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Submitted electronically via ProposedLCDComments@fcso.com and ProposedLCDComments@novitas-solutions.com

RE: Proposed LCD: Pharmacogenomics Testing - DL39073 (First Coast) and DL39063 (Novitas)

Dear Drs. Schaening and Bloschichak:

On behalf of the Association for Molecular Pathology (AMP) and the College of American Pathologists (CAP), we thank you for the opportunity to review and comment on the proposed policy for local coverage determinations, Pharmacogenomics Testing (DL39073 and DL39063).

The AMP is an international medical and professional association representing approximately 2,500 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 academic medicine, hospital-based and private clinical laboratories, the government, and the in vitro diagnostics industry.

The CAP is the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs. The CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

We are submitting joint comments because currently our organizations share the same position regarding these draft local coverage determinations (LCDs). We appreciate the effort that has gone into the development of these proposed LCDs, and we offer the following recommendations for your consideration.

Covered Indications

AMP and CAP applaud you for recognizing the importance of providing coverage to Medicare beneficiaries for pharmacogenomic (PGx) testing. We support the covered indications outlined in this draft LCD. In particular, both groups appreciate that you directly referred to the Clinical Pharmacogenetic Implementation Consortium (CPIC) guidelines. Utilization of CPIC guidelines will allow for modification as time goes on and for this coverage policy to evolve with the science. We encourage you to continue utilizing pharmacogenomic-related clinical practice guidelines, such as those created by CPIC, in addition to the

pharmacogenomic information included in FDA-labeling.[1]

Coverage Limitations

We disagree with the statement that "PGx tests are considered germline testing, and therefore only allowed once per lifetime." Not all PGx tests are the same and the comprehensive nature of PGx tests will improve as the associated science and evidence improves over time, which may warrant an additional PGx test to be performed in some circumstances. Restricting PGx tests to "once per lifetime" will prevent providers and patients from having access to future, state of the art PGx tests, which may improve quality and cost-effectiveness of care. This coverage limitation will ultimately restrict coverage for patients for whom testing would be medically necessary. For example, AMP and CAP have recently published guidelines for minimum requirements for PGx testing.[4] If a patient previously had testing that did not meet the minimum requirements for testing, the patient may need additional testing to ensure that they received appropriate testing. Additionally, current PGx tests are usually targeted variant testing. If the patient has had an adverse reaction to a medication, more comprehensive testing such as whole sequencing or duplication/deletion analysis may be warranted. **Therefore, we recommend deletion of the requirement that PGX tests be allowed only once per lifetime.**

Provider Qualifications

Both AMP and CAP have serious concerns as it pertains to the enforceability of the stated provider qualifications proposed in this draft policy. In many states, a PGx test can be ordered by a clinical provider that is not the treating clinician, such as pharmacists and genetic counselors. Restricting the ability to order PGx tests, to only treating clinicians, will lead to patient access issues. In many cases, genetic counselors and/or pharmacists are more, or as knowledgeable as to the actionability of the ordered test than the attending clinician. **Given this, we recommend that the term provider qualifications be broadened to include professionals other than solely the treating physician and recommend that the term "treating clinicians" be changed to "clinical provider".**

Coding Guidance

We are concerned about the following language within the coding articles that state:

> *"If a laboratory assays two or more genes in a patient in parallel, then those two or more genes will be considered part of the same panel.*
>
> *A panel constitutes a single procedural service, so one CPT code must be submitted for the panel."*

While this may be true in some cases, this is not always true. For example, when pursuing PGx testing to guide phenytoin therapy you need to examine both CYP2C9 and HLA-B; however, these two genes cannot typically be assayed together as one procedure. Independent interrogation of these genes each requires a different methodology. In this example, if a laboratory were to follow the guidance outlined in this article, they would only be able to submit reimbursement for one procedure. **We therefore recommend deletion of these two sentences within the guidance.**

As mentioned previously in this comment letter, AMP and CAP appreciate the reference to CPIC and FDA guidelines in this draft policy. Table 1 and Table 2 in the Billing and Coding Article includes a list of relevant gene/drug associations from CPIC and FDA sources, respectively. **AMP and CAP strongly recommend that First Coast and Novitas consider restructuring Table 1 and Table 2 to show the drug in the first column and then list the corresponding genes in the second column.** First Coast and Novitas reference the FDA's Table of Pharmacogenetic Associations,[2] which is structured the way in which we recommend. To avoid

[1] https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling
[2] https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

confusion and ensure accurate gene/drug associations, we ask that you revise Table 1 and 2 in the Billing and Coding Article in this way.

