April 11, 2018

Ms. Virginia Muir
LCD Comments
P.O. Box 7108
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PartBLCDComments@anthem.com

Re: Draft Local Coverage Determination: Genomic Sequence Analysis Panels in the Treatment of Hematolymphoid Diseases (DL37606)

Dear Ms. Muir:

Thank you for this opportunity to respond to your draft local coverage determination entitled Genomic Sequence Analysis Panels in the Treatment of Hematolymphoid Diseases (DL37606). The Association for Molecular Pathology (AMP) is an international medical professional association representing approximately 2,400 physicians, doctoral scientists, and medical technologists who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics and genomics. Membership includes professionals from the government, academic and commercial clinical laboratories, community hospitals, and the in vitro diagnostics industry.

As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the College of American Pathologists (CAP) serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

Members of both AMP and CAP are experts in molecular pathology and the implementation of this coverage policy will directly impact their practices. We are submitting joint comments because at this time both of our organizations share the same perspective regarding this draft LCD.

Proposed Coverage Policy

Both AMP and CAP would like to thank you for the thoughtful approach to coverage you took in this policy. We believe that as written this policy will ensure patients with acute myelogenous leukemia (AML), myelodysplastic syndromes (MDS), and myeloproliferative neoplasms (MPN) will have access to the molecular testing necessary to guide their treatment.

AMP and CAP recommend adding the gene mutations in *SH2B3, U2AF1* and *SH3B1* to the MPN Table to account for the update in 2018 NCCN guidelines and to recognize these may also affect management of the MPN subtype primary myelofibrosis (PMF). Although these gene mutations are listed as having a prognostic significance for essential thrombocythemia (ET), these "higher-risk" mutations may also be helpful in the decision making regarding allogeneic hematopoietic cell transplant in PMF since these "adverse variant/mutations also affect myelofibrosis-free survival." This change would be consistent with the framework of the existing LCD because "higher-risk" mutations may be helpful in the decision making regarding allogeneic hematopoietic cell transplant for patients with PMF. (NCCN Myeloproliferative Neoplasms 2018)

CPT Codes

We urge you to provide coverage for an additional CPT code:

81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed

It is now common for more than 50 genes to be implicated in the pathogenesis, molecular biology, and progression of myeloid disorders and acute leukemia. As many as 72 genes have been shown to be important in the diagnosis, prognosis, and therapy for acute and chronic myeloid diseases (Mukherjee et al., 2017). These 72 genes do not include the additional genes recently included in the 2017 World Health Organization classification of hematologic malignancies.

ICD-10 Codes

The proposed policy lists 16 ICD-10 codes for AML, 19 for MDS, and 3 for MPN. We agree that a specific myeloproliferative neoplasm diagnosis and ICD-10 should be required for previously diagnosed patients who have not responded to therapy or show evidence of relapse. However, the ICD-10 codes included in the policy do not accommodate diseases such as CMML, atypical CML, and others which demonstrate features of both MPN and MDS. In addition, we request addition of ICD-10 codes associated with the appropriate clinical criteria raising the suspicion of MPN that would appropriately trigger the hematologist's request for this testing. For example, NGS-based mutation profiling is certainly warranted in a patient with thrombocytosis, splenomegaly, and leukocytosis, but with a "borderline" bone marrow lacking minimal diagnostic criteria for an MPN. Such a patient could not appropriately be given one of the 3 specific MPN ICD-10 codes included in this draft LCD.

We recommend inclusion of additional ICD-10 codes for MPN that would fulfill criteria for this policy. The additional codes include, but may not be limited to, those listed below:

MPN

C88.8	Other malignant immunoproliferative diseases
C92.2	Atypical chronic myeloid leukemia, BCR/ABL-negative
C92.20	Atypical chronic myeloid leukemia, BCR/ABL-negative, not having achieved remission
C92.22	Atypical chronic myeloid leukemia, BCR/ABL-negative, in relapse
C94.40	Acute panmyelosis with myelofibrosis not having achieved remission
C94.41	Acute panmyelosis with myelofibrosis, in remission
C94.42	Acute panmyelosis with myelofibrosis, in relapse
C96	Other and unspecified malignant neoplasms of lymphoid, hematopoietic and related tissue
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
D47	Other neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue
D47.1	Chronic myeloproliferative disease
D47.4	Osteomyelofibrosis
D47.9	Neoplasm of uncertain behavior of lymphoid, hematopoietic and related tissue, unspecified
D47.Z	Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue
D47.Z9	Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue
D72	Other disorders of white blood cells
D72.8	Other specified disorders of white blood cells
D72.82	Elevated white blood cell count
D72.821	Monocytosis (symptomatic)
D72.828	Other elevated white blood cell count
D72.829	Elevated white blood cell count, unspecified
D72.89	Other specified disorders of white blood cells

D72.9	Disorder of white blood cells, unspecified
D75	Other and unspecified diseases of blood and blood-forming organs
D75.8	Other specified diseases of blood and blood-forming organs
D75.89	Other specified diseases of blood and blood-forming organs
D75.9	Disease of blood and blood-forming organs, unspecified
D77	Other disorders of blood and blood-forming organs in diseases classified elsewhere
D77	Other disorders of blood and blood-forming organs in diseases classified elsewhere
R16	Hepatomegaly and splenomegaly, not elsewhere classified
R16.1	Splenomegaly, not elsewhere classified
R16.2	Hepatomegaly with splenomegaly, not elsewhere classified

MPN/MDS (Myelodysplastic/myeloproliferative neoplasms) as defined by the WHO

C93.1	Chronic myelomonocytic leukemia (CMML)
C93.10	CMML not having achieved remission
C93.12	CMML in relapse
C93.Z	Other monocytic leukemia
C93.Z0	Other monocytic leukemia not having achieved remission
C93.Z2	Other monocytic leukemia in relapse
C95.1	Chronic leukemia of unspecified cell type
C95.10	Chronic leukemia of unspecified cell type not having achieved remission
C95.12	Chronic leukemia of unspecified cell type in relapse

We respectfully ask that you consider these comments, which were prepared by members of AMP and CAP and who provide services to Medicare beneficiaries covered by NGS. We are happy to be of assistance in providing additional clinical information, references, contacts, or whatever is needed to assist you with this draft LCD. Please direct your correspondence to Tara Burke, AMP Director of Public Policy and Advocacy, at tburke@amp.org or Nonda Wilson, CAP's Manager, Economic and Regulatory Affairs, at nwilson@cap.org. Sincerely, Association for Molecular Pathology College of American Pathologists.

Sincerely,

Association for Molecular Pathology
College of American Pathologists

References:

1. Mukherjee et al. Addition of chromosomal microarray and next generation sequencing to FISH and classical cytogenetics enhances genomic profiling of myeloid malignancies. Cancer Genet. 216-217: 128-141, 2017.

2. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, Myeloproliferative Neoplasms (Version 2.2018).