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September 8, 2021

Chiquita Brooks-LaSure, Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS–1753–P
Mail Stop C4–26–05
7500 Security Boulevard
Baltimore, MD 21244–1850

Re: CMS-1753-P — Hospital Outpatient Prospective Payment System, Proposed Rule – Laboratory Date of Service and Packaging Policy

Dear Administrator Brooks-LaSure:

On behalf of the Coalition for 21st Century Medicine (C21), we appreciate the opportunity to comment on the CY 2022 Hospital Outpatient Prospective Payment System (HOPPS) Proposed Rule. C21 continues to strongly support both the existing laboratory date of service (DOS) exceptions policy at 42 CFR 414.510(b)(5) and outpatient packaging exclusion, which have expanded beneficiary access to innovative clinical laboratory testing. As a follow up to the agency's inclusion of cancer-related protein-based multi-analyte assays with algorithmic analyses (MAAA) tests in the DOS policy and outpatient packaging exclusion in last year's rulemaking, we are writing to ensure consistency in applying the DOS policy and outpatient packaging exclusion to tests with a pattern of clinical use that is not connected with the primary hospital outpatient service. As discussed below, we recommend that CMS make the following adjustments to its current application of these policies:

1. **Apply the laboratory DOS policy and packaging policy exclusion to MAAA tests described by Proprietary Laboratory Analyses (PLA) codes; and**

2. **Make the laboratory DOS policy and packaging policy exclusion applicable to all MAAA tests if they are unrelated to the primary hospital outpatient service.**

C21 comprises many of the world's most innovative diagnostic technology companies, clinical laboratories, physicians, venture capital companies, and patient advocacy groups. C21's mission is to improve the quality of healthcare by encouraging research, development, and commercialization of innovative diagnostic technologies that will personalize patient care, improve patient outcomes, and substantially reduce healthcare costs. C21 has worked with CMS

and Congress on the laboratory DOS issue since 2005, and we appreciate the agency's efforts in establishing the current policy at § 414.510(b)(5) and its continued attention to these issues.

Support Laboratory DOS Policy and Outpatient Packaging Exclusion Applicability to Cancer-Related, Protein-Based MAAAs

C21 strongly supports the laboratory DOS policy at § 414.510(b)(5) and the outpatient packaging exclusion for tests that "have a different pattern of clinical use, which may make them generally less tied to a primary service in the hospital outpatient setting than the more common and routine laboratory tests." For the past several years, these policies have improved beneficiary access to precision tests and targeted treatment by removing barriers that once led to delayed and canceled orders.

We likewise support the update to the laboratory DOS policy and outpatient packaging exclusion promulgated in the CY 2021 HOPPS Final Rule, under which CMS added cancer-related protein-based MAAAs, as well as the rheumatoid arthritis-related protein-based MAAA described by CPT 81490, to these policies. C21 agrees with CMS that these revisions are appropriate because "these tests have a pattern of clinical use that make them relatively unconnected to the primary hospital outpatient service during which the specimen was collected and the results of these tests are typically used to determine post-hospital care."[1] We likewise agree that "expansion of the laboratory DOS policy exception at § 414.510(b)(5) to include cancer-related protein-based MAAAs…generally reduces delay with respect to access to these tests and subsequent results."[2] C21 commends the agency on this change, and agrees that it promotes consistency in billing responsibility between molecular pathology tests and protein-based MAAAs that aligns with the similarities in these tests' patterns of clinical use.

Clarify that Cancer-Related Protein-Based MAAAs Include Tests Assigned PLA Codes

A. PLA Code Does Not Impact MAAA's Pattern of Clinical Use

Although C21 strongly supports the inclusion of cancer-related protein-based MAAAs (and 81490) in the laboratory DOS policy and outpatient packaging exclusion, we continue to urge the agency to address the current application of these policies, which excludes cancer-related protein-based MAAAs described by PLA codes from § 414.510(b)(5) and from the outpatient packaging exclusion. As we explained in our comments on the CY 2021 HOPPS Proposed Rule, whether a test is assigned a PLA or Category I CPT code has no bearing on its pattern of clinical use. As such, the clinical rationale for including cancer-related protein-based MAAAs in the laboratory DOS policy and outpatient packaging exclusion applies with equal force to MAAAs described by PLA codes as to MAAAs described by Category I codes.

[1] 85 Fed. Reg. 85866, 86252 (Dec. 29, 2020).
[2] *Id.*

For example, our member Cernostics offers the TissueCypher test to identify high-risk Barrett's esophagus (BE) patients likely to progress to esophageal adenocarcinoma (EAC). TissueCypher has been assigned CPT code 0108U.[3] As evident from the code descriptor, TissueCypher is a cancer-related protein-based MAAA – it involves the algorithmic analysis of 9 protein biomarkers to determine risk of progression to cancer. TissueCypher's clinical use is exclusively to guide longer-term decision-making on BE surveillance intervals and treatment. Samples are collected during a BE patient's endoscopy, which may take place in the hospital outpatient setting. The TissueCypher test report is provided to the ordering physician approximately two weeks after the hospital outpatient visit at which the specimen is taken, and the information in the report is used to determine the patient's longer-term course of treatment. This may include modifying the surveillance interval for the subsequent endoscopy, and assessing whether endoscopic eradication therapy or other therapeutic intervention will be used during the subsequent endoscopy.

