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RE: Draft Local Coverage Determination – MGMT Promoter Methylation Analysis (DL36192, DL36188)

Dear Dr. Lurvey:

Thank you for the opportunity to comment on DL36192 and DL36188. 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.

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 we request that Noridian consider implementing the consensus recommendations outlined in this letter.

First, we thank you for your decision to cover MGMT Promoter Methylation Analysis under limited circumstances. We agree with your determination that this test is medically necessary, but believe that a certain critical clinical indication, namely the conundrum of tumor pseudo-progression, as detailed below, has been overlooked.

1. MGMT Testing for Glioma Patients with Pseudoprogression

The neuro-oncology community has recently come to recognize the concept of pseudo-progression in the treatment course of high grade gliomas. In particular, pseudo-progression is defined as apparent post-treatment radiographically-identified disease progression followed by subsequent improvement or stabilization without any additional treatment. Pseudo-progression is a transient phenomenon that likely represents a local tissue reaction to the therapy, and its presence has actually been shown to improve overall survival (DaCruz LCH Am J Neuroradiol 32:1978 – 85, 2011). Distinguishing pseudo-progression from its radiographic mimic, true tumor-specific disease progression, is thus critical, given that the best treatment option for pseudo-progression is to continue the current therapy, while the exact opposite

management, discontinuation of the current therapy, is the best treatment option for true disease progression. Although current radiographic imaging methods cannot distinguish (DaCruz LCH Am J Neuroradiol 32:1978 – 85, 2011) these two disparate diagnoses with radically different treatment ramifications, it has recently been determined that gliomas with MGMT promoter methylation have a significantly higher prevalence of pseudo-progression than non-methylated tumors (Brandes J Clin Oncol 26:2192-2197, 2008). In this study, 91% of patients with methylated MGMT had pseudo-progression (versus 41% of patients without methylated MGMT, P = .0002), and were best managed by continuing the current therapy. The determination of MGMT promoter methylation status in post-treatment patients with imaging consistent with progression/psuedo-progression is thus clinically critical to ensure that effective therapies are not inappropriately terminated under the false assumption of disease progression (versus the alternative diagnosis of transient good-prognosis pseudo-progression).

We therefore suggest that MGMT testing should be covered for all glioma patients with a post-treatment imaging study suggesting progression/pseudo-progression and that any ICD-10 codes relating to this diagnosis be added to this policy.

We respectfully ask that you consider these comments, which were prepared by a consortium of providers in the Noridian jurisdiction as well as other members of AMP and CAP, laboratory directors, staff and consultants who provide service to Medicare beneficiaries covered by Noridian. 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 Mary Steele Williams, AMP Executive Director, at mwilliams@amp.org or Nonda Wilson, CAP's Manager, Economic and Regulatory Affairs, at nwilson@amp.org.

Sincerely,

Association for Molecular Pathology
College of American Pathologists