MEDICAL POLICY

POLICY TITLE	NEXT-GENERATION SEQUENCING FOR THE ASSESSMENT OF MEASURABLE RESIDUAL DISEASE
POLICY NUMBER	MP 2.379

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	**RETIRED 7/1/2026**

I. POLICY

Next-generation sequencing (e.g. clonoSEQ) to detect measurable residual disease (MRD) at a threshold of 10^{-4} as an alternative test in individuals with acute lymphoblastic leukemia may be considered **medically necessary**.

Next-generation sequencing (e.g. clonoSEQ) to detect MRD at a threshold of less than 10^{-4} in individuals with acute lymphoblastic leukemia is considered **investigational**.

Next-generation sequencing (e.g. clonoSEQ) to detect MRD at a threshold of 10^{-4} as an alternative test in individuals with chronic lymphocytic leukemia may be considered **medically necessary**.

Next-generation sequencing (e.g. clonoSEQ) to detect MRD at a threshold of less than 10^{-4} in individuals with chronic lymphocytic leukemia is considered **investigational.**

Next-generation sequencing (e.g. clonoSEQ) detect MRD at a threshold of 10^{-5} as an alternative test in individuals with multiple myeloma may be considered **medically necessary**.

Next-generation sequencing (e.g. clonoSEQ) to detect MRD at a threshold of less than 10^{-5} in individuals with multiple myeloma is considered **investigational**.

Next-generation sequencing (e.g. clonoSEQ) to detect MRD in individuals with diffuse large B-cell lymphoma is considered **investigational**.

Next-generation sequencing (e.g. clonoSEQ) to detect MRD in individuals with mantle cell lymphoma is considered **investigational**.

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Next-generation sequencing to detect MRD is considered **investigational** in all other situations.

There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Cross-References:

MP 9.038 Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma
MP 9.044 Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome
MP 9.041 Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies.

III. DESCRIPTION/BACKGROUND

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Measurable residual disease (MRD), also known as minimal residual disease, refers to residual clonal cells in blood or bone marrow following treatment for hematologic malignancies. MRD is typically assessed by flow cytometry (FC) or polymerase chain reaction, which can detect 1 clonal cell in 100,000 cells. It is proposed that next-generation sequencing (NGS), which can detect 1 residual clonal sequence out of 1,000,000 cells, will improve health outcomes in patients who have been treated for hematologic malignancies such as acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), multiple myeloma (MM), diffuse large B-cell lymphoma (DLBCL), and mantle cell lymphoma (MCL).

Disease

There are 3 main types of hematologic malignancies: lymphomas, leukemias, and myelomas. Lymphoma begins in lymph cells of the immune system, which originate in the bone marrow and collect in lymph nodes and other tissues. Leukemia is caused by the overproduction of abnormal white blood cells in the bone marrow, which leads to a decrease in the production of red blood cells and plasma cells. The most common forms of leukemia are acute lymphoblastic leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, and chronic myeloid leukemia. Multiple myeloma (MM), also called plasma myeloma, is a malignancy of plasma cells in the bone marrow. The present evidence review will address B-cell acute lymphoblastic

leukemia, chronic lymphocytic leukemia, multiple myeloma, diffuse large B-cell lymphoma, and mantle cell lymphoma. As B-Cell acute lymphoblastic leukemia and B-Cell lymphoblastic lymphoma are generally considered clinically indistinct, reference to B-Cell acute lymphoblastic leukemia is intended to encompass both entities.

Treatment
Treatment depends on the type of malignancy and may include surgery, radiotherapy, chemotherapy, targeted therapy, plasmapheresis, biologic therapy, or hematopoietic cell transplant. Treatment of acute leukemias can lead to complete remission. Multiple myeloma and the chronic leukemias are treatable but generally incurable. Outcomes of lymphoma vary by subtype, and some forms are curable.

Measurable Residual Disease
Relapse is believed to be due to residual clonal cells that remain following "complete response" after induction therapy but are below the limits of detection using conventional morphologic assessment. Residual clonal cells that can be detected in the bone marrow or blood are referred to as measurable residual disease (MRD), also known as minimal residual disease. MRD assessment is typically performed by flow cytometry or polymerase chain reaction (PCR) with primers for common variants. Flow cytometry or next generation flow cytometry evaluates blasts based on the expression of characteristic antigens, while PCR assesses specific chimeric fusion gene transcripts, gene variants, and overexpressed genes. PCR is sensitive for specific targets, but clonal evolution may occur between diagnosis, treatment, remission, and relapse that can affect the detection of MRD. Next-generation sequencing (NGS) has 10- to 100-fold greater sensitivity for detecting clonal cells, depending on the amount of DNA in the sample (see Table 1) and does not require patient-specific primers. For both PCR and NGS a baseline sample at the time of high disease load is needed to identify tumor-specific sequences. MRD with NGS is frequently used as a surrogate measure of treatment efficacy in drug development.

