FoundationOne CDx

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan’s procedure code list for management requirements.

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What are somatic mutation tests

Definition

Somatic mutation tests are broadly defined here as any test that measures changes in DNA, RNA, or chromosomes found in tumor tissue that is used to make cancer management decisions.

- Somatic mutation tests are increasingly useful for therapy selection. Many cancer therapies are targeted at particular gene functions (therapeutic targets) and some require information about tumor genetics to use the therapies effectively (companion diagnostics). In these cases, NCCN as well as the FDA have outlined tumor testing that is recommended for specific cancers and the associated treatment implications.¹⁻⁵

Test information

- A variety of complex testing methodologies, combined with clinical information and patient preferences, are increasingly being used to inform clinical decision making among cancer patients with malignant solid tumors. One such test methodology is next-generation sequencing (NGS), frequently offered in the context of large gene panels that allow for the rapid and accurate sequencing of multiple genes at once. NGS is more frequently being used by oncologists in clinical practice to identify clinically actionable mutations that could be targeted by one or more appropriate cancer therapies. Concurrently, significant advancements in drug development have led to the introduction of specialty pharmaceuticals designed to target tumor-associated mutations identifiable by NGS. However, the extent to which the use of NGS in clinical practice, compared with routine methods (histopathology) or alternative commercial NGS tests, improves patient-important clinical outcomes is still unclear.⁶⁻⁷
• According to Foundation Medicine, the test manufacturer, FoundationOne CDx™ (F1CDx) is an in vitro diagnostic device that uses next generation sequencing (NGS) to detect substitutions, insertions, deletion alterations, and copy number alterations (CNAs) in 324 genes and select gene rearrangements. In addition to genomic signatures, the test also detects microsatellite instability (MSI) and tumor mutational burden (TMB) to inform treatment decisions about immunotherapies.\(^8\)

• The biomarker TMB is assessed by measuring the number of somatic mutations in genes sequenced in F1CDx and extrapolating to the whole genome. F1CDx is designed to include all somatically altered genes in human solid tumors that are validated targets for therapy, “either FDA approved or in clinical trials, and/or that are unambiguous drivers of oncogenesis based on current knowledge.”\(^8\)

• The manufacturer states that customized software and algorithms determine these genomic variants. Using a single DNA extraction method, patient DNA is extracted and isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. The F1CDx platform uses a whole-genome shotgun library construction and hybridization-based capture of DNA extracted from tumor tissue before sequencing. Custom software is then used to determine genomic variants.

• The F1CDx report provides the following information:\(^9\)
  
  o A listing of all alterations in tested genes that are known or likely to be cancer driver alterations and genomic signatures, some of which may also be associated with companion diagnostic information.
  
  o When indicated, the F1CDx report will include FDA-approved therapeutic options that may be considered based on detected alterations and tumor types for which F1CDx is approved as a companion diagnostic.
  
  o If an identified genomic alteration or genomic signature may be associated with treatment resistance, the F1CDx report will include a note notifying of potential resistance.
  
  o If no genomic alteration or genomic signatures associated with companion diagnostic–relevant information are identified, the F1CDx report will note that there are no reportable alterations with companion diagnostic claims.
  
  o The professional services section of the F1CDx report provides a list of potential clinical trials and investigational options to consider for identified genomic alterations or genomic signatures. Rationale, targets, and location of potential clinical trials are described in detail.

Guidelines and evidence

• The National Comprehensive Cancer Network (NCCN) provides the following guidance:
  
  o NCCN Guidelines for Treatment of Cancer by Site provide detailed guidelines on the use of individual tumor markers for each cancer type addressed.\(^5\)
NCCN also makes the following recommendations specifically for using multi-gene panels in the evaluation of non-small cell lung cancer (NSCLC): “The NCCN NSCLC Guidelines Panel strongly advises broader molecular profiling with the goal of identifying rare driver mutations for which effective drugs may already be available, or to appropriately counsel patients regarding the availability of clinical trials. Broad molecular profiling is a key component of the improvement of care of patients with NSCLC.”

NCCN also maintains a biomarker compendium stating “the goal of the NCCN Biomarkers Compendium is to provide essential details for those tests which have been approved by NCCN Guideline Panels and are recommended by the NCCN Guidelines.” Biomarkers for specific cancer types that are listed in the NCCN Biomarker Compendium have a level of evidence associated with their clinical utility.

The National Academy of Clinical Biochemistry (NACB, 2009) issued general tumor marker quality practice guidelines “to encourage more appropriate use of tumor marker tests.” They provide the following guidelines to determine if a tumor marker is useful:

- The marker results are appropriate precisely for the required application (i.e., risk assessment, screening, diagnosis, prognosis, prediction, or post-treatment monitoring)."
- “The marker results separate patients into two or more populations whose outcomes differ so strikingly that they and their caregiver would treat one group differently than another.”
- “The estimate of the separation in outcomes for marker positive and negative is reliable.”

On November 30, 2017, the FDA approved FoundationOne CDx panel testing as a companion diagnostic test for use in 5 disease indications 1) non-small cell lung cancer (NSCLC), 2) colorectal cancer (CRC), 3) melanoma, 4) breast cancer, and 5) ovarian cancer. Results of the F1CDx may help to inform disease management in accordance with approved drug labeling and clinical practice guidelines for particular individuals with NSCLC, melanoma, breast cancer, colorectal cancer, or ovarian cancer. See FDA document here.

Criteria

- No previous panel testing performed on the member’s tumor, AND
- Testing is being requested in order to effectively and safely prescribe a treatment or medication per an FDA label, AND
- The member has one of the following cancer types:
  - Non-small cell lung cancer, or
- Metastatic or unresectable melanoma, or
- Metastatic breast cancer, or
- Metastatic colorectal cancer, or
- Advanced ovarian cancer, or

- At least 5 tumor markers included in the panel individually meet criteria for the member’s tumor type based on one of the following:
  - All criteria are met from a test-specific guideline if one is available, or
  - An oncology therapy FDA label requires results from the tumor marker test to effectively or safely use the therapy for the member’s cancer type, or
  - NCCN guidelines include the tumor marker test in the management algorithm for that particular cancer type and all other requirements are met (specific pathology findings, staging, etc.); however, the tumor marker must be explicitly included in the guidelines and not simply included in a footnote as an intervention that “may be considered”, or
  - The NCCN Biomarker Compendium has a level of evidence of at least 2A for the tumor marker’s application to the member’s specific cancer type

**Note** This guideline addresses molecular markers only. It is intended to address those markers that are detected by next generation sequencing technology and those that are present on NGS panels. It does not address microsatellite instability (MSI), immunohistochemistry (IHC), or other markers that may be detected through other methods such as FISH, chromosomal microarray, routine chromosome analysis, etc.

**Billing and reimbursement**

This panel will only be considered for reimbursement when billed with an appropriate panel CPT code.

**References**


3. US Food and Drug Administration. Table of Pharmacogenomic Biomarkers in Drug Labeling. Available at: [http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm](http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm)


9. FoundationOne. FoundationONe CDxTM Technical Information. 2019. Available at: https://assets.ctfassets.net/vhrivb12lmne/6Rt6csmCPuaguuqmgi2YiY8/629ba4e5c7d9a3bd1f1f666085e1e4b1/FoundationOne_CDx_Label_Technical_Info.pdf

10. FoundationOne. CDx Sample Report. 2018. Available at: https://assets.ctfassets.net/vhrivb12lmne/P1UbtVjOoeAcaOCWoWQkW/613003bb4a62d6f06ab10b6e8367f92/FoundationOne_CDx_Sample_Report.pdf


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