



ASSOCIATION FOR MOLECULAR PATHOLOGY

Education. Innovation & Improved Patient Care. Advocacy.

9650 Rockville Pike, Suite 205, Bethesda, Maryland 20814

Tel: 301-634-7939 | Fax: 301-634-7995 | amp@amp.org | www.amp.org

October 22, 2018

Seema Verma, CMS Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building, Room 445-G
200 Independence Avenue, SW
Washington, DC 20201

RE: Preliminary Determinations for Calendar Year 2019 (CY2019) for New and Reconsidered Services on the Clinical Laboratory Fee Schedule (CLFS)

Dear Ms. Verma:

On behalf of the Association for Molecular Pathology (AMP), thank you for the opportunity to submit comments on preliminary determinations on the Clinical Laboratory Fee Schedule (CLFS) for calendar year 2019 (CY2019) for new and reconsidered codes. In this comment letter, we have concerns about CMS's "themed" approach to coding, which may lead to suboptimal code determinations. We also address specific codes which deserve additional consideration before their prices are finalized.

AMP is an international medical and professional association representing approximately 2,400 physicians, doctoral scientists, and medical technologists involved with laboratory testing based on knowledge derived from molecular biology, genetics and genomics. Our membership includes professionals from the government, academic medicine, private and hospital-based clinical laboratories, and the in vitro diagnostics industry.

Comments on the Four Themes

AMP recognizes that the evolution and expansion of molecular testing and coding have made it more difficult for CMS and the Advisory Panel to make sound pricing determinations. The themed approach to pricing represents a useful starting point to improve the process. However, AMP is concerned that creating broad parameters and fitting new codes into one of these categories may result in pricing determinations that fail to account for all relevant factors. Pricing determinations for new codes must be considered on a case by case basis and remain consistent with the federal regulations governing payment for clinical diagnostic laboratory tests.

When more than one theme applies to a particular code, the problem will be even greater. For example, consider likely new codes for procedures to analyze a large number of genes and for which stakeholders submit multiple recommendations, each with the same recommended crosswalk but different multipliers. In such scenarios, does CMS recommend (1) that codes be "crosswalked" sans multiplier; or (2) that they go to gapfill? The proposed themes do not provide adequate guidance for these cases.

AMP is also concerned that, if using these themes, CMS may fail to duly consider the Advisory Panel's recommendations. Below, we state our concerns with respect to each theme. We appreciate CMS' attempt to

improve this process, particularly as the number of codes that needs to be priced each year grows, and would welcome the opportunity to discuss our concerns in greater detail. AMP shares CMS's goal to ensure there is appropriate pricing for each code and would like to partner with CMS to refine the system to protect patient access and ensure equitable pricing of laboratory services.

Justification for use of multipliers

CMS is sometimes forced to choose between different proposed multipliers for the same code. AMP understands the CMS position to be that, as a general rule, if a crosswalk is correct, no multiplier will be applied. We agree most crosswalked codes will not require a multiplier with such a large number of molecular pathology procedures now available on the CLFS. However, multipliers may still be necessary and appropriate for certain crosswalks. This is consistent with federal regulations governing payment for clinical diagnostic laboratory tests. Specifically, 42 C.F.R. § 414.508 (2016) allows for the use of multipliers when determining a crosswalk, it states:

(1) Crosswalking. Crosswalking is used if it is determined that a new CDLT is comparable to an existing test, multiple existing test codes, or a portion of an existing test code.

(i) CMS assigns to the new CDLT code, the local fee schedule amounts and national limitation amount of the existing test.

(ii) Payment for the new CDLT code is made at the lesser of the local fee schedule amount or the national limitation amount.

If CMS will not allow the use of multipliers for codes with conflicting recommendations, the likely result will be incorrect pricing determinations. AMP recommends that when stakeholders recommend conflicting multipliers, that CMS consult with the Advisory Panel before making a final determination.

