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RE: Proposed LDC: MOLDX: Multiplex Nucleic Acid Amplification Test (NAAT) Panels for Infectious Disease Testing:

CGS Administrators, LLC (DL39038)
Noridian Healthcare Solutions (DL39001), (DL39003)
Palmetto GBA (DL38988)
Wisconsin Physicians Service Insurance Corporation (DL39044)

Dear Medical Directors:

On behalf of the Association for Molecular Pathology (AMP), the American Gastroenterological Association (AGA), and the College of American Pathologists (CAP), we thank you for the opportunity to review and comment on the proposed policy for MolDX: Multiplex Nucleic Acid Amplification Test (NAAT) Panels for Infectious Disease Testing (DL38988).

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 AGA is the trusted voice of the GI community. Founded in 1897, the AGA has grown to more than 16,000 members from around the globe who are involved in all aspects of the science, practice, and advancement of gastroenterology.

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 this draft LCD. Together, we would like to thank you for proposing limited coverage for outpatient testing with panels using NAATs for infectious disease testing, particularly panels with greater than 5 pathogens. We believe thoughtful consideration was given to the published literature and appreciate that you sought out input from subject matter experts by convening the Contractor Advisory Committee (CAC) in January; the resulting proposed LCD will positively impact patient care through early detection and implementation of appropriate treatment therapy, early in the illness when it is most effective. After reviewing the proposed policy's coverage criteria, we ask that Palmetto GBA consider incorporating the following AMP and CAP recommendations into the final coverage policy.

General Coverage Criteria

1. *"For immunocompetent patients, the clinical indication includes a presumption of active infection OR infection-associated complications (which may include exacerbation of underlying disease) that require the identification of a causative organism for appropriate management. Atypical clinical presentations of disease are considered appropriate indications for special populations who may not present with classic symptoms of infection (i.e., the elderly)."*

   Recommendation: The proposed LCD offers no definition of, or specific examples for, an underlying condition or immunocompromised patient. We fear that this will create coding issues leading to improper reimbursement and/or unwarranted denial of coverage. It is also necessary for providers to understand how the policy applies to patients. We recommend that the LCD provide examples of immunocompromised patients such as patients with weakened immune systems including those with HIV/AIDS, patients who are taking immunosuppressive drugs (e.g., corticosteroids); and those with inherited diseases that affect the immune system (e.g., congenital IgA deficiency).

Non-Coverage Criteria

1. *"If a previous panel test was performed with a similar/duplicative intended use, a subsequent test is only reasonable and necessary if the non-duplicative content of the second test is reasonable and necessary.*

   Exception: Repeat panel testing for the same clinical indication will only be covered if first panel yielded a negative result AND there is a high index of suspicion for a pathogen as the cause of symptoms AND the patient's clinical condition is not improving or is deteriorating after a clinically appropriate length of time. In such cases, 1 additional panel test may be covered

between 1 and 14 days after *the initial panel test, so long as the test fulfills the criteria for coverage as set forth in this policy."*

Recommendation: There are circumstances where repeat testing is warranted, such as if you were sampling too early or if sampling another body might be helpful as the disease progresses (e.g., lower respiratory tract when upper respiratory tract has become negative). It should only be considered a duplicate if it is a repeat of the same sample type, not just the same test. Therefore, we request that the following language be added for repeat testing: "For the same sample type and same clinical indication" if the "same sample had a negative result or a clinically insignificant finding."

Specific Panel Coverage Criteria

1. *"Respiratory (RP) & Pneumonia Panels (PNP): Testing is ordered by a clinician specialist in Infectious Diseases or Pulmonology for a patient with severe and established underlying respiratory pathology (i.e., severe asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis, pulmonary fibrosis, radiation therapy to the lung) AND treatment with antibiotics may be indicated according to established guidelines."*

   Recommendation: We believe that limiting ordering to the two named specialties will be problematic and produce substandard patient outcomes. We believe that a worrisome assumption is being made that there will be subspeciality experts at all points of care. This is not the case, especially in rural areas where critical care or other health specialists are not available. This requirement presents serious problems with access to care and patient safety.

   In many cases, the patient's infectious disease physician is not directly involved in the outpatient encounter. Requiring an infectious disease consultation, in the outpatient setting, will only add to the costs of the visit and delay test results. We ask that the following language be added after "testing is ordered by a clinician specialist in Infectious Diseases or Pulmonology": "or a healthcare guideline or algorithm with contribution of infectious disease or pulmonary specialist." This language should also be added for the section on immunocompromised patients.

