# Measurable Residual Disease Assessment for Hematological Cancers- clonoSEQ

Policy Number: **M20240726022**

Effective Date: **9/1/2024**

Sponsoring Department: **Health Care Services**

Impacted Department(s): **Health Care Services**

**Type of Policy:** ☐ Internal ☒ External

**Data Classification:** ☐Confidential ☐Restricted ☒Public

## Applies to (Line of Business):

☐ Corporate (All)

✦ State Products, if yes which plan(s): ☒MediSource; ☒MediSource Connect; ☒Child Health Plus; ☒Essential Plan

✦ Medicare, if yes, which plan(s): ☒MAPD; ☐PDP; ☒ISNP; ☒CSNP

✦ Commercial, if yes, which type: ☒Large Group; ☒Small Group; ☒Individual

☒ Self-Funded Services *(Refer to specific Summary Plan Descriptions (SPDs) to determine any pre-authorization or pre-certification requirements and coverage limitations. In the event of any conflict between this policy and the SPD of a Self-Funded Plan, the SPD shall supersede the policy.)*

## Excluded Products within the Selected Lines of Business (LOB)

N/A

**Applicable to Vendors?** Yes ☐ No☒

## Purpose and Applicability:

To set forth Independent Health's medical necessity criteria for **Measurable Residual Disease** Assessment utilizing clonoSEQ for members with **B-cell acute lymphoblastic leukemia (B-ALL)**, **multiple myeloma (MM)** and **chronic lymphocytic leukemia (CLL)**.

## Policy:

**Commercial and Self-Funded:**

clonoSEQ for the assessment of measurable residual disease (MRD) is considered medically appropriate to detect measurable residual disease (MRD) at a **threshold of 10-4** as an alternative test in patients with Leukemia, Lymphoma, and Multiple Myeloma.

**MediSource, MediSource Connect, Essential Plan and Child Health Plus:**
Measurable Residual Disease Assessment utilizing clonoSEQ is covered for MediSource, MediSource Connect, Essential Plan and Child Health Plus utilizing the Commercial criteria. Claims for MediSource, MediSource Connect, Essential Plan and Child Health Plus should utilize 81479 code for billing purposes.

**Medicare Advantage:**
There is currently a Local Coverage Determination (LCD) and a Local Coverage Article (LCA) for minimal residual disease testing for hematologic cancers. Please refer to the links listed in the Reference section for Medicare Advantage members.

**Background:**
Measurable residual disease assessment (MRD) for hematologic malignancies refers to the presence of residual malignant cells not detected by conventional methods. The presence or absence of MRD can be a prognostic biomarker for posttherapy risk stratification and guiding treatment approaches and may be performed via three different modalities: multiparameter flow-cytometry (MFC), quantitative polymerase chain reaction (qPCR), or next-generation sequencing (NGS) via clonoSEQ. Specimens for MRD assessment can be obtained via peripheral blood or from a small volume of first pull bone marrow to avoid hemodilution. Bone marrow is preferred, especially in cases of B-lineage acute lymphoblastic leukemia (ALL)/lymphoblastic lymphoma (LBL). A 2 to 5 mL sample from the first bone marrow aspirate usually provides sufficient numbers of bone marrow cells to achieve adequate sensitivity. Measurement of MRD after remission induction and/or consolidation therapy is highly prognostic for relapse, prognosis, and is routinely used in clinical care of patients with acute lymphoblastic leukemia /lymphoblastic lymphoma.

The clonoSEQ test measures MRD to monitor changes in the burden of disease during and after treatment for clinical decision making in conjunction with other clinicopathological factors in patients with B-cell acute lymphoblastic leukemia (B-ALL) and MM using bone marrow samples and in patients with chronic lymphocytic leukemia (CLL) using BM or peripheral blood (PB) samples.

According to the National Comprehensive Cancer Network Guidelines for Acute Lymphoblastic Leukemia, timing of MRD assessment includes upon completion of initial induction, and the end of consolidation. Additional time points should be guided by the regimen used and risk features. Serial monitoring frequency may be increased in patients with molecular relapse or persistent low-level disease burden. For some techniques, a baseline sample (i.e., prior to treatment) is needed to characterize the leukemic clone for subsequent MRD assessment.

## Pre-Authorization Required? Yes ☒ No ☐

Preauthorization is required for this service for the initial and subsequent requests for clonoSEQ testing.

## Definitions

B-cell acute lymphoblastic leukemia (B-ALL) is an aggressive type of leukemia characterized by the presence of too many lymphoblasts or lymphocytes in the bone marrow and peripheral blood, classified on the basis of B cell lineage. It can spread to the lymph nodes, spleen, liver, central nervous system (CNS), testicles, and other organs.

