Association for Molecular Pathology
Promoting Clinical Practice, Translational Research, and Education in Molecular Pathology
9650 Rockville Pike, Bethesda, Maryland 20814
Tel: 301-634-7939 ▪ Fax: 301-634-7990 ▪ Email: amp@amp.org ▪ www.amp.org

August 29, 2013

Elaine Jeter, MD
PO Box 100190
Columbia, SC 29202
J11B.policy@PalmettoGBA.com

RE: Draft Local Coverage Determination: **Genetic Testing for Lynch Syndrome (DL33779)**

Dear Dr. Jeter,

Thank you for the opportunity to comment on Draft Local Coverage Determination: Lynch Syndrome. We appreciate the effort involved in developing this local coverage determination. It may be useful at the outset to note that a consortium of professional associations are currently drafting practice guidelines that address molecular biomarkers in colorectal cancer testing, including Lynch Syndrome. We will alert Palmetto to their release, which is anticipated in the next year.

We have the following comments:

1. **Requirements for testing**
   The current recommendation by EGAPP and NCCN Guidelines for Colon Cancer Screening (V1.2013) and for Colon Cancer (V3.2013) is for universal testing for identifying Lynch syndrome patients regardless of the age at the time of diagnosis, and in persons with Stage II disease because MMR deficiency influences prognosis and response to 5-FU adjuvant therapy. Universal testing is supported by Myndura's findings as well. The incidence of Lynch Syndrome among patients with endometrial cancer is the same as among colorectal cancer patients, and it is logically appropriate to test all newly identified endometrial cancer for MMR as well.

2. **Variation from the algorithm as outlined in the DLCD.**
   The DLCD identifies the general principles outlined in the DLCD and a proscriptive algorithm for the sequence of testing. While we agree with the principles and initial testing, we note that in clinical practice, that algorithm will not always be followed for good reasons. The literature and clinical practice allow for some variation in the order of testing, based on a number of factors including tissue availability, prevalence, history, and test availability. It is the clinical judgment of the physician/molecular pathologist that determines the details. (Pino 2010).

   The DLCD does allow for use of alternate testing routine however it requires that documentation be submitted with each claim for review. This is labor intensive not only for Palmetto but also for the lab. As manual review, it represents an increase in medical review costs for the MAC; it slows down claim processing and delays payment.

We would suggest that Palmetto consider using an approach adopted by the DME MACS when there are restrictions or details to be met to qualify for coverage. The LCD coding section instructs the physicians or suppliers to attach a modifier to the CPT code to indicate that the coverage criteria in the LCD has been met. This serves many purposes: it ensures the payer that the providers know about the LCD and criteria and have met them; it expedites claim submission for the provider, it reduces medical review costs and expedites claims processing for the MAC.

The modifier is KX – "Requirements specified in the medical policy have been met. Documentation on file." Documentation would be submitted if Palmetto requested it.

REQUEST: In the coding guidelines, request that the KX modifier be submitted with the Group 1 CPT codes, except for BRAF, and documentation should be presented if Palmetto requests it.

3. ICD-9 Diagnoses codes – Group 1 for CPT Code 81210 - BRAF

We understand the place of BRAF testing in the algorithm for Lynch syndrome. We assume that the diagnoses codes would be applied to the CPT code, that means that claims submitted with other ICD-9 codes would be denied, that the test is not considered 'reasonable and necessary' for these other diagnoses.

However, BRAF testing is done for conditions other than Lynch syndrome. Palmetto recognizes the relationship between BRAF testing and melanoma in the inclusion of cobas 4800 BRAF V600 test in this draft LCD. The GeneReview database, gene registry, maintained by NIH states:

> "Mutations in this gene are associated with cardiofaciocutaneous syndrome, a disease characterized by heart defects, mental retardation and a distinctive facial appearance. Mutations in this gene have also been associated with various cancers, including non-Hodgkin lymphoma, colorectal cancer, malignant melanoma, thyroid carcinoma, non-small cell lung carcinoma, and adenocarcinoma of lung." (Genetic Testing Registry – BRAF)
>
> It is specifically cited for lung cancer. (Lung Cancer – Genetic Testing Registry)

REQUEST:

1) Remove CPT Code 81210 – BRAF from the Group list of codes for which medical necessity is only met by conditions related to Lynch Syndrome.
2) If additional control on testing is medically indicated by experience, please develop a separate coverage determination focusing only on indications for BRAF.

4. Coding guidelines

These are the only ICD-9-CM Codes That Support Medical Necessity for CPT codes 81301 or 88342.
Group 2 Codes:
V16.0 FAMILY HISTORY OF MALIGNANT NEOPLASM OF GASTROINTESTINAL TRACT
V84.04 GENETIC SUSCEPTIBILITY TO MALIGNANT NEOPLASM OF ENDOMETRIUM
V84.09 GENETIC SUSCEPTIBILITY TO OTHER MALIGNANT NEOPLASM

Diagnoses for CPT code 88301:

The list of diagnoses codes which support the initial IHC and MSI testing appear to be incomplete and do not match the clinical scenarios. A diagnosis of colorectal cancer or

endometrial cancer alone should be one of the ICD-9 codes that support the medical necessity of testing. That would be consistent with the recommendations for testing in those diagnosed with CRC without a known family history of neoplasm or known genetic susceptibility.