Further, AMP and CAP recommend the following additions to Table 1 in the Billing and Coding Article:

- **For the CFTR gene, the following CPT code(s) should be added**:
  - CPT code 81222[3] – *CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants*; and
  - CPT code 81223 – *CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence*.
- **For the CYP2C9 gene, the following CPT code(s) should be added**:
  - CPT code 81381[4] - *HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each.*

Documentation Requirements

The draft policy includes the following documentation requirements:

- *The order by the treating clinician must reflect whether the treating clinician is ordering a panel or single genes, and additionally, the patient's medical record must reflect that the service billed was medically reasonable and necessary.*
- *If two or more single genes are tested, rather than a multi-gene panel, then the record must reflect that a clinician individually ordered each gene.*

We believe that the above listed documentation requirements will cause significant confusion, given that what CMS designates as a gene panel may not constitute an actual panel from a laboratory perspective. **We request that this language be deleted to prevent confusion amongst both the clinical provider and clinical laboratory personnel.**

ICD-10 Coding

We request that additional ICD-10 codes be added to this policy include, but not be limited to the following list:

F20.0	Paranoid schizophrenia
F20.1	Disorganized schizophrenia
F20.2	Catatonic schizophrenia
F20.3	Undifferentiated schizophrenia
F20.5	Residual schizophrenia
F20.81	Schizophreniform disorder
F20.89	Other schizophrenia
F31.0	Bipolar disorder, current episode hypomanic
F31.11	Bipolar disorder, current episode manic without psychotic features, mild
F31.12	Bipolar disorder, current episode manic without psychotic features, moderate
F31.13	Bipolar disorder, current episode manic without psychotic features, severe
F31.2	Bipolar disorder, current episode manic severe with psychotic features
F31.31	Bipolar disorder, current episode depressed, mild

[3] https://cpicpgx.org/guidelines/guideline-for-ivacaftor-and-cftr/
[4] https://www.jmdjournal.org/article/S1525-1578(18)30594-4/fulltext

F31.32	Bipolar disorder, current episode depressed, moderate
F31.4	Bipolar disorder, current episode depressed, severe, without psychotic features
F31.5	Bipolar disorder, current episode depressed, severe, with psychotic features
F31.61	Bipolar disorder, current episode mixed, mild
F31.62	Bipolar disorder, current episode mixed, moderate
F31.63	Bipolar disorder, current episode mixed, severe, without psychotic features
F31.64	Bipolar disorder, current episode mixed, severe, with psychotic features
F31.71	Bipolar disorder, in partial remission, most recent episode hypomanic
F31.73	Bipolar disorder, in partial remission, most recent episode manic
F31.75	Bipolar disorder, in partial remission, most recent episode depressed
F31.77	Bipolar disorder, in partial remission, most recent episode mixed
F32.1	Major depressive disorder, single episode, moderate
F32.2	Major depressive disorder, single episode, severe without psychotic features
F32.3	Major depressive disorder, single episode, severe with psychotic features
F32.4	Major depressive disorder, single episode, in partial remission
F33.1	Major depressive disorder, recurrent, moderate
F33.2	Major depressive disorder, recurrent severe without psychotic features
F33.3	Major depressive disorder, recurrent, severe with psychotic symptoms
F33.41	Major depressive disorder, recurrent, in partial remission
F90.0	Attention-deficit hyperactivity disorder, predominantly inattentive type
F90.1	Attention-deficit hyperactivity disorder, predominantly hyperactive type
F90.2	Attention-deficit hyperactivity disorder, combined type
Z94.2	Lung transplant status
Z94.3	Heart and lungs transplant status
Z94.81	Bone marrow transplant status
Z94.82	Intestine transplant status
Z94.83	Pancreas transplant status
Z94.84	Stem cells transplant status

Thank you again for the opportunity to review and comment on this proposed policy. We are happy to be of assistance in providing additional clinical or other information to assist you with this draft LCD. Please direct your correspondence to either Tara Burke, Senior Director of Public Policy and Advocacy, 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 America Pathologists