2. *"Respiratory (RP) & Pneumonia Panels (PNP): For ALL patients: Only 1 of the following panels - RP OR PNP- will be covered for a given patient for the same clinical indication. The PNP should be prioritized in the evaluation of pneumonia from lower respiratory tract specimens (i.e., bronchoalveolar lavage samples (BALs))."*

   Recommendation: We believe that this language will negatively affect pediatric patients. In this patient population an upper respiratory panel is performed each time a respiratory disease or pneumonia is suspected. In addition, an upper viral respiratory tract infection may progress to a lower respiratory tract disease involving bacteria which may warrant PNP. PNP does not encompass RP completely. As a result, there should be an exception added for pediatric and adult Medicaid patients. If the upper respiratory is negative or non-diagnostic, then the lower respiratory should be covered.

3. *"Gastrointestinal (GI) Panels: Testing is ordered by a clinician specialist in Infectious Diseases or Gastroenterology for a patient with severe and established underlying GI pathology (i.e., inflammatory bowel disease (IBD), paralytic ileus, radiation therapy to the intestine) AND identification of an infectious cause is necessary to determine next steps in patient management."*

Recommendation: We believe that limiting ordering to the two named specialties will be problematic and produce substandard patient outcomes. In many cases, the patient's infectious disease physician and/or gastroenterologist is not directly involved in the outpatient encounter. A strict requirement for these consultations, in the outpatient setting, will only add time and cost to the visit and delay test results. We recommend that the following language be added after "Testing is ordered by a clinician specialist in Infectious Diseases or Gastroenterology": "or a healthcare guideline or algorithm with contribution of infectious disease or gastrointestinal specialist." This language should also be added for the section on immunocompromised patients.

4. *"Gastrointestinal (GI) Panels: The patient is seriously or critically ill (as defined by the American Hospital Association's "General Guide for the Release of Information on the Condition of Patients") as a result of a presumed GI infection AND the patient is being treated in an appropriate critical care facility. The patient's clinical indication for GI panel testing is diarrhea, and ALL the following apply: The diarrheal illness MUST be acute or persistent with signs or risk factors for severe disease (fever, bloody diarrhea, dysentery, dehydration, severe abdominal pain that may warrant hospitalization) AND/OR not resolving after 7 days, AND the patient has NOT taken laxatives within 24 hours of the test."*

   Recommendation #1: We believe that these criteria would hinder the ability of physicians to conduct vital public health surveillance. We recommend that an exception be made for "diarrhea with signs or symptoms of and epidemiologic indication of an event of public health significance."

   Recommendation #2: We request that the policy specify what constitutes an instance of severe dehydration. Specifically, we ask that the difference between mild, moderate, and severe dehydration, and what is enough to qualify as "severe disease" be specified.

   Recommendation #3: We believe that the requirement stating that a patient must not have used laxatives within 24 hours of the test, is overly restrictive. Patients who utilize laxatives are still capable of contracting an infection, regardless of laxative use. Further, there are other medications other than laxatives that may exacerbate normal bowel movements. This requirement would have negative impact on multiple patient groups; for example, those patients with CDIF. We recommend striking this language.

   Recommendation #4: We believe that it is unnecessary to wait for seven days to identify a massive outbreak and instead the language should state "or not resolving after 7 days" instead of "and/or."

5. *"Urogenital/Anogenital (UG/AG) Panels: For the UG/AG panels, epidemiologic indication or potential exposure to sexually transmitted pathogens (i.e., in the case of clinical concern for multiple sexually transmitted infections (STIs) due to a high-risk experience) is considered a covered clinical indication, even in the absence of clinical symptoms. Documentation of the high-risk reason for panel testing is clearly stated in the medical record.*

   In the absence of a high-risk experience, if the primary clinical concern is for 1 or few specific pathogens due to specific signs and symptoms (i.e., lesions suggestive of herpes simplex virus (HSV)), then it is expected that only a small, targeted panel (i.e., including HSV-1 and HSV-2) will be performed. In such cases, expanded panels are NOT considered reasonable and necessary and will NOT be covered."

Recommendation #1: We ask that clarification be made as to what other indications, outside of epidemiologic indication, would qualify as a covered clinical indication.

