ASSOCIATION FOR MOLECULAR PATHOLOGY
Education. Innovation & Improved Patient Care. Advocacy.
9650 Rockville Pike. Bethesda, Maryland 20814
Tel: 301-634-7939 | Fax: 301-634-7995 | amp@amp.org | www.amp.org

December 17, 2014

Elaine K. Jeter, MD
Medical Director
Palmetto GBA, Attn: MolDX
17 Technology Circle, Mail Code AG-315
Columbia, SC 29203
elaine.jeter@palmettogba.com
MolDX@palmettogba.com

Re: CDH1 Genetic Testing Coding and Billing Guidelines (M00087)

Dear Dr. Jeter:

On behalf of the Association for Molecular Pathology (AMP), I am writing in response to the addition of CDH1 testing to Palmetto's list of excluded tests in the MolDx program, and to urge Palmetto to reconsider this classification. AMP (Association for Molecular Pathology) 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. AMP members are experts in molecular pathology, and the implementation of coverage policies for these services has a direct impact on their practice.

Medical Evidence Supports Coverage of CDH1 Testing

AMP strongly disagrees with Palmetto's blanket non-coverage decision for CDH1 mutation testing based on the scientific consensus, well-documented in the medical literature, that CDH1 gene mutations are certainly not restricted to early-onset gastric cancer in young patients with Hereditary Diffuse Gastric Cancer (HDGC). In particular, and as referenced in consensus NCCN guidelines[i], CDH1 mutations are also not uncommonly found in patients with other cancers, especially breast and colon cancer, often presenting in elderly individuals with no obvious family history and with a consequent "sporadic" cancer.[ii] The COSMIC cancer mutation database (cancer.sanger.ac.uk), for example, reports 256 literature-confirmed cases of sporadic (non-inherited) cancers with a CDH1 mutation, only 77 of which are gastric cancers. Furthermore, the presence of a confirmed CDH1 mutation in a patient with a presumed "sporadic" cancer (of the breast, colon, or stomach; without an obvious family history) does have directly actionable medical consequences for the cancer patient (not just for the family members). Those directly actionable medical consequences for the Medicare enrollee include:

1) The confirmed presence of a CDH1 mutation implies an increased risk for the development of an aggressive cancer at a site other than the primary tumor. Such patients will benefit from enhanced cancer surveillance for early detection (and treatment). NCCN guidelines specifically recommend an "annual breast MRI" in these high-risk CDH1 mutation-positive patients.
2) The presence of a CDH1 mutation in a presumed "sporadic" cancer of the stomach, breast, or colon can be used as a specific residual disease tumor marker for that patient, during the course of therapy. Such cancer-specific mutations are now being utilized, not only to monitor cancer recurrence in biopsy samples, but, also to monitor early disease recurrence in circulating cell-free DNA from blood samples.

3) A critical fact is that a cancer patient (of any age) with a CDH1 mutation may present without a family history and with a consequent "sporadic" cancer (of the stomach, breast, or colon).

Another major concern is the proposed denial of multi-gene panel test coverage for panels that include CDH1. For the same reasons listed above, panel-based testing for "actionable" gene mutations in cancer patients (not their asymptomatic family members) is now considered standard of care, and the finding of a CDH1 mutation is clearly '"actionable" for the reasons specified above.

The Palmetto web notice listing CDH1 as an excluded test states the following: "Since the average age of onset for HDGC is thirty-eight years, the primary population for testing is below the age of the usual Medicare beneficiary." At the conclusion of the notice, it states: "In rare cases in which HDGC is suspected in a Medicare beneficiary, Palmetto GBA will review the documentation on a case-by-case basis." While the average age of onset for HDGC is indeed thirty-eight years, 17 percent of individuals eligible for Medicare are below thirty-five years of age and qualify for Medicare because they have end-stage renal disease (ESRD), Amyotrophic lateral sclerosis (ALS), or are disabled.[iii]We believe that consensus guidelines (as detailed above) dictate that a larger pool of patients on Medicare should receive this testing than this policy implies.

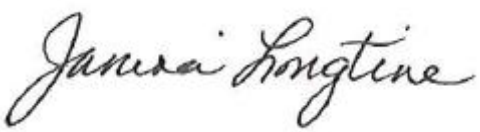
Palmetto Should be Utilizing the Formal LCD Process

AMP remains concerned that the process being employed by Palmetto to make decisions about molecular diagnostic tests that will be excluded from coverage is insufficient to comply with the LCD process – and its built-in inclusion of relevant input from the medical community. We assume that Palmetto's review of MOLDX program tests, like CDH1 testing, includes a review of the clinical utility of these tests and a review of the medical evidence to determine whether the "reasonable and necessary" criteria for coverage has been met. Because these are Palmetto-specific coverage decisions that are being applied to all Medicare beneficiaries, they should be subject to the LCD process for presentation and public comment before final implementation of coverage. The LCDs would include identification of the tests covered by the applicable CPT code or gene tested, the clinical indications, the patient selection limitations, the frequency of testing, the ICD-9 codes and reporting CPT codes, and presentation of the medical literature considered in making the determination.

The statements on Palmetto's website do not contain all of the information listed above or a section related to history and revisions. Without this information and a notice and comment period, these statements are insufficient to comply with the LCD process.

We respectfully ask that you re-consider your blanket non-coverage decision for CDH1 testing in consideration of these comments, which were prepared by a consortium of providers in the Palmetto jurisdiction as well as other members of the Association for Molecular Pathology, 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 in the reconsideration of this policy. Please direct your correspondence to Mary Steele Williams, AMP Executive Director, at mwilliams@amp.org.

Sincerely,



Janina A. Longtine
AMP President

---

[i] National Comprehensive Cancer Network. Gastric Cancer (Version 1.2014)

[ii] Giovanni Corso et al, *Frequency of CDH1 germline mutations in gastric carcinoma coming from high- and low-risk areas: metanalysis and systematic review of the literature,* BMC Cancer, 12:8 (2012).

[iii] http://kaiserfamilyfoundation.files.wordpress.com/2013/01/8100.pdf