Importantly, any future endoscopy (whether surveillance or treatment) will take place at least 30 days after delivery of the TissueCypher result, and more commonly will be 6 months to five years later. It would, in fact, be impossible for a TissueCypher result to impact treatment at the same outpatient visit at which the specimen is collected. An outpatient visit is, by definition, a single-day visit, whereas the TissueCypher result is not available until weeks after specimen collection and is used to guide endoscopy and/or other procedures that generally take place months after the test report. Another of our members' tests, OVERA from Asipira Labs (0003U[4]), is likewise a protein-based MAAA with a similar pattern of use to detect ovarian cancer risk in women with pelvic or adnexal masses in the interest of guiding future treatment.

Given this workflow, cancer-related protein-based MAAAs like TissueCypher and OVERA plainly satisfy CMS' requirement in the CY 2021 Final Rule that such tests "would need to demonstrate a pattern of clinical use that make them relatively unconnected to the primary hospital outpatient service during which the specimen was collected and the results of these tests are typically used to determine post-hospital care."[5] Accordingly, it is appropriate to include them under § 414.510(b)(5) and the outpatient packaging exclusion.

B. Inclusion of PLA Codes Aligns with Agency Practice and Definitions

Along with being inconsistent with the pattern of clinical use of cancer-related protein-based MAAAs like TissueCypher, the current application of the laboratory DOS policy and outpatient packaging exclusion is not in alignment with CMS' practices with regard to other categories of

[3] Gastroenterology (Barrett's esophagus), whole slide–digital imaging, including morphometric analysis, computer-assisted quantitative immunolabeling of 9 protein biomarkers (p16, AMACR, p53, CD68, COX-2, CD45RO, HIF1a, HER-2, K20) and morphology, formalin-fixed paraffin-embedded tissue, algo-rithm reported as risk of progression to high-grade dysplasia or cancer.

[4] Oncology (ovarian) biochemical assays of five proteins (apolipoprotein A-1, CA 125 II, follicle stimulating hormone, human epididymis protein 4, transferrin), utilizing serum, algorithm reported as a likelihood score.

[5] 85 Fed. Reg. 85866, 86254 (Dec. 29, 2020).

tests under the laboratory DOS policy. For example, CMS includes molecular pathology tests on its list of "Laboratory Tests Subject to Exceptions to Laboratory DOS Policy Defined at 42 C.F.R. § 414.510(b)(5)" regardless of whether they are assigned Category I or PLA codes. Tests described by PLA codes are likewise included in the laboratory DOS policy and the outpatient packaging exclusion if they are approved as ADLTs under section 1834A(d)(5)(A) of the Social Security Act. The agency has not articulated a clinical reason for distinguishing between PLA codes and Category I codes in this manner for cancer-related protein-based MAAAs, when it does not do so for other categories of test subject to the laboratory DOS policy and the outpatient packaging exception.

Nor does CMS' exclusion of protein-based MAAAs assigned PLA codes from the laboratory DOS and outpatient packaging exclusion policies find any support in the definition of the term "MAAA". In the CY 2021 HOPPS Final Rule, the agency refers to the AMA CPT definition of MAAAs as "procedures that utilize multiple results derived from panels of analyses of various types, including molecular pathology assays, fluorescent in situ hybridization assays, and non-nucleic acid based assays (for example, proteins, polypeptides, lipids, carbohydrates)."[6] This definition does not distinguish between a test that is assigned a Category I code and one that is assigned a PLA code.

To the contrary, AMA CPT guidance specifically provides that the "PLA Code section…may include a range of medical laboratory tests **including, but not limited to, Multianalyte Assays with Algorithmic Analyses (MAAA)** and Genomic Sequencing Procedures (GSP). The descriptor nomenclature follows, where possible, existing code conventions (e.g. MAAA, GSP)."[7] The application for a new PLA code requires applicants to select the type of test described by the code, listing MAAA as an option, and offering a sample descriptor to follow the MAAA nomenclature. The AMA CPT definition of MAAA and its interpretation of that definition thus support a consistent approach to cancer-related protein-based MAAAs described by Category I and PLA codes in applying the laboratory DOS policy and the outpatient packaging exclusion.

