Clinical Policy: Oncology Circulating Tumor DNA and Circulating Tumor Cells (Liquid Biopsy)

Reference Number: CP.MP.239
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Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Cell-free circulating tumor DNA (ctDNA) originates directly from the tumor tissue (primary or metastasis); as tumor cells die the contents are released into the bloodstream. Genetic tests performed on cell-free circulating tumor DNA (ctDNA), also referred to as a liquid biopsy, potentially offer a noninvasive alternative to tissue biopsy for detection of "driver mutations", or acquired genetic mutations that may guide targeted therapy, and may also be used to track progression of disease.

Circulating tumor cells (CTCs) are intact tumor cells that are shed from tumor cells into the bloodstream or lymphatic system. Most assays detect CTCs through the use of surface epithelial markers such as EpCAM and cytokeratins. The primary reason for detecting CTCs is prognostic rather than for guiding therapeutic choices, through quantification of circulating levels.

CPT® Codes	Example Tests (Labs)	Criteria Section	Common ICD Codes
0239U	FoundationOne® Liquid CDx (Foundation Medicine)	Comprehensive Molecular Profiling Panel Tests via Circulating Tumor DNA (ctDNA)	C15, C16, C25, C34
0242U	Guardant360® CDx (Guardant Health)	Comprehensive Molecular Profiling Panel Tests via Circulating Tumor DNA (ctDNA)	C15, C16, C25, C34
81455	Guardant360® LDT (Guardant Health NeoLAB® Solid Tumor Liquid Biopsy (NeoGenomics Laboratories) Tempus|xF: Liquid Biopsy Panel of 105 Genes (Tempus) PlasmaSELECT 64 (Personal Genome Diagnostics)	Comprehensive Molecular Profiling Panel Tests via Circulating Tumor DNA (ctDNA)	C15, C16, C25, C34

CPT® Codes	Example Tests (Labs)	Criteria Section	Common ICD Codes
0179U	Resolution ctDx Lung™ (Resolution Biosciences, LabCorp, Integrated Oncology)	Lung Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)	C34
81210, 81235, 81275, 81276	OncoBEAM™ Lung2: EGFR, KRAS, BRAF (Sysmex Inostics, Inc)	Lung Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)	C34
81445	Non-Small Cell Lung Cancer Expanded Profile (Biocept) InVisionFirst®-Lung Liquid Biopsy (inivata)	Lung Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)	C34
81210, 81275, 81276, 81311	OncoBEAM™ CRC1: KRAS, NRAS, BRAF, HRAS (Sysmex Inostics, Inc)	Colorectal Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)	C18-C20
81210, 81275, 81276	Colorectal Cancer Profile (Biocept)	Colorectal Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)	C18-C20
81210, 81311	OncoBEAM™ Melanoma1: BRAF, NRAS (Sysmex Inostics, Inc)	Melanoma Focused Panel Tests via Circulating Tumor DNA (ctDNA)	D03, D43
81235	cobas® EGFR Mutation Test v2	EGFR Variant Analysis via ctDNA	C34
81235	OncoBEAM™ Lung1: EGFR (Sysmex Inostics, Inc)	EGFR Variant Analysis via ctDNA	C34
81235	EGFR Exon 18, 19, 20, 21, Mutation Analysis Blood and Cell-Free DNA (Mayo Medical Laboratories)	EGFR Variant Analysis via ctDNA	C34
81235	Cell-Free DNA EGFR T790M Mutation Analysis Blood (Mayo Medical Laboratories)	EGFR Variant Analysis via ctDNA	C34
81235	EGFR T790M Mutation Detection in ctDNA (ARUP Laboratories)	EGFR Variant Analysis via ctDNA	C34