Stacking/bundling existing CDLT codes

AMP understands that CMS is concerned about its ability to make informed decisions regarding crosswalks for proprietary laboratory analysis (PLA) codes that recommend bundling of CLFS CDLT codes. CMS recommends gapfilling a PLA code when stakeholders recommend payment based on stacking or bundling of current codes.

Although PLA codes are created for a single manufacturer or laboratory, ensuring proper pricing of PLA codes is critical for the entire molecular pathology community and Medicare population. PLA codes can serve as crosswalk recommendations once incorporated onto the CLFS. It is important to reiterate that 42 CFR 414.508 allows crosswalking of codes that are comparable to "multiple test codes" and should not be wholly dismissed as a crosswalking option for PLA or any other code set that exists on the CLFS because more than one bundled option was presented.

AMP recognizes that PLA codes present new challenges and that CMS and the Advisory Panel are working diligently to understand the tests and put in place a system to ensure their appropriate valuation. However, as PLA codes become increasingly common, it is even more critical to accurately price them. A process that automatically channels PLA codes for gapfill would increase the risk of inaccurate pricing. AMP has significant concerns about the gapfill process that we recently raised with CMS. In the final rule implementing §216 of the Protecting Access to Medicare Act, CMS stated:

(4) EXPLANATION OF PAYMENT RATES.—In the case of a clinical diagnostic laboratory test for which payment is made under this subsection, the Secretary shall make available to the public an explanation of the payment rate for the test, including an explanation of how the criteria described in paragraph (2) and paragraph (3) are applied.”

Until CMS implements this provision consistently to create more transparency in the gapfill process, and further addresses the issues AMP and others have raised with the gapfill process as it is implemented today, the agency should not increase its reliance on the process.

The American Medical Association (AMA) has stated its willingness to serve as a resource for CMS with regards the unique challenges presented by PLA codes. We recommend that CMS and the Advisory Panel take advantage of AMA’s unique expertise in this area during the summer pricing process. This will result in better-informed and more accurate pricing determinations, which will serve the best interests of both the molecular pathology community and the Medicare patient population.

Codes that analyze a large quantity of genes

CMS acknowledges that there are new test codes with descriptors that include the ability to analyze large numbers of genes and that commenters recommended crosswalk to a code that generically analyzes 51 genes or more. In these cases, CMS states that when crosswalk to the 51+ somatic GSP code (81455) is recommended, they will instead recommend gapfill for these tests because code 81455 is “fairly generic.” Besides our concerns with the gapfill process stated above, we are concerned that automatically mandating codes for gapfill for which a crosswalk of 81455 was recommended in many cases dismisses the expertise and recommendations of the panel and others.

CMS comments that sending these types of codes to gapfill will “allow CMS and contractors the opportunity to gather current information in which the tests are performed and the resources necessary to provide these tests.” This statement implies that CMS did not receive any or adequate information for these services during the annual summer meeting. For instance, the owner of PLA code 0048U presented during the annual meeting and AMP recalls few, if any, follow-up questions asked by CMS seeking additional specifics on the procedure. Additionally, during the Advisory Panel meeting in July, the Panel unanimously recommended that 0048U be crosswalked to 81455. AMP recommends that CMS obtain all the information needed to make an accurate pricing recommendation on these tests during the stakeholder presentations rather than sending these codes automatically to gapfill.

AMP requests clarification on why CMS classifies the descriptor for 81455 as too generic to use for a crosswalk, but the descriptor for other genomic sequencing procedures (GSP) oncology codes for which a large number of genes are analyzed is sufficient (*e.g.*, 81545). Moreover, the sister code to the 51+ somatic GSP code (81455), which is the 5-50 somatic GSP code (81445), has a descriptor with similar language and comparable levels of language specificity, but CMS uses this as a crosswalk quite frequently. If CMS has issues with the descriptor of 81455, AMP recommends that CMS address that concern within the AMA CPT code change process and not dismiss the use of 81455 based on the descriptor language.

