ASSOCIATION FOR MOLECULAR PATHOLOGY

Providing global expertise in molecular testing that drives patient care

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Submitted via email to ProposedLCDComments@fcso.com and ProposedLCDComments@novitas-solutions.com

Dear Drs. Schaening-Perez and Stevens,

On behalf of the Association for Molecular Pathology (AMP), thank you for the opportunity to comment on Novitas Solutions, Inc. (Novitas) and First Coast Service Options, Inc. (First Coast) draft Local Coverage Determination (LCD) entitled Genetic Testing for Oncology.

AMP is an international medical and professional association representing approximately 2,900 physicians, doctoral scientists, and medical laboratory scientists (technologists) who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Membership includes professionals from academic medicine, hospital-based and private clinical laboratories, the government and the in vitro diagnostics industry.

AMP members play a crucial role in genetic testing in oncology. Widespread and equitable access to genetic testing in oncology is crucial to support accurate diagnoses, treatment plans, and the best health outcomes for cancer patients. Therefore, we ask that you consider the following recommendations and address the concerns we have listed below to ensure that patients have access to medically necessary cancer testing.

Using a subset of valid third-party systems may limit coverage. Medicare lacks jurisdiction to determine coverage systems.

Comment #1:

AMP is concerned that the draft Local Coverage Determination, as currently written, limits coverage in several ways. First, by narrowing coverage only to tests that meet the criteria established by at least one of the following three evidence-based databases and/or knowledge bases: National Comprehensive Cancer Network (NCCN), National Institute of Health funded Clinical Genome Resource (ClinGen), and Memorial Sloan Kettering Cancer Center Oncology Knowledge Base (OncoKB). These three knowledge bases have been identified as valid and reliable sources for their specified uses; however, none of them are designed to be test technology validators. As outlined by Section 4009 of the 21st Century Cures Act (codified at Social Security Act § 1862(l)(5)(D)) [1], this provision requires contractors to make substantive coverage decisions. AMP recognizes that the draft LCD includes a summary and analysis of evidence; however, it is not permissible to rely on a third-party database for a Medicare coverage determination.

Another worrisome provision within this draft LCD seeks to establish parameters around when genetic testing for oncology will be considered medically reasonable and necessary, as defined by Medicare. This is an additional coverage limitation that would have far-reaching implications by severely restricting coverage and could lead to decreased patient access for much needed diagnostic tests.

Request #1: Utilize all reputable sources for decisions of medical necessity

As previously stated, relying on these databases alone will create several coverage gaps. Therefore, we ask that First Coast and Novitas recognize alternative evidence-based guidelines, such as professional society guidelines, including but not limited to those from AMP, American Society of Clinical Oncology (ACSO), College of American Pathologists (CAP), and World Health Organization (WHO), as acceptable sources for coverage inclusion. Furthermore, the draft LCD limits coverage criteria to NCCN Category 1 and 2A recommendations. AMP recommends that First Coast and Novitas also include NCCN Category 2B recommendations in the covered indications because these represent a consensus position.

AMP would also like to highlight that by limiting decisions to the aforementioned three database systems, the coverage determination does not meet specific standards, namely, the evidentiary requirements set forth in the Program Integrity Manual (PIM), which states in §13.5.3:

In conducting a review, MACs shall use the available evidence of general acceptance by the medical community, such as published original research in peer-reviewed medical journals, systematic reviews and meta-analyses, evidence-based consensus statements and clinical guidelines[2].

It is important to note that important updates (e.g. FDA approval of a new therapy or diagnostic test) often take a long time to be included in databases like these. While there are certain medical or scientific panels that meet regularly for each in each database or guideline, there is a difference in the timing of coverage updates for lung cancer versus a rarer disease state. AMP believes it is not reasonable to use lack of inclusion in these specific databases as the basis for exclusion criteria for coverage due to the delays in updating evidence.

