April 12, 2023

Gabriel A. Bien-Willner, MD, PhD
Medical Director, MolDX
Chief Medical Officer, Palmetto GBA

Via email at: MOLDX.POLICY@palmettogba.com

RE: *Article - Billing and Coding: MolDX: Molecular Testing for Solid Organ Allograft Rejection (A58019)*

Dear Dr. Biel-Willner,

We are writing on behalf of the International Society for Heart and Lung Transplantation (ISHLT) to express grave concern that the article entitled *Billing and Coding: MolDX: Molecular Testing for Solid Organ Allograft Rejection (A58019)* (the "Billing Article")[1] in reference to the local coverage determination entitled MolDX: Molecular Testing for Solid Organ Allograft Rejection (L38568) (the "LCD")[2] substantively changes the intent of the LCD and has the potential to both harm patients and increase costs to Centers for Medicare & Medicaid Services, without affording beneficiaries and stakeholders the statutorily required public comment period. ISHLT is an international not-for-profit, multidisciplinary, professional organization dedicated to improving the care of patients with advanced heart or lung disease.

ISHLT acknowledges the following conflicts of interest in relation to this letter: Natera and CareDx provide financial support to ISHLT through educational grants and annual meeting support but were not involved in the drafting of this letter. Members of the Board of Directors who have active financial relationships with companies involved in this space did not contribute to the drafting of this letter and recused themselves from discussion and voting on it.

Molecular testing through measurement of circulating donor derived cell free DNA provides a noninvasive measurement of allograft injury. Gene expression testing can noninvasively assess for the presence of patterns of expression in the peripheral blood specific for allograft rejection. These tests are typically used as a component of surveillance and allograft dysfunction assessment protocols to both reduce the need for invasive biopsy testing (which carries direct and indirect risk and may be relatively contraindicated in patients with bleeding diatheses including Hermansky-Pudlak Syndrome). Moreover, these tests can provide complementary information to that provided by invasive testing (including cardiac catheterization and endomyocardial biopsy in the case of heart transplant recipients). The utility of these tests has been outlined in peer-reviewed consensus documents from ISHLT[3] as well as the American Society of Transplantation[4]. Moreover, the rationale for and evidence supporting the use of these tests is clearly summarized and referenced in the LCD[2].

Unfortunately, the Billing Article adds constraints to the use of these tests which in our estimation contradict the intent of the LCD. Specifically:

1) **It appears that the intent is to substitute medical review for the judgement of the treating physician in this instance. If that is the case, the LCD should state that explicitly.**

   The Billing Article states:

"For a given patient encounter, only one molecular test for assessing allograft status may be billed. Any additional molecular tests billed after the first will be denied and subject to medical review."

   The LCD states:

   "For a given patient encounter, only one molecular test for assessing allograft status may be performed UNLESS a second test, meeting all the criteria established herein, is reasonable and necessary as an adjunct to the first test," and

   "Additionally, there is evidence that while some cfDNA and GEP tests may have different intended uses, combining both may further improve graft rejection determination"

2) **It appears that the intent is to impose the timing and use of molecular testing into a protocol that forces biopsy if the test is not available or otherwise excludes surveillance biopsy rather than alternative protocols that might include molecular testing in lieu of a subset of surveillance biopsies. Moreover, given that a significant percentage of programs do not currently utilize a surveillance biopsy strategy due to benefit/risk profile concerns, this constraint would limit the use of molecular testing to a small subset of programs. In our estimation this inappropriately constrains the intent of the LCD.**

   The Billing article states:

   "…use of the molecular test for surveillance (protocol) testing is only compliant with the policy if the patient is enrolled at a center that utilizes this practice and would otherwise receive a surveillance (protocol) biopsy. Providers must demonstrate that such a practice (for protocol biopsies) is in place to meet coverage criteria of this policy."

   The LCD states:

   "To assist in the evaluation of adequacy of immunosuppression, wherein a non-invasive or minimally invasive test can be used in lieu of a tissue biopsy in a patient for whom information from a tissue biopsy would be used to make a management decision regarding immunosuppression," and

   "However, given the invasive nature and risks associated with a biopsy, tests that can potentially mitigate the need for a biopsy while still providing clinicians with actionable information that can be used to help optimize immunosuppressive therapy are reasonable and necessary."

3) **It appears that the intent is to undermine the complementary nature of molecular diagnostic testing to histology. In our estimation this contravenes the intent of the LCD**

The Billing article states:

"Performing this test is not compliant with the language of the policy if used for cause when it will not be performed in lieu of a biopsy or to further inform on the need for or results of a biopsy. As such, the test and the biopsy cannot be performed simultaneously or within a short window of time such that the test cannot reasonably inform medical management. Tests performed within a week AFTER a biopsy are not compliant with policy."

The LCD states:

"To assess rejection status in patients that have received a biopsy, but the biopsy results are inco nclusive or limited by insufficient material," and

"Additionally, ongoing studies have supported that cfDNA and GEP can accurately determine allograft status in several organ types, and that molecular characterization can both precede and enhance histologic findings."

4) **Although this statement appears to intend to exclude performing molecular testing concurren tly with surveillance biopsies it is overly vague and could, for example, be used to exclude molecular diagnostics when other less specific blood tests are obtained at the same time. This statement should be made more specific or removed.**

The Billing article states:

"Therefore, performing the molecular test at the same time as the pre-test is NOT compliant with the policy. The results of the pre-test must be available to the treating clinician to inform the need for a molecular test or biopsy…"

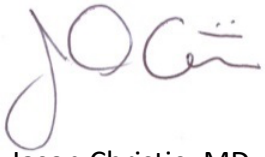
In summary, we are gravely concerned that the Billing article will establish a precedent constraining the use of Molecular Diagnostic testing that will apply to all LCDs in this area (including the essentially identical LCD for jurisdiction E)[5] and will impact similar regulatory decisions affecting our members and patients with end stage heart disease outside of the United States.

More importantly the Billing Article, if it remains in effect as written, sets a dangerous precedent that billing and coding articles can change the intent of an LCD without the statutorily required public comment, and is in conflict with feedback regarding the intent of billing and coding documents provided in a response to comments on a prior version of the Billing Document (point 3 in response to comment 1)[6].

As such the LCD can and should be subject to a reconsideration request and/or challenge per guidelines included in Chapter 13 of the Medicare Program Integrity Manual[7]. We request that you immediately rescind the Billing Article pending appropriate public comment and response.

We thank you for your attention to this matter of urgency to our patients and would welcome further dialogue on this matter.

Sincerely,



Andreas Zuckermann, MD
President
International Society for Heart and Lung Transplantation

Jason Christie, MD, MSCE
President-Elect
International Society for Heart and Lung Transplantation

References

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