It is proposed that by using a highly sensitive and sequential MRD surveillance strategy, one could expect better outcomes when therapy is guided by molecular markers rather than hematologic relapse. However, some patients may have hematologic relapse despite no MRD, while others do not relapse despite residual mutation-bearing cells. Age-related clonal hematopoiesis, characterized by somatic variants in leukemia-associated genes with no associated hematologic disease, further complicates the assessment of MRD. One available test (ClonoSEQ) uses both PCR and NGS to detect clonal DNA in blood and bone marrow. ClonoSEQ Clonality (ID) PCR assessment is performed when there is a high disease load (e.g., initial diagnosis or relapse) to identify dominant or “trackable” sequences associated with the malignant clone. NGS is then used to monitor the presence and level of the associated sequences in follow-up samples. As shown in Table 1, NGS can detect clonal cells with greater sensitivity than either flow cytometry or PCR, although next-generation flow techniques have reached a detection limit of 1 in 10^{-5} cells, which is equal to PCR and approaches the limit of detection of NGS (see Table 1).

Table 1. Sensitivity of Methods for Detecting Minimal Residual Disease

Technique	Sensitivity	Detection limit of blasts per 100,000 Nucleated Cells
Microscopy (complete response)		50,000
Multi-parameter flow cytometry	10^{-4}	10
Next-generation flow cytometry	10^{-5}	1.0
Polymerase chain reaction	10^{-5}	1.0
Quantitative next-generation sequencing	10^{-5}	1.0
Next-generation sequencing	10^{-6}	0.1

Regulatory Status

The clonoSEQ® Minimal Residual Disease Test is offered by Adaptive Biotechnologies. clonoSEQ® was previously marketed as clonoSIGHT™ (Sequenta), which was acquired by Adaptive Biotechnologies in 2015. clonoSIGHT™ was a commercialized version of the LymphoSIGHT platform by Sequenta for clinical use in MRD detection in lymphoid cancers. In September 2018, clonoSEQ received marketing clearance from the U.S. Food and Drug Administration (FDA) through the de novo classification process to detect MRD in patients with acute lymphoblastic leukemia or multiple myeloma. In 2020, clonoSEQ received marketing clearance from the FDA to detect MRD in patients with chronic lymphocytic leukemia. clonoSEQ is available for use in other lymphoid cancers, such as diffuse large B-cell lymphoma (DLBCL), as a CLIA-validated laboratory developed test (LDT).

IV. RATIONALE

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Summary of Evidence

For individuals with B-cell ALL (B-ALL) who are being monitored for residual disease following treatment who receive NGS for MRD at a threshold of 10^{-4}, the evidence includes a retrospective comparison of data from trials. Relevant outcomes are overall survival (OS), disease-specific survival, test validity, change in disease status, quality of life (QOL), and treatment-related morbidity. Comparison of NGS and the established standard of flow cytometry (FC) showed good concordance when the same threshold (10^{-4}) was used for both NGS and FC. OS in pediatric patients with MRD positivity was significantly lower than in pediatric patients who were MRD negative at this threshold. The relatively small subset of patients who were

discordant for FC and NGS results had outcomes that were midway between patients who were concordant as MRD positive or MRD negative for both tests. As the vast majority of patients had concordant results for NGS and FC at a threshold of 10^{-4}, NGS can be considered an alternative to FC for monitoring MRD in patients with B-ALL. The evidence is sufficient to determine that the technology results in an improvement in the net health outcomes.