Recommendation #2: We ask that clarification be made as to what qualifies as a "small, targeted panel." Specifically, we would like to inquire as to whether this would cover a bacterial vaginosis (BV) panel; given this represents one of the highest reasons for number of office visits.

6. *"Meningoencephalitis (ME) Panels: For immune-competent patients: the patient has at least 2 of the following indicators of central nervous system (CNS) infection: cerebrospinal fluid (CSF) markers, radiology, clinical signs, and symptoms consistent with meningitis or encephalitis, epidemiologic indication or exposure. For immune-compromised patients, at least 1 of these indicators is required.*

   For all patients: Testing is from a sample collected via lumbar puncture, and NOT an indwelling medical device (i.e., CSF shunts)."

   Recommendation: We believe that these indicators will prevent both adult and pediatric patients from getting covered treatment in an emergency room setting. This is since most immunocompromised and pediatric patients, presenting in the emergency room, will likely not have two of the stated indicators. We recommend that the language be changed from "at least 2" to state "one or more of the following indicators."

7. *"Bloodstream Infection (BSI) Panels will be covered according to the following additional criteria: There is clinical concern for bacteremia or sepsis AND microbe(s) were seen on a Gram stain from the patient's blood AND the patient is being managed in an appropriate critical care facility, AND personnel (i.e., an antimicrobial stewardship team) are equipped for rapid (same day) tailoring of antimicrobial therapy as a result of rapid testing."*

   Recommendation #1: We believe that the coverage requirement mandating a positive Gram stain does not reflect the reality of clinical treatment; especially in patient groups such as immunocompromised individuals. The results of a Gram stain are not always indicative of overall findings as it pertains to a diagnosis. We suggest that this coverage indication be reviewed for the general patient populations and all coverage requirements be waived for immunocompromised patients.

   Recommendation #2: We would ask for the removal of the coverage requirement for a patient to be managed in a critical care facility since this LCD is for diagnostic tests being performed in an outpatient setting. We recommend removal of "AND the patient is being managed in an appropriate clinical care facility" as this language is too restrictive. Alternatively, this language could be revised to state "or will be called back for re-admission or avoid unnecessary re-admission depending on the results of the panel identification".

   Recommendation #3: We think that the language on personnel is hard to quantify, and we request clarification on how this would be evaluated in a claim.

8. *"Urinary Tract Infection (UTI) Panels will be covered according to the following additional criteria: The patient is symptomatic AND at higher risk for UTI complications (i.e., the elderly, patients with recurrent symptomatic UTIs and/or complicated urinary tract anatomy) OR is seen in urogynecology or urology specialty care settings."*

Recommendation: We believe that limiting coverage to patients seen in urogynecology or urology specialty care settings is too restrictive. We request that the following language be added "or a healthcare guideline or algorithm with contribution of urogynecology or urology specialist."

9. *ICD-10 Codes*

Recommendation: We request that the following additional ICD-10 codes be added to the associated coverage article:

O98.7- Human immunodeficiency virus [HIV] disease complicating pregnancy, childbirth and the puerperium
098.71- Human immunodeficiency virus [HIV] disease complicating pregnancy
O98.711- Human immunodeficiency virus [HIV] disease complicating pregnancy, first trimester
O98.712- Human immunodeficiency virus [HIV] disease complicating pregnancy, second trimester
O98.713- Human immunodeficiency virus [HIV] disease complicating pregnancy, third trimester

C46.0 Kaposi's sarcoma of skin
C46.1 Kaposi's sarcoma of soft tissue
C46.2 Kaposi's sarcoma of palate
C46.3 Kaposi's sarcoma of lymph nodes
C46.4 Kaposi's sarcoma of gastrointestinal sites
C46.5 Kaposi's sarcoma of lung
C46.50 Kaposi's sarcoma of unspecified lung
C46.51 Kaposi's sarcoma of right lung
C46.52 Kaposi's sarcoma of left lung
C46.7 Kaposi's sarcoma of other sites

B25.8 Other cytomegaloviral diseases
B25.0 Cytomegaloviral pneumonitis
B25.1 Cytomegaloviral hepatitis
B25.9 Cytomegaloviral disease, unspecified
B25.2 Cytomegaloviral pancreatitis

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, Leslie Narramore, Director of Regulatory Affairs, at lnarramore@gastro.org; or Nonda Wilson, CAP's Manager, Economic and Regulatory Affairs, at nwilson@cap.org.

Sincerely,

Association for Molecular Pathology
American Gastroenterological Association
College of America Pathologists