Health Plans

Manual: IU Health Plans
Department: Utilization Management
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Medicare Advantage X Commercial

Detection of Circulating Tumor Cells Testing Policy

I. Purpose

Indiana University Health Plans (IU Health Plans) considers clinical indications when making a medical necessity determination for the Detection of Circulating Tumor Cells Testing

II. Scope

This policy applies to all IU Health Plans and Utilization Management staff having decision-making responsibilities where authorization is required for Fully Insured commercial plan.

III. Exceptions

1. Duplicate testing for the same biomarker (from the same type of sample and same clinical indication) using different methodologies is not covered.
2. Testing for circulating tumor cells is considered experimental and investigational in circumstances not specified in the policy section.

IV. Definitions

Biomarker: The state of Indiana defines biomarker as a characteristic that is objectively measured and evaluated as an indicator of:

1. Normal biological processes
2. Pathogenic processes; or
3. Pharmacologic responses to a specific therapeutic intervention, including known gene-drug interactions for medications being considered for use or already being administered.

The term includes gene mutations, characteristics of genes, and protein expression.

Biomarker Testing: The state of Indiana defines Biomarker Testing as the analysis of a patient's tissue, blood, or other biospecimen for the presence of a biomarker.
The term includes:

1. single-analyte tests;
2. multiplex panel tests;
3. protein expression; and
4. whole exome, whole genome, and whole transcriptome sequencing.

Circulating Tumor Cells (CTCs) are malignant cells found in peripheral blood originating from primary or metastatic tumors. Detections of CTCs has been associated with prognosis or response to

treatment in individuals with certain types of cancer breast, colorectal, and prostate). However evidence is insufficient to demonstrate that clinical decisions based on CTC levels improves the quality or duration of life or decreases adverse events.

Examples of Circulating Tumor Cell tests include but are not limited to:

The Cell Search System (Janssen Diagnostics)
FirstSight ^{CRC}
CellMax Life
CellSearch Circulating Multiple Myeloma Cell (CMMC) Test (Menarini Silicon Biosystems)
Cell Search HER2 Circulating Tumor Cell Test (Menarini Silicon Biosystems)

Liquid Biopsy is a term used for Circulating Tumor Cell (CTC) and Circulating Tumor DNA Testing due to the fact the it is a blood test.

Nationally Recognized Clinical Practice Guidelines: Nationally recognized clinical practice guidelines means evidence based clinical practice guidelines that were:

1. Developed by an independent organization or medical professional society with:
    a. transparent methodology and reporting structure
    b. conflict of interest policy.
2. Established standards of care informed by:
    a. Systemic review of evidence
    b. Assessment of benefit versus risk of alternative care options
3. Include recommendations intended to optimize patient care.

V. State of Indiana Biomarker Guidance

Indiana University Health Plans prioritizes following regulatory guidance in determining medical necessity and coverage of medical care**. For a test to be approved it must meet ALL of the supporting criteria.**

The state of Indiana has provided for coverage of biomarker testing under Indiana Code 27-8-14.3-10. (*As added by P.L.37-2024, SEC.2.*):

Sec. 10. (a) A health plan shall provide coverage for biomarker testing for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of an enrollee's disease or condition when biomarker testing is supported by medical and scientific evidence, including:

(1) labeled indications for a test approved or cleared by the United States Food and Drug Administration;
(2) indicated tests for a drug approved by the United States Food and Drug Administration;
(3) a warning or precaution on the label of a drug approved by the United States Food and Drug Administration;
(4) a national coverage determination of the Centers for Medicare and Medicaid Services (CMS);
(5) a local coverage determination of a Medicare administrative contractor; or
(6) nationally recognized clinical practice guidelines or consensus statements.

(b) The coverage required by this section must be provided in a manner that limits disruptions in care, including the need for multiple biopsies or biospecimen samples.

(c) Nothing in this section shall be construed to require coverage of biomarker testing for screening purposes.

(d) If a prior authorization requirement applies to biomarker testing under a health plan, the health plan or a third party acting on behalf of the health plan must:

(1) approve or deny a request for prior authorization for biomarker testing; and

(2) notify the covered individual and any person requesting prior authorization of the biomarker testing on behalf of the covered individual; in not more than five (5) business days after the request in the case of a nonurgent request or in not more than forty-eight (48) hours after the request in the case of an urgent request.

(e) A health plan shall ensure that a covered individual and the practitioner who prescribes biomarker testing for the covered individual have access to a clear, readily accessible, and convenient process for requesting an exception to:

(1) a coverage policy; or

(2) a prior authorization determination;

of the health plan that is adverse to the coverage of biomarker testing for the covered individual. The process required by this subsection shall be made readily accessible on the health plan's website.