For individuals with B-ALL who are being monitored for residual disease following treatment who receive NGS for MRD at a threshold of less than 10^{-4}, the evidence includes retrospective analysis of prognosis from trials. Relevant outcomes are OS, disease-specific survival, test validity, change in disease status, QOL, and treatment-related morbidity. NGS can be more sensitive than FC to detect the presence of residual leukemic cells, but specificity may be decreased at the more sensitive thresholds resulting in potential harm from overtreatment. Further study is needed to clarify whether MRD at levels lower than 1 in 10,000 cells represents clinically significant disease and if the more sensitive test can be used to risk-stratify patients with B-ALL. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with CLL who are being monitored for residual disease following treatment who receive NGS for MRD at a threshold of 10^{-4}, the evidence includes analysis of samples from clinical trials. Relevant outcomes are OS, disease-specific survival, test validity, change in disease status, QOL, and treatment-related morbidity. These studies evaluated the association between the level of MRD detected by NGS in bone marrow or blood and progression-free survival in completed phase 2 and 3 trials. Two studies demonstrated an association between the level of MRD and PFS (progression -free survival) with lower risk of progression in patients who exhibit MRD negativity below 10^{-4} compared to patients who have detectable residual disease. In one study of participants treated with ibrutinib+venetoclax, PFS at one year was high regardless of MRD status using threshold of 10-4 at the end of treatment. The evidence is sufficient to determine that the technology results in an improvement in the net health outcomes.

For individuals with CLL who are being monitored for residual disease following treatment who receive NGS for MRD at a threshold of less than 10^{-4}, the evidence includes analysis of samples from clinical trials. Relevant outcomes are OS, disease-specific survival, test validity, change in disease status, QOL, and treatment-related morbidity. NGS can be more sensitive than FC to detect the presence of residual leukemic cells, but it is not clear if prognosis is improved at the lower thresholds. Currently, no additional treatment is offered to eradicate low-level MRD ($<10^{-4}$) after first-line treatment of CLL. Further study is needed to clarify whether MRD at levels lower than 1 in 10,000 cells represents clinically significant disease and if the more sensitive test can be used for prognosis in patients with CLL. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

For individuals with MM who have achieved a complete response (CR) following treatment who receive NGS for MRD at a threshold of 10^{-5}, the evidence includes a retrospective comparison of NGS and FC data from MM treatment trials and from a clinical series. Relevant outcomes are OS, disease-specific survival, test validity, change in disease status, QOL, and treatment-

related morbidity. Concordance has been demonstrated between NGS and the established standard of FC at 10^{-4} as well as with next generation flow cytometry (NGF) at a threshold of 10^{-5}. PFS in patients with MRD positivity is significantly shorter than in patients who are MRD negative at these thresholds. The relatively small subset of patients who were discordant for FC and NGS results had outcomes that were, on average, midway between patients who were concordant as MRD positive or MRD negative for both tests. Retrospective studies also indicate improved PFS when MRD is less than 10^{-5} compared to patients who have MRD greater than 10^{-5}. This threshold is consistent with current guideline-based care for prognostication using either NGF or NGS. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with MM who have achieved a complete response (CR) following treatment who receive NGS for MRD at a threshold of less than 10^{-5}, the evidence includes retrospective studies on prognosis. Relevant outcomes are OS, disease-specific survival, test validity, change in disease status, QOL, and treatment-related morbidity. There is some evidence that MRD may be a prognostic marker, but there is insufficient evidence on the number of false positives in patients with CR at the more sensitive threshold provided by NGS for prognostication or to guide therapy. A chain of evidence regarding management changes based on the assessment of MRD with NGS to detect 1 malignant clonal sequence out of 1,000,000 cells cannot be completed. Direct evidence from randomized controlled trials is needed to evaluate whether patient outcomes are improved by changes in post-induction care (e.g., continuing or discontinuing therapy, avoiding unnecessary adverse events) following NGS assessment of residual disease at a threshold lower than 10^{-5}. Trials that will test the effectiveness of NGS to guide therapy in MM are ongoing. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

For individuals with DLBCL who are being monitored for residual disease following treatment who receive NGS for MRD, the evidence includes an analysis from a single-center, prospective trial. Relevant outcomes are OS, disease-specific survival, test validity, change in disease status, QOL, and treatment-related morbidity. Although both PFS and OS correlated with MRD positivity, the trial is limited by its small sample-size and inclusion of only patients eligible for HSCT from a single center. Guideline support for using MRD with any method or threshold to make management decisions is lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with MCL who are being monitored for residual disease the evidence includes retrospective analyses of NGS testing during therapeutic clinical trials. Relevant outcomes are OS, disease-specific survival, test validity, change in disease status, QOL, and treatment-related morbidity. A retrospective analysis of a "research version" of an NGS test has demonstrated concordance between NGS and FC at 10^{-4} during induction therapy. MRD positivity as determined by either the "research version" of NGS or FC was associated with worse PFS. An exploratory analysis found improved survival in patients who were MRD negative after 2 cycles of induction; however, this is based on a small number of samples with an undefined threshold for NGS testing. Overall, the literature is limited, and guidelines for NGS testing to detect MRD in patients with

MCL are lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

V. DEFINITIONS

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NA

VI. DISCLAIMER

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Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as required by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These polices are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.