Chronic lymphocytic leukemia (CLL) is one of the chronic lymphoproliferative disorders (lymphoid neoplasms). It is characterized by a progressive accumulation of functionally incompetent lymphocytes, which are usually monoclonal in origin.

Minimal/Measurable Residual Disease (MRD) refers to the presence of leukemic cells below the threshold of detection by conventional morphologic methods or standard immunophenotyping.

Multiple myeloma (MM) clonal plasma cell proliferative disorder typically characterized by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow and can result in extensive skeletal destruction with osteolytic lesions, osteopenia, and/or pathologic fractures.

Threshold of 10-4 is the ratio of total clonal cells to total nucleated cells.

## References

**Related Policies, Processes and Other Documents**

N/A

**Non-Regulatory References**

Advani AS, Aster JC. Clinical manifestations, pathologic features, and diagnosis of B cell acute lymphoblastic leukemia/lymphoma In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed on July 10, 2024.

Dekker SE, Rea D, Cayuela JM, et al. Using Measurable Residual Disease to Optimize Management of AML, ALL, and Chronic Myeloid Leukemia. Am Soc Clin Oncol Educ Book. 2023 Jun;43:e390010.

Hayes, Inc. Molecular Test Assessment clonoSEQ (Adaptive Biotechnologies). Lansdale, PA; June 2022.

Kumar S. Multiple myeloma: Evaluating response to treatment. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed on July 3, 2024.

Laubach JP. Multiple myeloma: Clinical features, laboratory manifestations, and diagnosis. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed on July 10, 2024.

Leukemia & Leukemia Society [web site]. Minimal Residual Disease (MRD). Available at: https://www.lls.org/sites/default/files/National/USA/Pdf/Publications/FS35_MRD_Final_2019.pdf Accessed June 24, 2024.

National Cancer Institute (NCI) [web site]. Acute Lymphoblastic Leukemia Treatment (PDQ®)–Health Professional Version. Updated March 28, 2024.Available at: https://www.cancer.gov/types/leukemia/hp/adult-all-treatment-pdq#_1 Accessed July 10, 2024.

National Comprehensive Cancer Network (NCCN) [web site]. Acute Lymphoblastic Leukemia; Version 1.2024 — June 14, 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf Accessed July 3, 2024.

National Comprehensive Cancer Network (NCCN) [web site]. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 3.2024 — March 26, 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf Accessed July 3, 2024.

National Comprehensive Cancer Network (NCCN) [web site]. Multiple Myeloma Version 4.2024 — April 26, 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf Accessed July 9, 2024.

Rai KR, Stilgenbauer S. Overview of the treatment of chronic lymphocytic leukemia. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed on July 10, 2024.

Riva G, Nasillo V, Ottomano AM, et al. Multiparametric Flow Cytometry for MRD Monitoring in Hematologic Malignancies: Clinical Applications and New Challenges. Cancers (Basel). 2021 Sep 12;13(18):4582.

Sánchez R, Ayala R, Martínez-López J. Minimal Residual Disease Monitoring with Next-Generation Sequencing Methodologies in Hematological Malignancies. Int J Mol Sci. 2019 Jun 10;20(11):2832.

Stock W, Zeev E. Detection of measurable residual disease in acute lymphoblastic leukemia/lymphoblastic lymphoma. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed on July 3, 2024.

Wierda WG, Rawstron A, Cymbalista F, et al. Measurable residual disease in chronic lymphocytic leukemia: expert review and consensus recommendations. Leukemia. 2021 Nov;35(11):3059-3072.

**Regulatory References**

Centers for Medicare and Medicaid (CMS) [web site]. Local Coverage Article - Billing and Coding: MolDX: Minimal Residual Disease Testing for Hematologic Cancers. A58997 Available at: https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=55672&ver=23 Accessed June 24, 2024.

Centers for Medicare and Medicaid (CMS) [web site]. Local Coverage Determination (LCD) MolDX: Minimal Residual Disease Testing for Cancer L38816. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=38816&ver=3&bc=0 Accessed June 24, 2024.

New York State Department of Health [web site]. New York State Medicaid Program Fee-For-Service Laboratory Procedure Codes. Version 6/2024 . Available at: https://www.emedny.org/ProviderManuals/Laboratory/PDFS/Laboratory_Procedure_Codes.pdf Accessed July 2, 2024.

## Version Control

Signature / Approval on File? Yes ☒ No☐

| Revision Date | Policy Author / Owner | Notes |
|---|---|---|
| 11/1/2024 | Health Care Services | Revised |
| Click here to enter a date. | Click here to enter text. | Click here to enter text. |
| Click here to enter a date. | Click here to enter text. | Click here to enter text. |
| Click here to enter a date. | Click here to enter text. | Click here to enter text. |