Evidence-Based Solid Tumor Minimal Residual Disease (MRD) Testing

I. Minimal residual disease (MRD) analysis for solid tumors using cell-free DNA with sufficient evidence of clinical utility and validity is considered **medically necessary** when**:**

A. The identification of recurrent, refractory, or progressive disease will require a change in management, **AND**

B. The member is not undergoing concurrent molecular laboratory testing for surveillance or monitoring for recurrent, refractory, or progressive disease, **AND**

C. The member meets one of the following:

1. The member is currently being treated for cancer, **AND**

a) The test has not previously been done for this cancer diagnosis, **OR**

2. The member is not currently being treated for their cancer, **AND**

a) The test has not been done in the past 12 months, **OR**

b) There is a clinical suspicion for tumor recurrence, **AND**

D. The member meets one of the following:

1. The member is being tested via Guardant Reveal and has one of the following:

a) Advanced colon cancer, **OR**

b) Colorectal cancer at any stage, **AND**

(1) The member is being monitored for response to immune checkpoint inhibitor therapy, **OR**

2. The member is being tested via Signatera and has one of the following:

a) Advanced colon cancer, **OR**

b) Muscle invasive bladder cancer, **OR**

c) Ovarian cancer, **OR**

d) Neoadjuvant (pre-surgery) breast cancer, **OR**

e) Advanced breast cancer, **AND**

(1) The member has a diagnosis of disease recurrence or relapse, **OR**

f) Any solid tumor, **AND**

(1) The member is being monitored for response to immune checkpoint inhibitor therapy, **OR**

3. The member is being tested via Oncodetect and has the following:

a) Advanced colorectal cancer, **OR**

4. The member is being tested via RaDaR and has one of the following:

a) HPV-negative head and neck squamous cell carcinoma, **OR**

b) Advanced breast cancer, **OR**

5. The member is being tested via NavDx and has the following:

a) HPV-driven oropharyngeal cancer.

II. Minimal residual disease (MRD) analysis for solid tumors using cell-free DNA with sufficient evidence of clinical utility and validity is considered **investigational** for all other indications where clinical utility and validity have not been demonstrated.

RATIONALE AND REFERENCES

Evidence-Based Solid Tumor Minimal Residual Disease (MRD) Testing

Centers for Medicare and Medicaid Services (CMS)

The CMS local coverage determination (LCD) entitled “MolDX: Minimal Residual Disease Testing for Cancer” states the following regarding the use of minimally invasive molecular DNA and RNA tests that detect minimal residual disease (MRD) in patients with a personal history of cancer:

- The patient has a personal history of cancer, the type and staging of which is within the intended use of the MRD test;
- 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;
- 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.
- 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”

“When the patient is NOT known to have cancer (specifically when there is no clinical, radiographical, or other biological evidence that tumor cells remain post treatment and subsequently the patient is no longer being subjected to therapeutic interventions for cancer), a second kind of test may exist wherein a single timepoint may constitute a single test. In such patients, the frequency of MRD testing is in accordance with national or society guidelines or recommendations.”

Centers for Medicare & Medicaid Services. Medicare Coverage Database: Local Coverage Determination. MolDX: Minimal Residual Disease Testing for Cancer (L38779). Effective Date: 12/26/2021. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=38779

Concert Note:

For use of minimal residual disease testing, absent clear, specific and evidence-based guideline recommendations for a particular regimen of testing, a default frequency of once per cancer diagnosis for patients with cancer or once every 12 months for patients without cancer will be adopted.

DEFINITIONS

1. **Advanced** cancer (advanced stages or advanced tumor or advanced/metastatic): Cancer that is unlikely to be cured or controlled with treatment. The cancer may have spread from where it first started to nearby tissue, lymph nodes, or distant parts of the body. Treatment may be given to help shrink the tumor, slow the growth of cancer cells, or relieve symptoms.
2. **Circulating tumor DNA (ctDNA)** is fragmented, tumor-derived DNA circulating in the bloodstream that is not being carried in a cell. ctDNA derives either directly from the tumor or from circulating tumor cells.
3. **Circulating Tumor Cells (CTCs)** are intact cells that have shed into the bloodstream or lymphatic system from a primary tumor or a metastasis site, and are carried around the body by blood circulation.
4. **Tumor mutational burden**: A measurement of mutations carried by tumor cells and is a predictive biomarker that is being studied to evaluate its association with response to immunotherapy.
5. **Widely metastatic**: A cancer for which local control cannot be delivered to all areas of disease (per NCCN guidelines).