C. CMS Can Update Application of the Laboratory DOS Policy Through Sub-regulatory Guidance

C21 believes that the agency can update its application of the laboratory DOS policy and outpatient packaging exclusion through sub-regulatory guidance (i.e., by adding codes to the agency's online list of "Laboratory Tests Subject to Exceptions to Laboratory DOS Policy Defined at 42 C.F.R. § 414.510(b)(5)", and updating status indicators for such codes to "A" in OPPS Addendum B). The regulatory text of § 414.510(b)(5) applies to "a molecular pathology test performed by a laboratory other than a blood bank or center, a test designated by CMS as an ADLT under paragraph (1) of the definition of an advanced diagnostic laboratory test in §

[6] *Id.* at 86252.
[7] AMA, CPT PLA Codes, *available at* https://www.ama-assn.org/practice-management/cpt/cpt-pla-codes (emphasis added).

414.502, a test that is a cancer-related protein-based Multianalyte Assays with Algorithmic Analyses, or the test described by CPT code 81490." Interpreting the term "Multianalyte Assays with Algorithmic Analyses" to align with the CPT Editorial Panel's interpretation by including PLA codes is not inconsistent with this regulatory language. We urge the agency to announce this adjustment in application of the laboratory DOS policy and outpatient packaging policy in the Final Rule.

Moreover, implementing the inclusion of cancer-related, protein-based MAAAs described by PLA codes in the laboratory DOS policy and the outpatient packaging policy should not be laborious. CMS can identify the protein-based MAAAs in the PLA section of the CPT code book by determining which codes' descriptors include **both** multiple proteins and reference to an algorithm. Alternatively, CMS could work with the CPT Editorial Panel to notify the agency of approved PLA codes that are classified as MAAAs. As discussed above, this information is included in the PLA code application, so the CPT Editorial Panel has access to it. An even less effort-intensive option would be for CMS to add a PLA code that describes a cancer-related, protein-based MAAA to the list of "Laboratory Tests Subject to Exceptions to Laboratory DOS Policy Defined at 42 C.F.R. § 414.510(b)(5)" and change the status indicator for the code to "A" upon request by the performing laboratory and CMS confirmation (based on the code descriptor) that the test is protein-based and a MAAA.

Include Non-Cancer Protein-Based MAAAs

Finally, C21 also believes that the laboratory DOS policy and outpatient packaging exclusion should include all protein-based MAAAs, whether cancer-related or not, because MAAAs generally have a pattern of clinical use that make them relatively unconnected to the primary hospital outpatient service during which the specimen was collected. As discussed in our comment letter on the CY 2021 HOPPS Proposed Rule, we do not believe that a relationship to cancer is an appropriate proxy for whether a protein-based MAAA's clinical use is distinct from the primary outpatient service.

Rather, MAAA tests related to complex conditions other than cancer are similar to cancer-related MAAAs in their typical use, as the results are used to guide longer-term patient care after the patient's outpatient encounter. The agency has already made this determination for one non-cancer related protein-based MAAA. In the CY 2021 HOPPS Final Rule, CMS concluded, based on stakeholder input, that "the pattern of clinical use for [the Vectra rheumatoid arthritis test described by] CPT code 81490 is generally unconnected to the hospital outpatient encounter during which the specimen is collected, as it is typically used to determine potential interventions outside of the hospital outpatient encounter and is generally used by the rheumatologist to make longer-term changes in RA treatment."[8] Most protein-based MAAA tests for complex conditions other than cancer are similarly unconnected in pattern of clinical use from the primary outpatient service.

[8] 85 Fed. Reg. 85866, 86254 (Dec. 29, 2020).

Lastly, including protein-based MAAAs in the laboratory DOS policy will not cause tests performed in the outpatient setting to be included in § 414.510(b)(5) because the existing regulations require tests performed and used during the outpatient encounter to be billed by the hospital. Under § 414.510(b)(5)(i) and (iv), the test must satisfy the requirement that it be "performed following a hospital outpatient's discharge from the hospital outpatient department" along with the requirement that its results "do not guide treatment provided during the hospital outpatient encounter." If the test is either performed before the outpatient's discharge or guides treatment provided at the outpatient encounter at which the specimen is collected, § 414.510(b)(5) does not apply and the DOS is the date of specimen collection, requiring the hospital to bill for the test.

Conclusion

C21 strongly supports CMS' laboratory DOS policy at § 414.510(b)(5) and its outpatient packaging exclusion, as well as the extension of these policies to cancer-related, protein-based MAAAs. To ensure consistency with respect to billing jurisdiction and packaging status for tests that are unconnected to the primary outpatient service, we urge CMS to modify its interpretation of the term "cancer-related protein-based MAAA" to include MAAA tests assigned PLA codes. We believe this change can be implemented through sub-regulatory guidance with minimal effort. C21 likewise encourages the agency to include in the laboratory DOS policy and outpatient packaging exclusion those non-cancer related protein-based MAAAs that, like the Vectra test, are unconnected to the primary outpatient service.

Thank you for considering our comments. Please contact me at hmurphy@c21cm.org or (916) 835-5117 should you have any questions or if we can provide you with further information.

Sincerely,

Hannah Murphy
Executive Director
Coalition for 21st Century Medicine