Approved Revised: Do Not Implement Until 7/31/26

Circulating Tumor DNA (Liquid Biopsy)

DESCRIPTION

Liquid biopsy (e.g., FoundationOne® Liquid CDx, Guardant360® CDx) refers to the analysis of circulating tumor DNA (ctDNA) or circulating tumor cells (CTCs) as a method of noninvasively characterizing tumors and tumor genome from the peripheral blood. This method may be used to test for single genes or multiple genes using a panel.

Both malignant and nonmalignant cells release small fragments of DNA into the blood, which is referred to as cell-free DNA. Most cell-free tumor DNA is derived from apoptotic and/or necrotic tumor cells, either from the primary tumor or metastases. Analysis of circulating tumor DNA allows multiple samples of blood to be analyzed over time to monitor the molecular changes taking place in a tumor and possibly determining sensitivity to certain treatments.

Signatera™ is a personalized, tumor-informed circulating tumor DNA assay designed to detect molecular residual disease following treatment in individuals with cancer. The test uses prior sequencing of an individual's tumor to identify individualized tumor-specific variants and monitors plasma samples for these variants over time. Signatera™ is offered as a laboratory-developed test; FDA review for a companion diagnostic indication is ongoing.

POLICY

- Circulating tumor DNA (liquid biopsy) companion diagnostic assays are considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**

- Tumor-informed circulating tumor DNA (ctDNA) testing using Signatera™ is considered ***investigational*** for all indications.

MEDICAL APPROPRIATENESS

- Circulating tumor DNA (liquid biopsy) companion diagnostic assays to guide in prescribing certain medications is considered **medically appropriate** when **ALL** of the following are met:

    - Diagnosis of advanced or metastatic cancer (solid tumors)
    - Treatment with a medication in which there is a liquid biopsy-based FDA- approved (e.g., FoundationOne Liquid CDx®, Guardant360® CDx) companion diagnostic being considered
    - FDA label for the drug and indication being considered states companion diagnostic testing is necessary
    - Individuals have not had previous somatic tumor testing to identify genetic changes required to prescribe medication

IMPORTANT REMINDERS

- Any specific products referenced in this policy are just examples and are intended for illustrative purposes only. It is not intended to be a recommendation of one product over another and is not intended to represent a complete listing of all products available. These examples are contained in the parenthetical e.g., statement.
- We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a member is entitled to receive under his or her health plan, the Member's

health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

ADDITIONAL INFORMATION

For guidance on testing criteria, refer to the FDA's List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools) (https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools) for an updated list of FDA-approved tumor markers.

SOURCES

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EFFECTIVE DATE 7/31/2026

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