Tumor-Type Agnostic Solid Tumor Molecular Profiling Panels

I. Tumor-type agnostic solid tumor molecular profiling panels are considered **medically necessary** when:

A. The member meets both of the following:

1. The member has a diagnosis of:

a) Recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer, **OR**

b) Histiocytosis, **OR**

c) Non-small cell lung cancer (NSCLC) regardless of stage, **OR**

d) Resectable or borderline resectable pancreatic adenocarcinoma, **OR**

e) Central nervous system tumor, **OR**

f) Resectable colon cancer, **AND**

2. The member is seeking further cancer treatment (e.g., therapeutic chemotherapy), **OR**

B. The member meets one of the following:

1. The member is being evaluated for a suspected metastatic malignancy of unknown type, **OR**

2. The member is undergoing initial evaluation for a known or suspected gastric cancer, **OR**

3. The member has a diagnosis of uterine neoplasm, **AND**

a) The member is undergoing initial evaluation, **OR**

4. The member is undergoing initial evaluation for a known or suspected gastrointestinal stromal tumor (GIST), **AND**

a) The tumor is negative for *KIT* and *PDGFRA* mutations.

II. Repeat testing via a tumor-type agnostic solid tumor molecular profiling panel is considered **medically necessary** when:

A. The member has progression of:

1. Advanced or metastatic non-small cell lung cancer (NSCLC), **OR**
2. Advanced or metastatic gastric adenocarcinoma, **OR**
3. Metastatic prostate cancer, **OR**
4. Metastatic colorectal cancer.

III. Tumor-type agnostic solid tumor molecular profiling panels are considered **investigational** for all other indications.

NOTE: Additional codes representing additional IHC and/or cytogenetics analyses may be billed alongside the PLA or GSP codes.

RATIONALE AND REFERENCES

Tumor-Type Agnostic Solid Tumor Molecular Profiling Panels

National Comprehensive Cancer Network (NCCN): Breast Cancer (4.2025)

This guideline recommends comprehensive somatic testing to aid in clinical management of patients with recurrent/stage IV breast cancer (p. BINV-18).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer 4.2025 https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

National Comprehensive Cancer Network (NCCN): Occult Primary (2.2025)

This guideline recommends tumor mutation burden (TMB), MSI and MMR testing as part of the initial work up for patients with cancer of unknown primary. The guideline further recommends consideration of somatic tumor profiling to identify actionable genomic aberrations after a histological determination of the tumor has been made (p. OCC-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Occult Primary 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/occult.pdf

National Comprehensive Cancer Network (NCCN): Non-Small Cell Lung Cancer (7.2025)

This guideline has several recommendations regarding biomarker testing:

- Broad molecular profiling is recommended to be performed for stage IV / advanced or metastatic adenocarcinoma, large cell, or NSCLC not otherwise specified. NCCN also recommends consideration of broad molecular profiling for advanced or metastatic squamous cell carcinoma of the lung (p. NSCL-14, NSCL-15, NSCL-19).
- Generally, it is recommended that broad, panel-based genomic profiling be performed via NGS when feasible. NCCN defines broad molecular profiling as a panel which includes all the following biomarkers in either one assay or several smaller assays: *EGFR, ALK, KRAS, ROS1, BRAF, NTRK1/2/3*, *MET*ex14 skipping, *RET, ERBB2 (HER2),* and *PD-L1* (p. NSCL-19 and NSCL-H 1 and 2 of 8).
- Repeat somatic genetic testing can be helpful to aid in deciding next therapeutic steps when a patient's tumor shows evidence of progression on targeted therapy. Broad genomic profiling may be the best testing method to ensure all possible therapeutic biomarkers are analyzed (p. NSCL-H 7 of 8).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer 7.2025 https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

National Comprehensive Cancer Network (NCCN): Colon Cancer (4.2025)

This guideline recommends all patients with metastatic colorectal cancer have molecular testing which should be done, if possible, via a broad NGS panel to identify rare and actionable alterations including fusions (p. COL-2, COL-B 4 of 10). Testing can be performed on the primary tumor and/or metastases (p. COL-B 4 of 10). Repeat testing can be considered by clinicians to guide future therapy decisions (p. COL-B 4 of 10).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Colon Cancer 4.2025 https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf

National Comprehensive Cancer Network (NCCN): Gastric Cancer (2.2025)

