GUIDELINES
This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder contract. Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards. This guideline is solely for explaining correct procedure reporting and does not imply coverage and reimbursement.

DESCRIPTION
Clinical laboratory diagnostic tests can include tests that predict the risk associated with one or more genetic variations within a cancer or tumor (i.e. somatic mutations). In addition, in vitro companion diagnostic laboratory tests provide a report of test results of genetic variations and are essential for the safe and effective use of a corresponding therapeutic product. Next Generation Sequencing (NGS) is one technique that can detect genetic variations within a cancer or tumor. Other techniques that could be utilized include (but are not limited to): Sanger sequencing, multiplex ligation-dependent probe amplification (MLPA), quantitative real-time PCR (polymerase chain reaction), allele specific PCR, and fluorescence in situ hybridization (FISH).

Patients with advanced cancer can have recurrent, metastatic, and/or stage IV disease. Some genetic variations in a patient’s cancer can, in concert with clinical factors, predict how each individual responds to specific treatments.

In application, molecular profiling panels (i.e., information on the cancer’s genetic variations) can contribute to predicting a patient’s response to a given drug: good, bad, or none at all. Applications of molecular profiling panels to predict a patient’s response to treatment occurs ideally prior to initiation of the drug. In the setting of hematolymphoid malignancies, molecular profiling panels also help with predicting prognosis.

Examples of FDA approved companion diagnostic tests for use include (but are not limited to) the following:

- FoundationOne® CDx
- Praxis™ Extended RAS Panel
- Oncomine™ Dx Target Test

An up-to-date listing of FDA Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools) can be found here: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools

Examples of other commercial molecular profiling panels that are not necessarily FDA approved as companion diagnostic tests but are performed at CLIA-certified laboratories include (but are not limited to) the following:

- Caris Life Sciences MI Profile™
- Aurora Diagnostics Auraseq-Solid Tumor
- Tempus│X

POLICY
Molecular Profiling (Somatic Testing) Panels require prior authorization for all product lines (81445, 81450, 81455, 81479, 0022U, 0037U).

Somatic Mutation Testing Panels through Foundation Medicine are non-covered for Advantage.

If the servicing laboratory selects to use multiple CPT codes (i.e. unbundled or stacked version) for billing purposes, and the medical necessity criteria are met below for a panel, the laboratory will be strongly encouraged to use an applicable panel CPT code.
HMO, PPO, Individual Marketplace, Advantage
Genomic profiling (somatic testing) of a solid tumor is considered medically necessary only for non-small cell cancer, breast cancer, ovarian cancer, colorectal cancer, and melanoma when the following criteria are met:

1. The test is performed in a CLIA-certified laboratory and is ordered by a treating physician

2. Patient has:
   a. either recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer; and
   b. either not been previously tested using the same test for the same primary diagnosis of cancer or repeat testing using the same test only when a new primary cancer diagnosis is made by the treating physician; and
   c. decided to seek further cancer treatment (e.g., therapeutic chemotherapy).

3. The diagnostic laboratory test must have results provided to the treating physician for management of the patient using a report template to specify treatment options.

Elite
Genomic profiling (somatic testing) of an advanced cancer is considered medically necessary when the following criteria are met:

1. The test is performed in a CLIA-certified laboratory and is ordered by a treating physician

2. Patient has:
   i. either recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer; and
   ii. either not been previously tested using the same test for the same primary diagnosis of cancer or repeat testing using the same test only when a new primary cancer diagnosis is made by the treating physician; and
   iii. decided to seek further cancer treatment (e.g., therapeutic chemotherapy).

3. The diagnostic laboratory test must have:
   i. FDA approval or clearance as a companion in vitro diagnostic; and
   ii. an FDA approved or cleared indication for use in that patient's cancer; and
   iii. results provided to the treating physician for management of the patient using a report template to specify treatment options.

HMO, PPO, Individual Marketplace, Advantage, Elite
InvisionFirst™ - Lung (Inivata, Research Triangle Park, NC) (hereafter InVision)
InvisionFirst™ is a plasma-based, somatic comprehensive genomic profiling test (CGP) for patients with advanced (Stage IIIIB/IV) non-small cell lung cancer (NSCLC). This test is considered medically necessary when one of the following criteria are met:

- At diagnosis-
  o When results for EGFR single nucleotide variants (SNVs) and insertions and deletions (indels); rearrangements in ALK and ROS1; and SNVs for BRAF are not available AND when tissue-based CGP is infeasible [i.e., quantity not sufficient (QNS) for tissue-based CGP or invasive biopsy is medically contraindicated].

or

- At progression-
  o For patients progressing on or after chemotherapy or immunotherapy who have not been tested for EGFR SNVs and indels; rearrangements in ALK and ROS1; and SNVs for BRAF, and for whom tissue-based CGP is infeasible;

or

  o For patients progressing on EGFR tyrosine kinase inhibitors (TKIs).