VI. Policy Statements

IU Health Plans considers the detection of circulating tumor cells (CTC) in the blood as investigational and not medically necessary in the management of individuals with cancer EXCEPT for the following situations where there is clear documentation in the medical record of ONE of the following:

1. HER2 tumor marker cancers where all of the following are met:
   a. Tissue based testing (quantity insufficient or invasive biopsy -example brain lesions) is contra-indicated on cancers not previously tested
   b. Testing for the biomarker can be done using circulating tumor cells
2. Androgen Receptor AR-V7 in Metastatic castration resistant prostate cancer (mCRPC) with progression on abiraterone or enzalutamide.
3. Next Generation Sequencing of Tumor DNA (ClonoSEQ, ClonoSIGHT) is considered medically necessary to detect or quantify Measurable (Minimal) Residual Disease (MRD) for ONE of the following conditions:
   a. Acute Lymphocytic Leukemia
   b. Multiple Myeloma following transplant

Codes:

Code	Description
0091U	Oncology (colorectal screening, cell enumeration of CTC utilizing whole blood algorithm, for the presence of adenoma or cancer. Reported as a positive or negative result -FirstSight ^{CRC} , Cell Max Life
81479	Oncology circulating plasma cell immunologic selection, identification, morphological characterization, and enumeration of plasma cells, peripheral blood, CELLSEARCH CMMC Test
81479	Oncology circulating plasma cell immunologic selection, identification, morphological characterization, and enumeration of plasma cells, peripheral blood, CELLSEARC CTC-HER2 Test

81479	Unlisted genetic testing code- This is used for AR-V7 testing
86152	Cell enumeration using immunologic selection and identification in fluid specimen (eg circulating tumor cells in the blood)
86153	Cell enumeration using immunologic selection and identification in fluid specimen (eg circulating tumor cells in the blood); physician interpretation and report when required

VII. Procedures

None

VIII. References/Citations

1. Bidard, F. C., Jacot, W., Kiavue, N., Dureau, S., Kadi, A., Brain, E., Bachelot, T., Bourgeois, H., Gonçalves, A., Ladoire, S., Naman, H., Dalenc, F., Gligorov, J., Espié, M., Emile, G., Ferrero, J. M., Loirat, D., Frank, S., Cabel, L., Diéras, V., … Pierga, J. Y. (2021). Efficacy of Circulating Tumor Cell Count-Driven vs Clinician-Driven First-line Therapy Choice in Hormone Receptor-Positive, ERBB2-Negative Metastatic Breast Cancer: The STIC CTC Randomized Clinical Trial. *JAMA oncology*, *7*(1), 34–41. https://doi.org/10.1001/jamaoncol.2020.5660
2. Center for Medicare and Medicaid Services. Local Coverage Determination (LCD Reference Article) Billing and Coding Article. Billing and Coding: MolDx: Phenotypic Biomarker Detection from Circulating Tumor Cells. A58205. Contractor: Wisconsin Physician Service Insurance Corporation. Revision Effective Date 5/26/2022. Article - Billing and Coding: MolDX: Phenotypic Biomarker Detection from Circulating Tumor Cells (A58205) (cms.gov)
3. Center for Medicare and Medicaid Services. Local Coverage Determination (LCD) MolDx: Phenotypic Biomarker Detection from Circulating Tumor Cells. L38678. Contractor: Wisconsin Physician Service Insurance Corporation. Revision Effective Date 5/26/2022. LCD - MolDX: Phenotypic Biomarker Detection from Circulating Tumor Cells (L38678) (cms.gov)
4. National Comprehensive Cancer Network (NCCN). NCCN Guidelines Version 4.2024. Prostate Cancer. prostate.pdf (nccn.org)
5. State of Indiana. Indiana Code for 2024. Title 27; Article8; Chapter 14.3 Coverage for Biomarker Testing. IGA | 2024 Indiana Code
6. Vasseur, A., Kiavue, N., Bidard, F. C., Pierga, J. Y., & Cabel, L. (2021). Clinical utility of circulating tumor cells: an update. *Molecular oncology*, *15*(6), 1647–1666. https://doi.org/10.1002/1878-0261.12869
7. Wang, H., Zhang, Y., Zhang, H., Cao, H., Mao, J., Chen, X., Wang, L., Zhang, N., Luo, P., Xue, J., Qi, X., Dong, X., Liu, G., & Cheng, Q. (2024). Liquid biopsy for human cancer: cancer screening, monitoring, and treatment. *MedComm*, *5*(6), e564. https://doi.org/10.1002/mco2.564

IX. Forms/Appendices

None

X. Responsibility

Medical Director