ASSOCIATION FOR MOLECULAR PATHOLOGY
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National Government Services Medical Policy Unit
P.O. Box 7108
Indianapolis, IN 46207-7108
NGSDraftLCDComments@anthem.com

RE: Proposed LCD: Pharmacogenomics Testing

On behalf of the Association for Molecular Pathology (AMP), we thank you for the opportunity to review and comment on the proposed policy for local coverage determinations, Pharmacogenomics Testing (DL 39995).

AMP is an international medical and professional association representing approximately 3000 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. Many of our members are highly involved in the field of pharmacogenetics and provide testing procedures relevant to DL 39995 for their patients, and we appreciate the opportunity to share our expertise.

AMP works extensively on pharmacogenetic testing and recently released joint guidelines with the American College of Medical Genetics and Genomics, Clinical Pharmacogenetics Implementation Consortium, College of American Pathologists, Dutch Pharmacogenetics Working Group of the Royal Dutch Pharmacists Association, European Society for Pharmacogenomics and Personalized Therapy, Pharmacogenomics Knowledgebase, and Pharmacogene Variation Consortium. These experts developed a consensus recommendation that defines the key attributes of pharmacogenetic testing with recommended alleles/variants for clinical testing, instructing laboratories to test the proper alleles for *DYPD*[1], *CYP3A4* and *CYP3A5*[2], *TPMT* and *NUDT15*[3] *CYP2D6*[4], Warfarin[5], *CYP2C9*[6], and *CYP2C19*[7]. consensus recommendation. AMP supports these recommendations in order achieve the best patient outcomes.

Covered Indications

AMP appreciates your recognition of the importance of providing coverage to Medicare beneficiaries for pharmacogenomic (PGx) testing. We greatly appreciate that DL 39995 directly refers to the Clinical Pharmacogenetic Implementation Consortium (CPIC) guidelines as meeting the necessary criteria for rigorous, standardized evaluation of PGx testing. AMP believes a benefit of crafting the coverage policy to

[1] https://www.jmdjournal.org/article/S1525-1578(24)00154-5/fulltext
[2] https://www.jmdjournal.org/article/S1525-1578(23)00136-8/fulltext
[3] https://www.jmdjournal.org/article/S1525-1578(22)00194-5/fulltext
[4] https://www.jmdjournal.org/article/S1525-1578(21)00164-1/fulltext
[5] https://www.jmdjournal.org/article/S1525-1578(20)30298-1/fulltext
[6] https://www.jmdjournal.org/article/S1525-1578(18)30594-4/fulltext
[7] https://www.jmdjournal.org/article/S1525-1578(17)30519-6/fulltext

specifically reference CPIC guideline level A or B, as well as the Food and Drug Administration (FDA) table of known gene-drug interactions and FDA labeling will allow coverage to evolve along with the science. We strongly urge you to continue to refer to these evidence sources for demonstrating actionability in clinical decisions in the final LCD.

Coverage Limitations

AMP disagrees with the coverage limitation stating "PGx tests are considered germline testing, and therefore only allowed once per lifetime." Not all PGx panels include the same genes and variants, and PGx tests will become more comprehensive as additional evidence of utility is generated over time about variants, especially for underserved populations, which may warrant an additional or repeat PGx test(s) 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, that further improve quality and cost-effectiveness of care. For example, as referenced earlier in this letter, AMP recently published updated guidelines for minimum requirements for PGx testing and clinical laboratories are integrating this new standard into practice. If a patient had testing prior to the new practice guideline, the patient may need additional testing to ensure that they received testing that reflects the current recommendations. Additionally, current PGx tests are usually targeted panel tests. However, if the patient subsequently has had an adverse reaction to a medication, further testing such as whole gene sequencing or duplication/deletion analysis may be warranted. Therefore, we recommend deleting the requirement that PGx tests be allowed only once per lifetime.

Suggestions for Associated Billing Article DA59915

AMP makes the following recommendations for the Billing and Coding Article Pharmacogenetic Testing:

Relevant Gene and Drug Associations

AMP recommends the inclusion of the gene *CYP3A4* to the tables for relevant gene and drug associations. *CYP3A4* contributes significantly to the first-pass and systemic metabolism of substrate drugs[2]. *CYP3A4* is also associated with genetic variants for a drug response to quetiapine, an atypical antipsychotic indicated for the treatment of schizophrenia and bipolar disorder[2].

Inclusion of Genes in Specified Groups

Within the document, under coding information, Group 15 and 16 have the codes 81401 and 81406, respectively. AMP believes that since 81401 and 81406 are Tier 2 Molecular Pathology codes, it is recommended that a gene name be included to denote what tests you would deem applicable under these groups.

Nomenclature Clarification

DA59915 refers to *IFLN3* and *IFLN4* as separate genes. AMP would like to note that current nomenclature denotes *IFLN3* and *IFLN4* to refer to the same variant as it is intragenic. We request that the billing article update their language to reflect this.

ICD-10 Coding

AMP requests additional ICD-10 codes for this policy include, but not be limited to, the following lCD-10 codes:

F90.0	Attention-deficit hyperactivity disorder, predominantly inattentive 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

Thank you again for the opportunity to review and comment on this proposed policy. We attended your public meeting on this dLCD and we are happy to be of assistance in providing additional clinical, or other information, to assist you with this draft LCD. Also, please consider AMP as a resource to connect you with subject matter experts in the development of future policies. Please direct your correspondence to Annie Scrimenti, Associate Director, Public Policy and Advocacy, at ascrimenti@amp.org .

Sincerely,

Maria E. Arcila, MD
President, Association for Molecular Pathology