CPT® Codes	Example Tests (Labs)	Criteria Section	Common ICD Codes
81235	EGFR T790M Mutation Detection Blood (University of Washington Medical Center)	EGFR Variant Analysis via ctDNA	C34
81210	Cell-Free DNA BRAF V600 Test (Mayo Medical Laboratories)	BRAF Variant Analysis via ctDNA	C18-C20, C24, C43, C71, C73, C91.4
81210	OncoBEAM™ Melanoma2: BRAF (Sysmex Inostics, Inc)	BRAF Variant Analysis via ctDNA	C18-C20, C24, C43, C71, C73, C91.4
81210	Melanoma Cancer Profile (Biocept	BRAF Variant Analysis via ctDNA	C18-C20, C24, C43, C71, C73, C91.4
81275, 81276	Cell-Free DNA KRAS 12, 13, 61, 146 Blood (Mayo Medical Laboratories)	KRAS Variant Analysis via ctDNA	C18-C20
81311	NeoLAB® NRAS Mutation Analysis - Liquid Biopsy (NeoGenomics Laboratories)	NRAS Variant Analysis via ctDNA	C18-C20
0177U	therascreen® PIK3CA RGQ PCR Kit (QIAGEN)	PIK3CA Variant Analysis via ctDNA	C50
81309	PIK3CA Mutation CDx (NeoGenomics Laboratories)	PIK3CA Variant Analysis via ctDNA	N/A
81479	AR-V7 Prostate Cancer (Johns Hopkins Medical Institutions - Pathology Laboratory OncotypeDx AR-V7 Nucleus Detect (Genomic Health Inc.)	AR-V7 Androgen Receptor Splice Variant Analysis in Circulating Tumor Cells (CTCs)	C61, Z19.2
86152, 86153, S3711	Circulating Tumor Cells (CTC) for Colorectal Cancer by CellSearch (Mayo Medical Laboratories)	Circulating Tumor Cell (CTC) Enumeration Analysis	C00.0-C96.9

CPT® Codes	Example Tests (Labs)	Criteria Section	Common ICD Codes
	Circulating Tumor Cells for Prostate Cancer by CellSearch (Mayo Medical Laboratories) Circulating Tumor Cells (CTC) Count (Biocept)		

This policy document provides criteria for circulating tumor DNA (ctDNA) and circulating tumor cells testing (liquid biopsy). For other oncology-related testing, please refer to:

- ***CP.MP.241 Oncology: Molecular Analysis of Solid Tumors and Hematologic Malignancies*** for criteria related to DNA testing of a solid tumor or a blood cancer.
- ***CP.MP.225 Genetic Testing: Hereditary Cancer Susceptibility Syndromes*** for criteria related to genetic testing to determine if an individual has an inherited cancer susceptibility syndrome.
- ***CP.MP.237 Oncology: Algorithmic Testing*** for criteria related to gene expression profiling and tumor biomarker tests with algorithmic analyses.
- ***CP.MP.238 Oncology: Cancer Screening*** for criteria related to the use of non-invasive fecal, urine, or blood tests for screening for cancer.
- ***CP.MP.222 Genetic Testing: General Approach to Genetic Testing*** for criteria related to circulating tumor DNA or circulating tumor cell testing that is not specifically discussed in this or another non-general policy.

Policy/Criteria

Molecular Profiling Panel Tests Via Circulating Tumor DNA (CTDNA)

Comprehensive Molecular Profiling Panel Tests via Circulating Tumor DNA (ctDNA)

I. It is the policy of health plans affiliated with Centene Corporation® that Comprehensive molecular profiling panel tests via circulating tumor DNA (liquid biopsy) (0239U, 0242U, 81455) is considered **medically necessary** when meeting all of the following:

A. The member/enrollee has a diagnosis of one of the following:

1. Advanced (stage IIIb or higher) or metastatic lung adenocarcinoma,
2. Advanced (stage IIIb or higher) or metastatic large cell lung carcinoma,
3. Advanced (stage IIIb or higher) or metastatic squamous cell lung carcinoma,
4. Advanced (stage IIIb or higher) or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS),
5. Locally advanced / metastatic pancreatic adenocarcinoma,

6. Gastric cancer,
7. Esophageal or Esophagogastric Junction cancer,
8. Metastatic prostate cancer,

B. The member/enrollee is a candidate for an anti-cancer therapy,

C. At least one of the following:

1. The member/enrollee is medically unfit for invasive tissue sampling (biopsy),
2. The member/enrollee does not have a biopsy-amenable lesion.

II. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support comprehensive molecular profiling panel tests via circulating tumor DNA (liquid biopsy) (0239U, 0242U, 81455) for all other indications.

III. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support comprehensive molecular profiling panel tests via circulating tumor DNA (liquid biopsy) (0239U, 0242U, 81455) performed simultaneously with, or subsequent to, solid tumor tissue testing.

Lung Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)

I. It is the policy of health plans affiliated with Centene Corporation® that lung cancer focused panel tests via circulating tumor DNA (ctDNA) (0179U, 81210, 81235, 81276) are considered **medically necessary** when meeting all of the following:

A. The member/enrollee has a diagnosis of any of the following:

1. Advanced (stage IIIb or higher) or metastatic lung adenocarcinoma,
2. Advanced (stage IIIb or higher) or metastatic large cell lung carcinoma,
3. Advanced (stage IIIb or higher) or metastatic squamous cell lung carcinoma,
4. Advanced (stage IIIb or higher) or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS),

B. The member/enrollee is a candidate for an anti-cancer therapy,

C. At least one of the following:

1. The member/enrollee is medically unfit for invasive tissue sampling (biopsy),
2. The member/enrollee does not have a biopsy-amenable lesion.

II. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support lung cancer focused panel tests via circulating tumor DNA (ctDNA) for all other indications.

Colorectal Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)

I. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support colorectal cancer focused panel tests via circulating tumor DNA (ctDNA) (81210, 81275, 81276, 81311).

Melanoma Focused Panel Tests via Circulating Tumor DNA (ctDNA)

I. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support melanoma focused panel tests via circulating tumor DNA (ctDNA) (81210, 81311).

Single Gene Molecular Profiling Panel Tests Via Circulating Tumor Dna (CtDNA)

EGFR Variant Analysis via ctDNA

I. It is the policy of health plans affiliated with Centene Corporation® that *EGFR* variant analysis (81235) via cell-free circulating tumor DNA (ctDNA) is considered **medically necessary** when meeting all of the following:

   A. The member/enrollee has a diagnosis of any of the following:

      1. Advanced (stage IIIb or higher) or metastatic lung adenocarcinoma,
      2. Advanced (stage IIIb or higher) or metastatic large cell lung carcinoma,
      3. Advanced (stage IIIb or higher) or metastatic squamous cell lung carcinoma,
      4. Advanced (stage IIIb or higher) or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS),

   B. The testing is being done at time of diagnosis or at the time of progression,

   C. Treatment with an *EGFR* tyrosine kinase inhibitor therapy (eg, erlotinib [Tarceva], gefitinib [Iressa], afatinib [Gilotrif], or osimertinib [Tagrisso]) is being considered,

   D. At least one of the following:

      1. The member/enrollee is medically unfit for invasive tissue sampling (biopsy),
      2. The member/enrollee does not have a biopsy-amenable lesion.

II. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support *EGFR* variant analysis (81235) via cell-free circulating tumor DNA (ctDNA), as a stand alone test, for all other indications.

BRAF Variant Analysis via ctDNA

I. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support *BRAF* variant analysis (81210) via circulating tumor DNA (ctDNA), as a stand alone test.

KRAS Variant Analysis via ctDNA

I. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support *KRAS* variant analysis (81275, 81276) via circulating tumor DNA (ctDNA), as a stand alone test.

NRAS Variant Analysis via ctDNA

I. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support *NRAS* variant analysis (81311) via circulating tumor DNA (ctDNA), as a stand alone test.

PIK3CA Variant Analysis via ctDNA

I. It is the policy of health plans affiliated with Centene Corporation® that *PIK3CA* variant analysis (0177U, 81309) via circulating tumor DNA (ctDNA) is considered **medically necessary** when:

   A. The member/enrollee has recurrent or stage IV hormone receptor-positive/ HER2-negative breast cancer.

II. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support *PIK3CA* variant analysis (0177U, 81309) via circulating tumor DNA (ctDNA), as a stand alone test, for all other indications.