VII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational therefore not covered:

Procedure Codes							
0306U	0307U	0340U					

Covered when medically necessary:

Procedure Codes							
0171U	0364U	0560U	0561U	81479	81599		

ICD-10-CM Diagnosis Codes	Description
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission

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ICD-10-CM Diagnosis Codes	Description
C90.02	Multiple myeloma in relapse
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.11	Chronic lymphocytic leukemia of B-cell type in remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse

VIII. REFERENCES

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1. *National Comprehensive Care Network. NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia. Version 2.2024*
2. *Berry DA, Zhou S, Higley H, et al. Association of Minimal Residual Disease With Clinical Outcome in Pediatric and Adult Acute Lymphoblastic Leukemia: A Meta-analysis. JAMA Oncol. Jul 13 2017; 3(7): e170580. PMID 28494052*
3. *Wood B, Wu D, Crossley B, et al. Measurable residual disease detection by high-throughput sequencing improves risk stratification for pediatric B-ALL. Blood. Mar 22 2018; 131(12): 1350-1359. PMID 29284596*
4. *Pulsipher MA, Carlson C, Langholz B, et al. IgH-V(D)J NGS-MRD measurement pre- and early post-allotransplant defines very low- and very high-risk ALL patients. Blood. May 28 2015; 125(22): 3501-8. PMID 25862561*
5. *Pulsipher MA, Han X, Maude SL, et al. Next-Generation Sequencing of Minimal Residual Disease for Predicting Relapse after Tisagenlecleucel in Children and Young Adults with Acute Lymphoblastic Leukemia. Blood Cancer Discov. Jan 2022; 3(1): 66-81. PMID 35019853*
6. *Liang EC, Dekker SE, Sabile JMG, et al. Next-generation sequencing-based MRD in adults with ALL undergoing hematopoietic cell transplantation. Blood Adv. Jul 25 2023; 7(14): 3395-3402. PMID 37196642*
7. *Hallek M, Cheson BD, Catovsky D, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. Blood. Jun 21 2018; 131(25): 2745-2760. PMID 29540348*
8. *National Comprehensive Care Network. NCCN clinical care practice guidelines in Oncology: Chronic lymphocytic leukemia/ small lymphocytic lymphoma. Version 1.2025*
9. *clonoSEQ Assay: Technical Information*
10. *Thompson PA, Srivastava J, Peterson C, et al. Minimal residual disease undetectable by next-generation sequencing predicts improved outcome in CLL after chemoimmunotherapy. Blood. Nov 28 2019; 134(22): 1951-1959. PMID 31537528*