Comment #2:

The current coverage indication states: "The provider has either established a diagnosis of cancer or found significant evidence to create suspicion for cancer in their patient. Both a clinical evaluation AND

[1] https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.htm
[2] https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/pim83c13.pdf

abnormal results from histologic, cytologic and/or flow cytometric examination are required to establish a diagnosis of cancer or suspicion of cancer. If then, as a next step in the clinical management of the patient, genetic testing would directly impact the management of the patient's specific condition, the testing would be indicated."

AMP interprets this to mean that liquid biopsy methods, such as cell free DNA (cfDNA) testing is not covered. However, the draft LCD notes "In rare circumstances where patients have significant evidence to create suspicion for cancer AND are not candidates for a tissue biopsy due to high risk for complications AND genetic testing would directly impact the management of the patient's specific condition, cell-free genetic testing could be indicated."

Request #2: Clarify use of Liquid biopsy when patient's ineligible for Tissue biopsy.

AMP requests clarification that First Coast and Novitas would provide coverage if a good quality tissue sample is unavailable, then a liquid biopsy would be indicated for testing. For example, lung cancer relapse where a tissue biopsy cannot be obtained or a tumor on the thyroid that would be too invasive to perform a biopsy. We believe this would be a legitimate use of a liquid biopsy test. Other instances a liquid biopsy is needed include when insufficient tissue biopsy remains for molecular testing after a standard morphology and immunological work-up.

Comment #3:

The draft LCD also states that the FDA-approved UroVysion fluorescence in situ hybridization (FISH) is not considered medically reasonable and necessary. UroVysion FISH has been the standard of care since 2003 and is medically reasonable and necessary in-patient care for monitoring response to therapy and in diagnosis when cystoscopy or cytology results are equivocal[3][4][5]. Any barriers in coverage can lead to worse health outcomes and exacerbated health disparities. UroVysion is a non-proprietary test that has been used in laboratories certified through the Clinical Laboratory Improvement Amendments (CLIA) or the College of American Pathologists (CAP) across the Unites States for approximately 20 years.

Request #3: AMP strongly recommends that First Coast and Novitas reverse this proposal and provide coverage for UroVysion FISH.

Comment #4:

AMP would like to highlight that there is no explicit coverage of multi-gene panels and genomic sequencing procedures. The current standard of care in oncology includes the use of multi-gene panels to best diagnosis patients. AMP believes that standard of care and the needed corresponding coverage is not addressed within this proposed LCD.
AMP acknowledges that in the Response to Comments: Genetic Testing for Oncology A59417, comment #26, your response states:

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[3] Skacel, M et al. Multitarget fluorescence in situ hybridization assay detects transitional cell carcinoma in the majority of patients with bladder cancer and atypical or negative urine cytology. 2003. J. Urol. 169:210-2105.
4 Sarosdy, M.F. et al. 2002. J. Urol. Nov;168(5):1950-4.
5 Halling, K.C. et al. 2000. J. Urol. 164:1768-1775.

> "For tests that are genomic sequencing procedures that simultaneously assay multiple genes or genetic regions, coverage would be dependent on the genetic content examined and whether the content is covered for the patient's specific medical condition by the LCD."

AMP has interpreted this comment to mean that there will be individual assessments of genetic assays for patients to determine coverage. This assessment process will likely be a burden to laboratories and patients and could lead to a lack of access to needed tests for patients.

Request #4: AMP requests that Novitas and First Coast explicitly cover multi-gene panels and genomic sequencing procedures within this LCD as this has become the standard of care in advanced cancer clinical practice.

Provider Qualifications

The draft LCD proposes provider qualifications that do not reflect current clinical practice, specifically situations where care teams include pathologists and oncologists. The draft LCD states that the ordering provider of a genetic test for a patient with an established diagnosis of cancer or substantiated suspicion of cancer: (1) Understands how the test result will impact the patient's condition; (2) Must be the treating clinician who is responsible for the management of the patient's cancer; and (3) Has presented this information to the patient eliciting patient understanding.

