, 81310, 81315, 81316, 81334, 81401, 0040U, 81261, 81263, 81264, 81340, 81342, and 81450) to policy which will continue to require PA for ALOB.

This Medical Policy is intended to represent clinical guidelines describing medical appropriateness and is developed to assist Presbyterian Health Plan and Presbyterian Insurance Company, Inc. (Presbyterian) Health Services staff and Presbyterian medical directors in determination of coverage. The Medical Policy is not a treatment guide and should not be used as such.

For those instances where a member does not meet the criteria described in these guidelines, additional information supporting medical necessity is welcome and may be utilized by the medical director in reviewing the case. Please note that all Presbyterian Medical Policies are available online at: ***Click here for Medical Policies***

Web links:

At any time during your visit to this policy and find the source material web links has been updated, retired or superseded, PHP is not responsible for the continued viability of websites listed in this policy.

When PHP follows a particular guideline such as LCDs, NCDs, MCG, NCCN etc., for the purposes of determining coverage; it is expected providers maintain or have access to appropriate documentation when requested to support coverage. See the References section to view the source materials used to develop this resource document.