Circulating Tumor Cell Tests

AR-V7 Androgen Receptor Splice Variant Analysis in Circulating Tumor Cells (CTCs)

I. It is the policy of health plans affiliated with Centene Corporation® that *AR-V7* androgen receptor splice variant analysis (81479) in circulating tumor cells (CTCs) is considered **medically necessary** when meeting both of the following:

   A. The member/enrollee has metastatic castration-resistant prostate cancer (M1 CRPC),

   B. The member/enrollee has had a progression after first-line treatment with enzalutamide (Xtandi®) or abiraterone (Zytiga®).

II. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support *AR-V7* androgen receptor splice variant analysis (81479) in circulating tumor cells (CTCs) for all other indications.

Circulating Tumor Cell (CTC) Enumeration

I. It is the policy of health plans affiliated with Centene Corporation® that current evidence does not support circulating tumor cell (CTC) enumeration (86152, 86153).

Notes and Definitions

Cell-free 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.

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.

Cell-free circulating tumor DNA analysis should not be used in lieu of a histologic tissue diagnosis, however there are specific clinical considerations, outlined above, where the use of ctDNA may be considered.

Cell-free circulating tumor DNA analysis should not be performed simultaneously with tissue testing of a solid tumor.

If cell-free circulating tumor DNA analysis is negative, follow-up with tissue-based analysis is recommended.

Background

National Comprehensive Cancer Network (NCCN):

Non-Small Cell Lung Cancer
NCCN guidelines (v.4.2021) support the use of cell-free circulating tumor DNA (ctDNA) testing if a patient is either not medically fit for invasive tissue sampling, or if there is insufficient tissue for molecular analysis. If ctDNA testing is negative, there should be follow-up with tissue-based analysis. NCCN recognizes that studies have shown generally high sensitivity, but a significantly compromised sensitivity with up to 30% false-negative rate and does not support the use of ctDNA testing in lieu of a histologic tissue diagnosis, if it is possible and feasible.

Prostate Cancer
NCCN guidelines (v.1.2022) suggest the consideration of AR-V7 tests to help guide selection of therapy for patients with disease progression in the post-abiraterone/enzalutamide metastatic castration resistant prostate cancer setting.

NCCN guidelines (v.1.2022) strongly advocates evaluating tumor for alterations in homologous recombination DNA repair genes in individuals with metastatic prostate cancer and states that ctDNA assay is an option when biopsy for histologic and molecular evaluation is not possible.

Colorectal Cancer
NCCN guidelines (v.3.2021) state that there is insufficient data to recommend the use of circulating tumor DNA (ctDNA) for patients with colorectal cancer to estimate the risk of recurrence or to determine adjuvant therapy. The NCCN Panel encourages enrollment in clinical trials in order to aide in generation of additional data for these assays.

Melanoma
NCCN guidelines (v.2.2021) do not currently have a recommendation for the use of circulating tumor DNA (ctDNA) for patients with melanoma.

Breast Cancer
NCCN guidelines (v.2.2021) states that PIK3CA mutation testing can be done on tumor tissue or ctDNA in peripheral blood (liquid biopsy) and if liquid biopsy is negative, tumor tissue testing is recommended.
NCCN guidelines (v.2.2021) recognize that patients with metastatic breast cancer and persistently increased CTC after 3 weeks of first-line chemotherapy have a poor PFS and OS; however, while CTC count has prognostic ability, it has failed to show a predictive value at this time.

Gastric Cancer
NCCN guidelines (v.2.2021) recognize the use of liquid biopsy in patients with advanced disease who are unable to have a clinical biopsy for disease surveillance or management, and that the DNA shed from gastric carcinomas can identify targetable alterations or the evolution of clone with altered treatment response profiles. NCCN also cautions the interpretation of negative results, as it does not exclude the presence of tumor mutation or amplifications that are clinically relevant.

Pancreatic Cancer
NCCN guidelines (v.2.2021) state that while testing of tumor tissue is preferred, cell-free DNA testing can be considered if tumor tissue testing is not feasible.

Esophageal or Esophagogastric Junction Cancer
NCCN guidelines (v.2.2021) recognize the use of liquid biopsy in patients with advanced disease who are unable to have a clinical biopsy for disease surveillance or management, and that the DNA shed from esophageal and EGJ carcinomas can identify targetable alterations or the evolution of clone with altered treatment response profiles. NCCN also cautions the interpretation of negative results, as it does not exclude the presence of tumor mutation or amplifications that are clinically relevant.