If no genetic alteration is detected by InVision or if circulating tumor DNA (ctDNA) is insufficient/not detected, tissue-based genotyping should be considered.
Guardant360® (Guardant Health, Redwood City, CA) is a plasma-based comprehensive somatic genomic profiling test (hereafter called CGP) for patients with Stage IIIB/IV non-small cell lung cancer (NSCLC). This test is considered medical necessary when one of the following criteria are met:

- **At diagnosis** – Untreated Patient
  - When results for EGFR single nucleotide variants (SNVs) and (insertions and deletions (indels); rearrangements in ALK and ROS1; and SNVs for BRAF are not available AND when tissue-based CGP is infeasible (i.e., quantity not sufficient for tissue-based CGP or invasive biopsy is medically contraindicated),

- **OR**

- **At progression** - Treated Patient
  - For patients progressing on or after chemotherapy or immunotherapy who have never been tested for EGFR SNVs and indels; rearrangements in ALK and ROS1; and SNVs for BRAF, and for whom tissue-based CGP is infeasible (i.e., quantity not sufficient for tissue-based CGP from original biopsy); OR
  - For patients progressing on any tyrosine kinase inhibitors (TKIs).

If no genetic alteration is detected by Guardant360, or if circulating tumor DNA (ctDNA) is insufficient/not detected, tissue-based genotyping should be considered.

**HMO, PPO, Individual Marketplace, Advantage, Elite**

Genomic profiling (somatic testing) as an evaluation for Acute Myeloid Leukemia (AML) is considered medically necessary when the following criteria are met:

- The test is performed by a CLIA-certified laboratory and is ordered by a treating physician
- The test must include KIT, FLT3 (ITD and TKD), NPM1, CEBPA, IDH1, IDH2, and TP53.
- The member has not been previously tested using the same NGS panel
- The member has decided to seek further cancer treatment (e.g., therapeutic chemotherapy).

**Advantage**

Per the Ohio Department of Medicaid, Providers can request prior authorization to exceed coverage or benefit limits for members under age 21.

**CODING/BILLING INFORMATION**

The appearance of a code in this section does not necessarily indicate coverage. Codes that are covered may have selection criteria that must be met. Payment for supplies may be included in payment for other services rendered.

<table>
<thead>
<tr>
<th>CPT CODES</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81455</td>
<td>Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (e.g., ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFR, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed</td>
</tr>
<tr>
<td>81450</td>
<td>Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA analysis and RNA analysis when performed, 5-50 genes (e.g., BRAF, CEBPA, DNMT3A, EZHA, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed</td>
</tr>
<tr>
<td>81455</td>
<td>Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (e.g., ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFR, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed</td>
</tr>
<tr>
<td>81479</td>
<td>Unlisted molecular pathology procedure</td>
</tr>
<tr>
<td>0022U</td>
<td>Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence/absence of variants and associated therapy(ies) to consider</td>
</tr>
<tr>
<td>0037U</td>
<td>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</td>
</tr>
</tbody>
</table>

**TAWG REVIEW DATES:** 05/24/2018, 09/27/2018

**REVISION HISTORY EXPLANATION**
Effective 03/16/18 Next Generation Sequencing (NGS) tests for advanced cancer [i.e., FoundationOne CDx™ (F1CDx) [0037U], Oncomine™ Dx Target Test (81455)] may be covered with prior authorization for Elite per CMS guidelines. Next Generation Sequencing (NGS) tests for advanced cancer are non-covered for HMO, PPO, Individual Marketplace & Advantage. Policy created to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

09/27/18: Added code 0022U as covered with prior authorization for Elite per CMS guidelines and non-covered for HMO, PPO, Individual Marketplace & Advantage. Code 81445 should be billed for Oncomine™ Dx Target Test for DOS 06/22/2017-09/30/2017. Code 0022U should be billed for Oncomine™ Dx Target Test for DOS after 10/01/2017. Policy created to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

8/14/19: Policy name changed/updated from NGS for Advanced Cancer to Molecular Profiling (Somatic Testing) Panels for Cancer. Policy reviewed and updated to reflect the most current clinical evidence per National Comprehensive Cancer Network®. Molecular profiling for advanced colorectal, breast, ovarian, melanoma, and non-small cell cancer when criteria are met is now covered for HMO, PPO, Individual Marketplace and Advantage. Criteria were added for InvisionFirst™, Guardant360®, and molecular profiling related to AML.

REFERENCES/RESOURCES
Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services
Ohio Department of Medicaid http://jfs.ohio.gov/
American Medical Association, Current Procedural Terminology (CPT®) and associated publications and services
Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets
Industry Standard Review
Hayes, Inc.
U.S. Food & Drug Administration, List of Cleared or Approved Diagnostic Devices (In Vitro and Imaging Tools)