I. **Policy:** Molecular Profiling of Malignant Tumors to Identify Targeted Therapies

II. **Purpose/Objective:**
To provide a policy of coverage regarding Molecular Profiling of Malignant Tumors to Identify Targeted Therapies

III. **Responsibility:**
A. Medical Directors  
B. Medical Management

IV. **Required Definitions**
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. **Additional Definitions**
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

   a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
   b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
   c. in accordance with current standards of good medical treatment practiced by the general medical community.
   d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
   e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

**Medicaid Business Segment**
Medical Necessity shall mean a service or benefit that is compensable under the Medical Assistance Program and if it meets any one of the following standards:

   (i) The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
   (ii) The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or development effects of an illness, condition, injury or disability.
   (iii) The service or benefit will assist the Member to achieve or maintain maximum functional
capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for members of the same age.

**DESCRIPTION:** Molecular profiling is a method for identifying multiple biomarkers in the malignant tumors of persons who have cancer. The biomarker information can be used to identify treatment options.

**INDICATIONS:**

**REQUIRES PRIOR AUTHORIZATION BY A PLAN MEDICAL DIRECTOR OR DESIGNEE**

Molecular profiling to identify targeted therapies utilizing one of the following tests: FoundationOne, Foundation One CDx, Memorial Sloan Kettering Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT), or Target Now Molecular Profiling Service (Caris Diagnostics) will be considered medically necessary when all of the following criteria are met:

- A diagnosis of recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer has been established; and
- A decision has been made to seek further cancer treatment, such as therapeutic chemotherapy; and
- The member has not been previously tested using the same NGS test for the same primary diagnosis of cancer;
- The test is being used:
  - To establish eligibility for checkpoint inhibition immunotherapy including but not limited to Bavencio (avelumab), Imfinzi (durvalumab), Keytruda (pembrolizumab), Opdivo (nivolumumab), Tecentriq (atezolizumab), Yervoy (ipilimumab); and/or
  - As a companion diagnostic for drugs including but not limited to: Alecensa (alectinib), Cotellic (cobimetinib) in combination with Zelboraf (vemurafenib), Erbitux (cetuximab), Gilotrif (afatinib), Herceptin (trastuzumab), Iressa (gefitinib), Kadcyla (ado-trastuzumabemtansine), Mekinist (trametinib), Perjeta (pertuzumab), Rubraca (rucaparib), Tarceva (erlotinib), Tafinlar (dabrafenib), Tafinlar (dabrafenib) in combination with Mekinist (trametinib), Tagrisso (osimertinib), Vectibix (panitumumab), Xalkori (crizotinib), Zelboraf (vemurafenib), Zykdadia (ceritinib)

**FoundationOne Liquid:** Circulating tumor cell free DNA (cfDNA) molecular profiling testing is considered to be medically necessary when the following criteria are met:

- A diagnosis of non-small cell lung cancer is suspected but the member’s physical condition poses unacceptable risk for invasive biopsy; or
- A diagnosis of non-small cell lung cancer has been confirmed on pathology, but insufficient tumor sample is available for molecular testing;

  and

- The treating physician will use the results to guide therapy

**Guardant360:** Molecular profiling to identify targeted therapies utilizing Guardant360 will be considered medically necessary when all of the following criteria are met:

The member has been diagnosed with advanced (Stage IIIB or IV) non-small cell lung cancer (NSCLC); and

At Diagnosis:

- The member is untreated and results for EGFR - single nucleotide variants (SNV) and indels; rearrangements in ALK and ROS1; and SNVs for BRAF AND tissue-based comprehensive somatic genomic profiling (CGP) is infeasible (i.e., quantity not sufficient for tissue-based CGP or invasive biopsy is medically contraindicated); or

At Progression:

- The member is progressing on or after chemotherapy or immunotherapy and has never been tested for EGFR SNVs and indels; rearrangements in ALK, and ROS1; or SNVs for BRAF, and tissue-based CGP is infeasible (i.e. quantity not sufficient for tissue-based CGP); or
- The member is progressing on any tyrosine kinase inhibitors (TKI’s)

