April 8, 2016

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Re: Draft Coverage Determination: MOLDX: Chromosome 1p/19q Deletion Analysis (DL36542)

Dear Dr. Lurvey, Dr. Haley, Dr. Hecker, and Dr. Oakes:

Thank you for the opportunity to comment on Noridian's proposed local coverage determination policy (LCD) for MolDX: Chromosome 1p/19q deletion analysis (DL36542). 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 18,000 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 Noridian consider the joint recommendations outlined in this letter.

We support your decision to provide coverage for 1p/19q deletion analysis under certain circumstances; however we request that you consider the following additions to coverage.

Indications for Testing

Some tumor types other than those listed in the draft LCD will often require 1p/19q testing to arrive at the correct diagnosis. For example, small cell glioblastomas can be confused with anaplastic oligodendrogliomas as both can exhibit round hyperchromatic nuclei and small droplets of eosinophilic cytoplasm. In these instances, the presence of a 1p/19q co-deletion is diagnostically useful in making the distinction, and indicative of a much better prognosis and a different therapeutic approach. In addition, neurocytic tumors (e.g. central neurocytomas, extraventricular neurocytomas, cerebellar liponeurocytomas, and dysembryoplastic neuroepithelial tumors) exhibit small round cell features that are histologically similar to oligodendroglioma and are often appropriately tested for 1p/19q co-deletions to adjudicate the diagnosis.

Request: We ask that the following tumor types be added to the "medically necessary" list under "Indications for Testing": Small cell glioblastomas, neurocytic tumors (e.g. central neurocytomas, extraventricular neurocytomas, cerebellar liponeurocytomas, and Dysembryoplastic Neuroepithelial tumors).

Limitations of Coverage

We disagree with your decision to only cover one 1p/19q deletion analysis per patient. Some clinical scenarios will demand more than one 1p/19q assay per patient. For example, recurrent oligodendrogliomas often exhibit histologic features of astrocytic gliomas as a result of therapeutic interventions raising the possibility of an oligoastrocytoma, a tumor with a worse prognosis.

Also, small biopsies of treated sites (areas which have received prior therapy) can produce histologic features of astrocytic hyperplasia that can be confused with recurrent tumor. In such instances, 1p/19q-testing is indicated, as distinguishing recurrent tumor versus treatment response is of obvious diagnostic and therapeutic significance. Needle biopsies after treatment may demonstrate features similar to those of an oligoastrocyoma, raising questions about the original diagnosis versus treatment effect where tumor is gone and replaced by benign reactive changes. The presence of a 1p/19q co-deletion is diagnostic of a significantly different tumor type. Oligodendroglioma with 1p/19q co-deletion is a diagnostic marker used to guide therapy, not a prognostic marker. As such, it should be covered in these circumstances.

Request: We request that your "one service" restriction be changed to reflect the clinical scenarios described above.

CPT/HCPCS Codes

We request that you consider coverage for the following CPT codes, which are commonly used in the course of common lab practice to evaluate the 1p/19q co-deletion:

81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenetic array analysis for neoplasia)
88374	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), using computer-assisted technology, per specimen; each multiplex probe stain procedure
88377	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), manual, per specimen; each multiplex probe stain procedure

The 81406 CPT code will be used by labs that evaluate the 1p/19q co-deletion using micro-array technology, a well-documented method for evaluating deletion events in tumor cells. The 88374 (computer-assisted FISH) and 88377 (manual FISH) CPT code will be used by labs that evaluate the 1p/19q co-deletion using semi-quantitative morphometric fluorescence in situ hybridization, which is probably the most popular method for evaluating large chromosome-level deletion events in tumor cells. These "quantitative multiplex" FISH codes are required in order to quantitatively evaluate the ratio of the deleted 1p and 19q chromosome arms in comparison to the control 1q and 19p chromosome arms.

Request: We request that you consider coverage for the following ICD-10 codes which are not any of the specific tumor types that are known to be positive for the 1p/19q deletion, but rather are non-specific "rule out" diagnoses that often require specialized testing (including 1p/19q) to definitively exclude the specific 1p/19q -associated diagnoses detailed above. Coverage is thus requested for the diagnoses listed below where a negative test result will also be useful to assign an accurate diagnosis and inform the most appropriate therapy.

C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum

C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.9	Malignant neoplasm of central nervous system, unspecified
C79.31	Secondary malignant neoplasm of brain
C79.32	Secondary malignant neoplasm of cerebral meninges
D33.0	Benign neoplasm of brain, supratentorial
D33.1	Benign neoplasm of brain, infratentorial
D33.2	Benign neoplasm of brain, unspecified
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D33.7	Benign neoplasm of other specified parts of central nervous system
D33.9	Benign neoplasm of central nervous system, unspecified
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D43.1	Neoplasm of uncertain behavior of brain, infratentorial
D43.2	Neoplasm of uncertain behavior of brain, unspecified
D43.8	Neoplasm of uncertain behavior of other specified parts of central nervous system
D43.9	Neoplasm of uncertain behavior of central nervous system, unspecified
D49.6	Neoplasm of unspecified behavior of brain
G93.89	Other specified disorders of brain
G93.9	Disorder of brain, unspecified
G94	Other disorders of brain in diseases classified elsewhere
H47.611	Cortical blindness, right side of brain
H47.612	Cortical blindness, left side of brain
H47.619	Cortical blindness, unspecified side of brain
H47.631	Disorders of visual cortex in (due to) neoplasm, right side of brain
H47.632	Disorders of visual cortex in (due to) neoplasm, left side of brain
H47.639	Disorders of visual cortex in (due to) neoplasm, unspecified side of brain
Z85.841	Personal history of malignant neoplasm of brain
Z86.011	Personal history of benign neoplasm of the brain

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 the Association for Molecular Pathology, College of American Pathologists, 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 Tara Burke, AMP Policy Analyst, at tburke@amp.org or Nonda Wilson, CAP Manager, Economic and Regulatory Affairs, at nwilson@cap.org.

Sincerely,

Association for Molecular Pathology
College of American Pathologists