August 8, 2015

Cahaba Government Benefit Administrators®
Comments for Draft LCDs
ATTN: Contractor Medical Director
P.O. Box 13384
Birmingham, AL 35202-3384
LCDComment@cahabagba.com

RE: Pathology and Laboratory: BRCA1 and BRCA2 Genetic Testing (DL36741)

Dear Dr. Graves, Dr. Humpert and Dr. Mitchell,

Thank you for the opportunity to comment on DL36741. The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 2,300 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 medicine, private and hospital-based clinical laboratories, and the in vitro diagnostics industry.

The College of American Pathologists (CAP) is a national medical specialty society representing more than 17,000 physicians who practice anatomic and/or clinical pathology. College members practice their specialty in clinical laboratories, academic medical centers, research laboratories, community hospitals and federal and state health facilities.

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 concerns regarding this draft LCD, and, as such, we request that Cahaba consider the joint recommendations outlined in this letter.

First, we thank you for your decision to cover BRCA1 and BRCA2 testing under many circumstances. In particular, we agree that a personal history of female breast cancer should certainly be a clinical indication for testing, although (as discussed below), we request a clarification of policy regarding those patients who have been adopted, or for whom there is no available family history. Additionally, we believe that certain other critical indications have been overlooked in this LCD, as described below, and that the LCD should be appropriately revised to incorporate these changes.

Indications

Policy statement: "This is a limited coverage policy for BRCA 1 and BRCA 2 genetic testing. BRCA 1 and BRCA 2 genetic testing has been found to be reasonable and necessary in the following instances.

1. Personal History of Female Breast Cancer

   BRCA1 and BRCA2 genetic testing for susceptibility to breast or ovarian cancer is covered in adults……. as medically reasonable and necessary when there is a personal history of breast cancer…. and ANY of the following indications"

The following additional indications are part of the consensus definition for a possible familial case of breast cancer, and are copied verbatim from the coverage policy of another Medicare contractor [see Palmetto MolDX: BRCA1 and BRCA2 Genetic Testing LCD (L36082)]. For consistency, we request that that the same language be included in the Cahaba LCD.

Request: Include the following instances in the final LCD

- Diagnosed at age 45 or younger;
- Diagnosed at age 50 or younger with at least one close blood relative with breast cancer at any age;
- Diagnosed with two breast primaries (includes bilateral disease or cases where there are two or more clearly separate ipsilateral primary tumors) when the first breast cancer diagnosis occurred prior to age 50

2. Personal History of Other Cancer

AMP and CAP commend Cahaba for recognizing that BRCA1 and BRCA2 should be performed in high-risk patients with cancers other than female breast cancer. We would like to point out that founder mutations similar to the three identified in the Ashkenazi Jewish population have also been identified in other cultural and geographic populations[1]. BRCA1 and BRCA2 genes were identified through the screening of individuals, affected and unaffected, in burdened families among varied cohorts. Therefore, similarly burdened families should thus also qualify for coverage.

Request: Include testing for other populations found to be at high-risk.

Limitations

1.. "Once in a Lifetime" Testing Requirement

With regard to "genetic testing," there is an important distinction between inherited and acquired conditions: while a specific molecular diagnostic test for an inherited condition would typically be indicated only once in a lifetime for a beneficiary, more frequent molecular testing may be medically reasonable and necessary in acquired conditions such as malignancies, including separate malignancies developing at different times and/or locations, and recurrent malignancies as they are treated and followed, in order to assess response or other relevant clinical criteria. A not uncommon scenario would be a woman with a family and personal history of breast cancer who initially tests negative for a germline BRCA1/2 mutation (when she is first diagnosed with breast cancer) and then, years later, develops a (perhaps secondary?) ovarian cancer with an acquired somatic cancer cell-specific BRCA1/2 mutation that would render the tumor susceptible to PARP inhibitor therapy[2,3]. Without BRCA re-testing of the tumor tissue (not germline), this patient would be denied effective therapy.

Request: On this basis, we recommend rather than an absolute prohibition on retesting, that the final LCD be modified to acknowledge that any such repeat testing would be on the basis of individual consideration.

Clarify Indicators for Individuals who have Been Adopted

In situations where patients with a personal history of breast or another BRCA-related malignancy have been adopted or do not otherwise have access to accurate family health information, we recommend clarification on coverage for BRCA1 and BRCA2 testing. These individuals should be covered for this testing in most circumstances.

We respectfully ask that you consider these comments which were prepared by a consortium of providers in the Cahaba jurisdiction as well as other members of the Association for Molecular Pathology, College of American Pathologists, laboratory directors, staff and consultants who provide service to Medicare beneficiaries covered by Cahaba. 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 Policy Analyst, 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

References:

1. Fackenthal JD and Olopade OI. Breast cancer risk associated with BRCA1 and BRCA2 in diverse populations. Nature Reviews Cancer 7, 937-948, 2007.
2. Ledermann J, Harter P, Gourley C et al. Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: a preplanned retrospective analysis of outcomes by BRCA status in a randomised phase 2 trial. Lancet Oncol 2014; 15: 852–861.
3. M. Moschetta, A. George, S. B. Kaye & S. Banerjee. BRCA somatic mutations and epigenetic BRCA modifications in serous ovarian cancer . Annals of Oncology 27: 1449–1455, 2016