AMP believes these requirements, if finalized, will detrimentally impact workflow and potentially delay care, and we strongly recommend that they be removed from this policy. These stipulations also contradict the recommended procedures for ordering molecular tests for cancer. Many times, the treating oncologist may not be assigned to the patient this early in the care continuum, making it extremely difficult and unnecessarily burdensome for the ordering provider to be the treating clinician. For example, a pathologist may require a molecular test (e.g. ALK gene fusion/translocation) in order to make a diagnosis of Inflammatory Myofibroblastic Tumor (IMT) with Anaplastic Lymphoma Kinase (ALK Translocation). Requiring the "treating oncologist" to order the ALK gene fusion/translocation assay will delay the diagnosis and treatment with an ALK kinase inhibitor. The approach proposed by First Coast and Novitas could result in costly delays in diagnosis and care for patients. Multi-disciplinary teams, including molecular pathologists, oncologists, surgeons, interventional radiologists and pulmonologists, and other proceduralists, are the gold-standard in oncology care; thus, coverage policies should align with the workflows that support this model.

In addition, it is very difficult, if not impossible, for the laboratory to know if or when test results are presented to a patient and if the patient comprehends the results. It is important to note that pathologists rarely have direct conversations with patients, and in the reference lab context often do not have access to patients' medical records. For these reasons, this requirement would be impossible for most laboratories to implement.

General Information

Within the coverage policy, AMP believes that there is still a conflation between somatic and germline testing. AMP submitted comments on the previously proposed LCD that stated a clear delineation of the requirements for each type of testing was needed. AMP appreciates the inclusion of the definitions in

the revised draft policy. However, AMP believes that the placement of germline and somatic testing do not represent what the requirements are for coverage and will cause confusion with providers. In order to clearly delineate the requirements for each type of testing, AMP requests the indications, databases, and indications for repeat testing to be listed separately for germline and somatic testing.

Billing and Coding

In accordance with the recommendations above and to ensure that appropriate coverage is maintained for tests included in the Biomarkers for Oncology LCD, AMP requests that the following CPT codes and ICD-10 diagnosis codes be added to the draft policy. Please note that the lists are non-exhaustive and serve to show as examples of the necessary additions to allow for needed patient access.

CPT Codes

We recommend the inclusion of the following additional CPT codes:

CPT Code	Long Code Descriptor
81503	Oncology (ovarian), biochemical assays of five proteins (CA-125, apolipoprotein A1, beta-2 microglobulin, transferrin, and pre-albumin), utilizing serum, algorithm reported as a risk score
81538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival
81540	Oncology (tumor of unknown origin), mRNA, gene expression profiling by real-time RT-PCR of 92 genes (87 content and 5 housekeeping) to classify tumor into main cancer type and subtype, utilizing formalin-fixed, paraffin-embedded tissue, algorithm reported as a probability of a predicted main cancer type and subtype

ICD-10 codes:

There are numerous ICD-10 codes which represent indications for which coverage is medically reasonable and necessary and are omitted from the draft LCD. AMP would like to point out that any ICD-10 with the term “unspecified” within its definition has been defined as a non-covered diagnosis, despite the term being the most appropriate and specific coding by an oncologist and will cause patient access issues if implemented. Unspecified codes are used during late-stage cancer treatment when the type of cancer or location of cancer is too numerous to delineate. Non-coverage of unspecified ICD-10 codes will cause patient lack of access in these circumstances, when patients need access to treatment the most. It is also common to leave the location of a cancer unspecified in certain circumstances. For example, in metastatic lung cancer, targeted therapies are systemic, not local, and treated the same, no

matter if the cancer is located in the right or left lung. Furthermore, there is no way for laboratories to change the ICD-10 codes once a biopsy has been received.

ICD-10 code request:

Due to the expansive nature of the policy as written, an appendix including but not limited to numerous ICD-10 codes is required for appropriate coverage and access. Please find in the attached Appendix A non-exhaustive list of ICD-10 codes that we request be added to the local coverage articles DA59123 and DA59125.

Thank you again for the opportunity to review and comment on this draft policy. We are happy to be of assistance in providing additional clinical or other information to assist you with this draft LCD. Please direct your correspondence to Annie Scrimenti, Associate Director, Public Policy and Advocacy, at ascrimenti@amp.org.

Sincerely,

Samuel Caughron, M.D.
Chair, Economic Affairs Committee
Association for Molecular Pathology