<u>American Society of Clinical Oncology and College of American Pathologists</u>
The American Society of Clinical Oncology and College of American Pathologists (2018) published a joint review on the use of circulating tumor DNA analysis in patients with cancer, concluding the following:

> "The evidence indicates that testing for ctDNA is optimally performed on plasma collected in cell stabilization or EDTA tubes, with EDTA tubes processed within 6 hours of collection. Some ctDNA assays have demonstrated clinical validity and utility with certain types of advanced cancer; however, there is insufficient evidence of clinical validity and utility for the majority of ctDNA assays in advanced cancer. Evidence shows discordance between the results of ctDNA assays and genotyping tumor specimens and supports tumor tissue genotyping to confirm undetected results from ctDNA tests. There is no evidence of clinical utility and little evidence of clinical validity of ctDNA assays in early-stage cancer, treatment monitoring, or residual disease detection. There is no evidence of clinical validity and clinical utility to suggest that ctDNA assays are useful for cancer screening, outside of a clinical trial. Given the rapid pace of research, re-evaluation of the literature will shortly be required, along with the development of tools and guidance for clinical practice."

The ASCO (2016) made the following guideline in regard to the use of biomarkers to guide decisions on adjuvant systemic therapy for women with early-stage invasive breast cancer:

> "The clinician should not use circulating tumor cells to guide decisions on adjuvant systemic therapy. Type: evidence based. Evidence quality: intermediate. Strength of recommendation: strong."

College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology

The College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology (2018) published a guideline on molecular testing for the selection of lung cancer patients for treatment with targeted tyrosine kinase inhibitors and noted the following recommendations regarding liquid biopsy for activating EGFR mutations and a consensus opinion regarding liquid biopsy for the T790M resistance mutation:

- Recommendation: "In some clinical settings in which tissue is limited and/or insufficient for molecular testing, physicians may use a cfDNA assay to identify [activating] EGFR mutations."
- Expert Consensus Opinion: "Physicians may use plasma cfDNA methods to identify EGFR T790M mutations in lung adenocarcinoma patients with progression or secondary clinical resistance to EGFR targeted TKIs; testing of the tumor sample is recommended if the plasma result is negative."
- No recommendation: "There is currently insufficient evidence to support the use of circulating tumor cell molecular analysis for the diagnosis of primary lung adenocarcinoma, the identification of EGFR or other mutations, or the identification of EGFR T790M mutations at the time of EGFR TKI resistance."

U.S. Food and Drug Administration (FDA)

Cobas EGFR Mutation Test v2:

"On June 1, 2016, the U. S. Food and Drug Administration approved cobas EGFR Mutation Test v2 (Roche Molecular Systems, Inc.) using plasma specimens as a companion diagnostic test for the detection of exon 19 deletions or exon 21 (L858R) substitution mutations in the epidermal

growth factor receptor (EGFR) gene to identify patients with metastatic non-small cell lung cancer (NSCLC) eligible for treatment with Tarceva® (erlotinib). The cobas EGFR Mutation Test v2 is already approved for this indication using formalin-fixed paraffin-embedded (FFPE) tissue specimens. The new use is for detection of these specific mutations in circulating-free tumor DNA (cfDNA) isolated from plasma specimens, also called liquid biopsy specimens, to aid physicians in identifying patients who may be treated first with TARCEVA (erlotinib). This is the first "liquid biopsy test" approved for use by FDA. This new test may benefit patients who may be too ill or are otherwise unable to provide a tumor specimen for EGFR testing. Patients positive by cobas EGFR Mutation Test v2 using plasma specimens for the presence of EGFR exon 19 deletions or L858R mutations are candidates for treatment with Tarceva (erlotinib). Patients who are negative by this test should undergo routine biopsy and testing for EGFR mutations with the FFPE tissue sample type."

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2021, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed.	02/22	02/22

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of member/enrollees. This clinical policy is not intended to recommend treatment for member/enrollees. Member/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid member/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare member/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and

Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.