11. *Munir T, Moreno C, Owen C, et al. Impact of Minimal Residual Disease on Progression-Free Survival Outcomes After Fixed-Duration Ibrutinib-Venetoclax Versus Chlorambucil-Obinutuzumab in the GLOW Study. J Clin Oncol. Jul 20 2023; 41(21): 3689-3699. PMID 37279408*
12. *Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol. Aug 2016; 17(8): e328-e346. PMID 27511158*
13. *Bal S, Weaver A, Cornell RF, et al. Challenges and opportunities in the assessment of measurable residual disease in multiple myeloma. Br J Haematol. Sep 2019; 186(6): 807-819. PMID 31364160*
14. *Martinez-Lopez J, Lahuerta JJ, Pepin F, et al. Prognostic value of deep sequencing method for minimal residual disease detection in multiple myeloma. Blood. May 15 2014; 123(20): 3073-9. PMID 24646471*
15. *Perrot A, Lauwers-Cances V, Corre J, et al. Minimal residual disease negativity using deep sequencing is a major prognostic factor in multiple myeloma. Blood. Dec 06 2018; 132(23): 2456-2464. PMID 30249784*
16. *Martinez-Lopez J, Wong SW, Shah N, et al. Clinical value of measurable residual disease testing for assessing depth, duration, and direction of response in multiple myeloma. Blood Adv. Jul 28 2020; 4(14): 3295-3301. PMID 32706892*
17. *Cavo M, San-Miguel J, Usmani SZ, et al. Prognostic value of minimal residual disease negativity in myeloma: combined analysis of POLLUX, CASTOR, ALCYONE, and MAIA. Blood. Feb 10 2022; 139(6): 835-844. PMID 34289038*
18. *Oliva S, Genuardi E, Paris L, et al. Prospective evaluation of minimal residual disease in the phase II FORTE trial: a head-to-head comparison between multiparameter flow cytometry and next-generation sequencing. EClinicalMedicine. Jun 2023; 60: 102016. PMID 37396800*
19. *Kriegsmann K, Hundemer M, Hofmeister-Mielke N, et al. Comparison of NGS and MFC Methods: Key Metrics in Multiple Myeloma MRD Assessment. Cancers (Basel). Aug 18 2020; 12(8). PMID 32824635*
20. *Costa LJ, Chhabra S, Medvedova E, et al. Minimal residual disease response-adapted therapy in newly diagnosed multiple myeloma (MASTER): final report of the multicentre, single-arm, phase 2 trial. Lancet Haematol. Sep 27 2023. PMID 37776872*
21. *Hematologic Cancer Incidence, Survival, and Prevalence. Centers for Disease Control and Prevention*
22. *Types of B-cell lymphoma. American Cancer Society. Revised January 29, 2019*
23. *Herrera AF, Armand P. Minimal Residual Disease Assessment in Lymphoma: Methods and Applications. J Clin Oncol. Dec 01 2017; 35(34): 3877-3887. PMID 28933999*
24. *Chase ML, Merryman R, Fisher DC, et al. A prospective study of minimal residual disease in patients with diffuse large B-cell lymphoma using an Ig-NGS assay. Leuk Lymphoma. Feb 2021; 62(2): 478-481. PMID 33236969*
25. *Thiruvengadam SK, Hunter B, Varnavski A, et al. Ofatumumab, Etoposide, and Cytarabine Intensive Mobilization Regimen in Patients with High-risk Relapsed/Refractory Diffuse Large B-Cell Lymphoma Undergoing Autologous Stem Cell Transplantation. Clin Lymphoma Myeloma Leuk. Apr 2021; 21(4): 246-256.e2. PMID 33288485*

26. *Smith M, Jegede O, Parekh, et al. Minimal Residual Disease (MRD) Assessment in the ECOG1411 Randomized Phase 2 Trial of Front-Line Bendamustine-Rituximab (BR)-Based Induction Followed By Rituximab (R) Lenalidomide (L) Consolidation for Mantle Cell Lymphoma (MCL). 2019;134(Suppl_1):751*
27. *Lakhotia R, Melani C, Dunleavy K, et al. Circulating tumor DNA predicts therapeutic outcome in mantle cell lymphoma. Blood Adv. Apr 26 2022; 6(8): 2667-2680. PMID 35143622*
28. *National Comprehensive Care Network. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 1.2025*
29. *National Comprehensive Care Network. NCCN clinical care practice guidelines in Oncology: B-cell lymphomas. Version 3.2024*
30. *Blue Cross Blue Shield Association Medical Policy Reference Manual. 2.04.147, Next-Generation Sequencing for the Assessment of Measurable Residual Disease, January 2025*

IX. POLICY HISTORY

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MP 2.379	**07/22/2021 New Policy.** Partial BCBSA adoption. Medically necessary criteria for NGS to detect MRD in patients with ALL (threshold 10^{-4}), CLL (threshold 10-4) and MM (threshold 10-5). NCCN statement added.
	03/04/2022 Consensus Review. No change to policy statement. References reviewed and updated. FEP language updated.
	03/11/2022 Administrative Update Added new codes 0306U and 0307U as investigational; effective 04/01/2022
	09/12/2022 Administrative Update. Added New code 0340U as E/I effective 10/01/2022
	01/30/2023 Minor Review. Added that NGS for MRD in diffuse large B cell lymphoma and mantle cell lymphoma are investigational. Background, Rationale and References updated. Added ICD 10 codes C90.00, C90.01 and C90.02.
	02/05/2024 Minor Review. Policy statements edited to clarify that MRD testing with NGS for individuals with diffuse large B-cell lymphoma and mantle cell lymphoma is investigational at any sensitivity threshold. Background and Rationale updated. References added.
	11/20/2024 Administrative Update. Removed NCCN statement.
	01/24/2025 Consensus Review. No change to policy statement. Background and References updated.
	06/04/2025 Administrative Update. Removing the Benefit Variations and updating the Disclaimer. Added New Codes 0561U & 0560U
	03/06/2026 Retirement Review. Service to be managed by the vendor Evicore.

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