REQUEST: Please consider adding the following to the diagnoses that support medical necessity:

ICD-9 diagnosis codes for CRC and for endometrial cancer
V10.05 Personal history of malignant neoplasm of large intestine
V10.06 Personal history of malignant neoplasm of rectum rectosigmoid junction and anus
V10.42 Personal history of malignant neoplasm of other parts of uterus
V12.72 Personal history of colonic polyps

Diagnoses Associated with 88342 – IHC

This is a general immunohistochemistry procedure performed for many other clinical indications. If this policy is put into place as stated, all other indications for use will be denied as not having met 'reasonable and necessary' criteria. This will have serious far reaching, unintended negative consequences for patient care.

REQUEST:

1) Remove CPT Code 88342 – IHC from the Group 2 list of codes for which medical necessity is only met by conditions related to Lynch Syndrome or history of malignance.
2) If additional control on testing is medically indicated by experience, please develop a separate coverage determination through the LCD process, focusing only on indications for IHC.

5. ICD-9 diagnoses codes – Group 1

We would suggest that the codes for malignancy of the anus be moved from the excluded list and added to the list of codes which support medical necessity. Despite our best efforts, there are times that the diagnosis is selected by general location and does not take into consideration the fact that the mass appeared to originate in the anus but was in fact a metastasis. While the physician may amend the diagnosis, the medical record / coding process may not.

154.2 Malignant neoplasm of anal canal
154.3 Malignant neoplasm of anus unspecified site
197.5 Secondary malignant neoplasm of large intestine and rectum

We respectfully ask that you consider our comments which were prepared by a consortium of members of the Association for Molecular Pathology and Laboratory directors, staff and consultants who provide service to Medicare beneficiaries covered by Palmetto. We are happy to be of assistance in providing additional clinical information, references, contacts, or whatever is needed to assist you with this DLCD. Please direct your correspondence to Dr. Andrea Ferreira-Gonzalez:

Andrea Ferreira-Gonzalez, PhD
Director, Molecular Diagnostics Laboratory
Virginia Commonwealth University/Medical College of Virginia
Richmond, VA
aferreira-gonzalez@mcvh-vcu.edu
(804) 828-9564

Sincerely,

Jennifer L. Hunt, MD, MEd
President

References:

Funkhouser, WK, *et al*. Relevance, pathogenesis, and testing algorithm for mismatch repair-defective colorectal carcinomas: a report of the Association for Molecular Pathology. *J Mol Diagn* 2012, 14(2):91-103.

Myundra M, Grooss SC, *et al*. The cost-effectiveness of genetic testing strategies for Lynch syndrome among newly diagnosed colorectal cancer. *Genet Med* 2010, 12(2):93–104.

Pino and Chung. Application of molecular diagnostics for the detection of Lynch syndrome. *Expert Rev Mol Diagn* 2010, 10(5):651-665.

The following individuals co-sign this letter:

Robert A. Bray, PhD, D(ABHI), HCLD/CC(ABB)
Director, HLA Laboratory
Sentara Norfolk General Hospital
rab@mlcgroupllc.com

Dongfeng Chen, PhD, D(ABHI)
Director, Clinical Transplantation Immunology Lab
Duke University Medical Center
dongfeng.chen@duke.edu

Michael D. Gautreaux, PhD, D(ABHI)
Director, HLA/Immunogenetics Laboratory
Department of General Surgery
Wake Forest School of Medicine
mgautrea@wakehealth.edu

Howard M. Gebel, PhD, D(ABHI)
Director, Transplant Immunology
Henrico Doctors' Hospital
hgebel@gmail.com

Margaret L. Gulley, MD
Professor
Dept of Pathology
University of North Carolina
margaret_gulley@med.unc.edu

J. Charles Jennette, MD
Chair, Dept of Pathology & Laboratory Medicine
University of North Carolina-Chapel Hill School of Medicine
charles_jennette@med.unc.edu

Peter J. Kragel, MD
Chair, Dept of Pathology & Laboratory Medicine
Brody School of Medicine/East Carolina University
kragelp@ecu.edu

Peter N. Lalli, PhD, D(ABHI)
Director, Histocompatibility and Flow Cytometry Laboratory
Carolinas Laboratory Network
peter.lalli@carolinashealthcare.org

Edward H. Lipford, MD
Medical Director
Carolinas Laboratory Network
ned.lipford@carolinashealthcare.org

Gerard J. Oakley, III MD
Assistant Professor of Pathology
Marshall University
joey.oakley.2002@owu.edu

Salvatore V. Pizzo, MD, PhD
Chair, Dept of Pathology & Biochemistry
Duke University School of Medicine
salvatore.pizzo@duke.edu

Lorita M Rebellato, PhD, D (ABHI)
Laboratory Director
Department of Pathology
The Brody School of Medicine at ECU/Vidant Medical Center
REBELLATOL@ecu.edu

Mary S. Richardson, MD
Interim Chair, Dept of Pathology and Laboratory Medicine
Director, Surgical Pathology
Medical University of South Carolina
richardm@musc.edu

John Schmitz, PhD
Professor, Pathology & Laboratory Medicine
Director, HLA, Flow Cytometry and Immunology Laboratories
UNC Hospitals
jschmitz@unch.unc.edu

Karen E. Weck, MD
Professor of Pathology & Laboratory Medicine and Genetics
Director, Molecular Genetics
University of North Carolina at Chapel Hill
kweck@unc.edu

David S. Wilkinson, MD, PhD
Professor
Director of Molecular Genetic Pathology Fellowship
Associate Director of Transfusion Medicine
Department of Pathology
Virginia Commonwealth University
dwilkinson@mcvh-vcu.edu