This guideline recommends consideration of NGS testing during the workup for gastric cancer (p. GAST-1). NGS testing can be considered in place of sequential testing for individual biomarkers if there is limited tissue or traditional biopsy cannot be done in patients with inoperable locally advanced, recurrent or metastatic adenocarcinoma of the stomach considering an FDA approved therapy (p. GAST-B 6 of 7). The guidelines also recommend that repeat tumor testing can be considered when there is clinical or radiologic evidence for disease progression of advanced gastric cancer (p. GAST-B, 3 of 7).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Gastric Cancer 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf

National Comprehensive Cancer Network (NCCN): Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer (3.2025)

This guideline recommends that patients with recurrent disease undergo comprehensive tumor molecular analysis to identify alterations that would be amenable to targeted therapeutics that have tumor specific or tumor-agnostic benefit (p. OV-6). These guidelines also recommend that molecular testing be performed on the most recent tumor tissue available (p. OV-B, 1 of 3).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer 3.2025 https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf

National Comprehensive Cancer Network (NCCN): Pancreatic Adenocarcinoma (2.2025)

This guideline recommends tumor/somatic molecular profiling to identify targetable alterations for patients with locally advanced or metastatic disease and recommends consideration of this testing for patients with resectable or borderline resectable disease who are candidates for systemic therapy. Testing can include but is not limited to fusions (*ALK, NRG1, NTRK, ROS1, FGFR2, RET*), mutations (*BRAF, BRCA1/2*, *KRAS*,

PALB2), amplifications (*HER2*), MSI, tumor mutational burden and mismatch repair deficiency (p. PANC-1A, PANC-F, 1 of 13).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf

National Comprehensive Cancer Network (NCCN): Prostate Cancer (2.2025)

This guideline recommends consideration of somatic multigene tumor testing to identify alterations in HRR genes in addition to MSI and TMB testing for patients with metastatic prostate cancer. NCCN recommends consideration of this testing in patients with regional prostate cancer. This guideline also recommends that repeat tumor profiles can be considered at the time of progression of disease (p. PROS-C, 2 of 2).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf

National Comprehensive Cancer Network (NCCN): Histiocytic Neoplasms (1.2025)

This guideline recommends molecular mutation profiling in the work-up/evaluation of Langerhans Cell Histiocytosis (LCH), Erdheim-Chester Disease (ECD) and Rosai-Dorfman Disease (RDD) for prognostic and treatment information (p. HIST-C, 1 of 5).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Histiocytic Neoplasms 1.2025
https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf

National Comprehensive Cancer Network (NCCN): Uterine Neoplasms (3.2025)

This guideline recommends comprehensive molecular profiling in the initial evaluation of uterine neoplasms, including uterine sarcoma (p. UTSARC-A1 of 8). This can be done on the initial biopsy or the hysterectomy specimen (p. ENDO-A 2 of 4).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms 3.2025 https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf

National Comprehensive Cancer Network (NCCN): Ampullary Adenocarcinoma (2.2025)

This guideline recommends somatic molecular profiling to identify uncommon and potentially actionable mutations including fusions, amplifications, MSI, dMMR, and TMB for patients with locally advanced or metastatic disease who are candidates for systemic therapy (p. AMP-6).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Ampullary Adenocarcinoma 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/ampullary.pdf

National Comprehensive Cancer Network (NCCN): Gastrointestinal Stromal Tumors (1.2025)

This guideline recommends molecular testing for a suspected or confirmed gastrointestinal stromal tumor when systemic therapy is being considered (p. GIST-1). If testing does not show a KIT or PDGFRA mutation, NGS testing is recommended to look for alternative driver mutations that will identify targeted therapy options (p. GIST-B).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Gastrointestinal Stromal Tumors (GIST) 1.2025
https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf

National Comprehensive Cancer Network (NCCN): Central Nervous System Cancers (1.2025)

This guideline recommends next-generation sequencing in the pathologic workup of CNS tumors, since there are now multiple prognostic and diagnostic biomarkers that should be tested to aid in treatment decisions (p. BRAIN-E 2 of 9).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Central Nervous System Cancers 1.2025 https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf

National Comprehensive Cancer Network (NCCN): Rectal Cancer (2.2025)

This guideline states that repeat molecular testing can be considered by clinicians to guide future therapy decisions (p. REC-B 5 of 11).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Rectal Cancer 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf

Food and Drug Administration (FDA)

The FoundationOne CDx test has been approved by the FDA as a companion diagnostic test for several therapies, including some that are indicated for early stage non-small cell lung cancer diagnoses.

U.S. Food and Drug Administration. FoundationOne CDx: device labeling. PMA No. P170019. Published November 30, 2017. https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170019C.pdf

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).