**For the MEDICARE BUSINESS SEGMENT:**

Guardant360 is covered when the member
- has been diagnosed with a recurrent, relapsed, refractory, metastatic, or advanced solid tumor that did not originate from the central nervous system, and
- is untreated for the primary cancer being tested, or is not responding to treatment, and
- has decided to seek further cancer treatment with the following conditions:
  - The member is a candidate for further treatment with a drug that is either FDA-approved for that cancer, or has an NCCN 1 or NCCN 2A recommendation for that cancer, and
  - The FDA-approved indication or NCCN recommendation is based upon information about the presence or absence of a genetic biomarker tested for in the Guardant360® assay; and
- Tissue-based, CGP is infeasible

**EXCLUSIONS:**
The Plan currently considers the use of molecular profiling tests such as, but not limited to EXaCT-1 Whole Exome Sequencing, GeneKey, GeneTrails Solid Tumor Panel, MatePair, MyAML, OmniSeq, OnkoMatch, OncInsights, and SmartGenomics to be experimental, investigational or unproven and NOT COVERED. At this time, published, peer-reviewed, medical literature to support the use of these tests is limited and insufficient to establish their analytical validity or clinical utility.

**Note:** A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

**CODING ASSOCIATED WITH:** Molecular Profiling of Malignant Tumors
*The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.*

- 0037U Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden [FoundationOne CDx (F1CDx)]
- 0048U Oncology (solid organ neoplasm), DNA, targeted sequencing of protein-coding exons of 468 cancer-associated genes, including interrogation for somatic mutations and microsatellite instability, matched with normal specimens, utilizing formalin-fixed paraffin-embedded tumor tissue, report of clinically significant mutation(s) [MSK-IMPACT (Memorial Sloan Kettering Integrated Mutation Profiling of Actionable Cancer Targets)]
- 81445 Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
- 81455 Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
- 0013U Oncology (solid organ neoplasm), gene rearrangement detection by whole genome next-generation sequencing, DNA, fresh or frozen tissue or cells, report of specific gene rearrangement(s) [MatePair Targeted Rearrangements]
- 0014U Hematology (hematolymphoid neoplasm), gene rearrangement detection by whole genome next-generation sequencing, DNA, whole blood or bone marrow, report of specific gene rearrangement(s) [MatePair Targeted Rearrangements]
- 0036U Exome (ie, somatic mutations), paired formalin-fixed paraffin-embedded tumor tissue and normal specimen, sequence analyses [EXaCT-1 Whole Exome Testing]
- 0050U Targeted genomic sequence analysis panel, acute myelogenous leukemia, DNA analysis, 194 genes, interrogation for sequence variants, copy number variants or rearrangements [MyAML NGS Panel]
- 0056U Hematology (acute myelogenous leukemia), DNA, whole genome next generation sequencing to detect gene rearrangement(s), blood or bone marrow, report of specific gene rearrangement(s) [MatePair Acute Myeloid Leukemia Panel]
- 0057U Oncology (solid organ neoplasm), mRNA, gene expression profiling by massively parallel sequencing for analysis of 51 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a normalized percentile rank
RNA-Sequencing by NGS; [OmniSeq]


LINE OF BUSINESS:
Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD’s and NCD’s will supersede this policy. For PA Medicaid Business segment, this policy applies as written.

REFERENCES:
Centers for Medicare and Medicaid Services (CMS). Decision memo for next-generation sequencing (NGS) for Medicare beneficiaries with advanced cancer. CAG-00450N. March 16, 2018.

MolDx LCD L37649 Guardant360® Plasma-Based Comprehensive Genomic Profiling in Non-Small Cell Lung Cancer (NSCLC)


U.S. Food & Drug Administration. FoundationOne CDx - P170019


Centers for Medicare & Medicaid Services. National Coverage Determination (NCD90.2): Next Generation Sequencing (NGS)


MoIDX: Plasma-Based Genomic Profiling in Solid Tumors (L38043)

This policy will be revised as necessary and reviewed no less than annually.

Devised: 12/18

Revised: 12/19 (add FoundationOne Liquid); 2/20(Add Medicare Guardant360 indication)

Reviewed: