Medical Coverage Policy | Minimal Residual Disease Testing for Cancer

EFFECTIVE DATE: 06|01|2023
POLICY LAST UPDATED: 05|31|2023

OVERVIEW

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).

The following tests are addressed in this policy:

- clonoSEQ (Adaptive Biotechnologies)

MEDICAL CRITERIA

Medicare Advantage Plans and Commercial Products

clonoSEQ may be considered medically necessary to detect MRD in patients with a personal history of cancer when ALL of the following are true (1 – 10):

1. If Next-Generation Sequencing (NGS) methodology is used in testing, the conditions in A OR B below are met or are not applicable (the patient does not have cancer as defined below);

   A. Somatic (Acquired) Cancer:
      I. Patient has:
         a. either recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; and
         b. not been previously tested with the same test using NGS for the same cancer genetic content, and
         c. decided to seek further cancer treatment (e.g., therapeutic chemotherapy).

   AND

      II. The diagnostic laboratory test using next generation sequencing (NGS) must have:
         a. Food & Drug Administration (FDA) approval or clearance as a companion in vitro diagnostic; and,
         b. an FDA-approved or -cleared indication for use in that patient's cancer; and,
         c. results provided to the treating physician for management of the patient using a report template to specify treatment options.

   OR

   B. Germline (Inherited) Cancer:
      I. Patient has:
         a. ovarian or breast cancer; and,
         b. a clinical indication for germline (inherited) testing for hereditary breast or ovarian cancer; and,
         c. a risk factor for germline (inherited) breast or ovarian cancer; and
         d. not been previously tested with the same germline test using NGS for the same germline genetic content.

   AND

      II. The diagnostic laboratory test using NGS must have all of the following:

a. FDA-approval or clearance; and,
b. results provided to the treating physician for management of the patient using a report template to specify treatment options.

2. The patient has a personal history of cancer, the type and staging of which is within the intended use of the MRD test;
3. The identification of recurrence or progression of disease within the intended use population of the test is identified in the National Comprehensive Cancer Network (NCCN) or other established guidelines as a condition that requires a definitive change in patient management;
4. The test is demonstrated to identify molecular recurrence or progression before there is clinical, biological or radiographical evidence of recurrence or progression AND demonstrates sensitivity and specificity of subsequent recurrence or progression comparable with or superior to radiographical or other evidence (as per the standard-of-care for monitoring a given cancer type) of recurrence or progression;
5. To be reasonable and necessary, it must also be medically acceptable that the test being utilized precludes other surveillance or monitoring tests intended to provide the same or similar information, unless they either (a) are required to follow-up or confirm the findings of this test or (b) are medically required for further assessment and management of the patient;
6. If the test is to be used for monitoring a specific therapeutic response, it must demonstrate the clinical validity of its results in published literature for the explicit management or therapy indication (allowing for the use of different drugs within the same therapeutic class, so long as they are considered 'equivalent and interchangeable' for the purpose of MRD testing, as determined by national or society guidelines);
7. Clinical validity (CV) of any analytes (or expression profiles) measured must be established through a study published in the peer-reviewed literature for the intended use of the test in the intended population;
8. The test is being used (a) in a patient who is part of the population in which the test was analytically validated and (b) according to the intended use of the test;
9. The MRD test [unless it is a Food and Drug Administration (FDA) approved and established standard-of-care single-gene polymerase chain reaction (PCR)] satisfactorily completes a technical assessment (TA) that will evaluate and confirm that the analytical validity, clinical validity, and clinical utility criteria set in this policy are met to establish the test as Reasonable and Necessary;
10. Tests utilizing a similar methodology or evaluating a similar molecular analyte to a test for which there is a generally accepted testing standard or for which existing coverage exists must demonstrate equivalent or superior test performance (i.e., sensitivity and/or specificity) when used for the same indication in the same intended-use population.

PRIOR AUTHORIZATION

Prior authorization is required for Medicare Advantage Plans and recommended for Commercial Products.

Note: Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

POLICY STATEMENT

Medicare Advantage Plans and Commercial Products

The following test may be considered medically necessary when the medical criteria above are met:

- clonoSEQ

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable laboratory benefits/coverage.

BACKGROUND

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, by 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.

Evidence supports that MRD testing can be used to accurately predict disease recurrence or progression before clinical or radiographical evidence is evident (establishing molecular recurrence) and performs better than other established methods for disease surveillance such as serial CEA monitoring, physical exams, imaging, or flow cytometry. Although this is a logical progression of the understanding of the development and evolution of cancer (that tumor cells grow and shed DNA at proportional levels until such a time there is macroscopic disease in organs or bone marrow), the evidence clearly establishes that MRD testing can demonstrate acceptable clinical validity in the determination of disease recurrence; a condition whose identification has pre-established utility as it is an event that in the proper clinical context requires altering or modifying patient management. Current medical practice, including as defined in the NCCN guidelines, clearly advocate for changing or re-establishing treatment when such a diagnosis is rendered. As such, determining molecular recurrence before there is clinical or radiographical evidence of it is likely to further improve patient outcomes and is consistent with current guidelines that advocate for early detection of and treatment for recurrence. Furthermore, additional uses of MRD have been established, such as for monitoring treatment response, although it is based on the same principle. Studies demonstrate the clinical validity of molecular progression as predictive of failure to respond to treatment and demonstrate futility in continued therapy. The utility of such testing in maintenance therapy monitoring to improve patient outcomes is therefore similarly inherent; preclusion of potentially hazardous compounds that are not likely to have clinical benefit and prevention of adverse events have demonstrated improved patient outcomes.

This remains a rapidly evolving field, and it is anticipated that new evidence may emerge either showing limitations of the clinical utility underlying MRD testing or additional strengths and new applications.

CODING

The following CPT code may be medically necessary for Medicare Advantage Plans and Commercial Products when medical criteria above are met:

This code can be used for clonoSEQ:

0364U Oncology (hematolymphoid neoplasm), genomic sequence analysis using multiplex (PCR) and next-generation sequencing with algorithm, quantification of dominant clonal sequence(s), reported as

presence or absence of minimal residual disease (MRD) with quantitation of disease burden, when appropriate (New Code Effective 4/1/2023)

RELATED POLICIES

Proprietary Laboratory Analyses (PLA)

PUBLISHED

Provider Update, April 2023

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