Determining crosswalks for new BRCA codes

CMS provides additional rationale for its preliminary recommendations for the *BRCA1* and *BRCA2* codes. In subsequent sections of this letter, AMP addresses specifically the preliminary determinations for 81X78 and 81X81 as well as concerns surrounding use of CPT code 81406 for any code. Additionally, we have concerns about dismissal of stakeholder recommendations that contained a percentage of the NLA for CPT

code 81162. A crosswalk recommendation that is comprised of a percentage or portion of a code is consistent with federal regulations governing payment for clinical diagnostic laboratory tests and should not be dismissed solely based on use of a portion/percentage of a code. Specifically, 42 C.F.R. § 414.508 (2016) allows for a portion of an existing test code when determining a crosswalk, it states:

(1) Crosswalking. Crosswalking is used if it is determined that a new CDLT is comparable to an existing test, multiple existing test codes, or a portion of an existing test code.

(i) CMS assigns to the new CDLT code, the local fee schedule amounts and national limitation amount of the existing test.

(ii) Payment for the new CDLT code is made at the lesser of the local fee schedule amount or the national limitation amount.

AMP seeks clarification on the rationale for CMS' justification for the BRCA new codes preliminary determinations, namely that "the comparable lower payment rate will support a more competitive landscape for these tests to be accessible to a greater Medicare beneficiary population." Under PAMA, market-based pricing is reported by applicable laboratories but pricing for new codes remains dependent on crosswalk and gapfill. AMP disagrees that the recommended pricing will result in a more competitive market and concludes exactly the opposite result if these prices are finalized; a lower reimbursement will pose an insurmountable barrier to entry for new and smaller laboratories. This preliminary pricing falls well below the resources and work required to perform this testing, and as a result, laboratories would likely be forced to cease testing for BRCA.

CY2019 CLFS Preliminary Determinations for New and Reconsidered Codes

AMP presented public comment at both the June 2018 CLFS meeting and the July 2018 Panel meeting, as well as provided written comments to CMS after the meeting. We wish to thank CMS for recommending crosswalks for many of the new CPT codes, however we are concerned that some of the preliminary recommendations provided by CMS differ vastly from both Advisory Panel recommendations and stakeholder input and, in many cases, do not represent the best options for crosswalks. AMP believes these crosswalk recommendations should be adjusted using a pricing determination that more appropriately relate the new CPT codes to existing services already priced on the CLFS.

As dictated by 42 CFR 414.508, crosswalking is used when it is determined that a new CDLT is comparable to an existing test, multiple existing test codes, or a portion of an existing test code¹. In order to determine if this requirement is met, AMP analyzes and compares a number of factors to determine the most appropriate crosswalk, including the analytical methods employed, the overall resources utilized, the types of genetic variants tested (e.g., single nucleotide polymorphisms, deletions, duplications, etc.) and the amount of genetic material interrogated. As we have stated, a large number and wide spectrum of molecular pathology codes are included in the current CLFS, which allows for appropriate crosswalking of new codes to existing codes. It's important to note that crosswalking based on a single criterion (e.g., the type of genetic variant tested) often will not yield the most appropriate crosswalk. For example, for a new code representing a full gene sequence procedure, a number of existing codes may appear to be a viable crosswalk candidate as a handful of full gene sequence codes exist on the CLFS. However, one must also consider other factors before choosing the most appropriate as gene size and content can vary enormously, resulting in vast variability in the amount of resources utilized. It appears from our analysis that a large number of CMS's preliminary recommendations only account for one factor and thus may not be the most appropriate or applicable crosswalk for the new procedures. To assist CMS in finalizing the CY2019 determination, we provide a more detailed rationale for

¹ <https://www.law.cornell.edu/cfr/text/42/414.508>

some of the new codes below and request that CMS reconsider and adopt the crosswalk recommendations provided by AMP, which are also supported by other stakeholders and the experts on the Advisory Panel.

Specific Recommendations for Reconsidered, New Molecular Pathology, Genomic Sequencing and Microbiology Procedures

2019 Reconsidered Procedures

81326 - PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; known familial variant.

CMS proposes to maintain a crosswalk of 81326 (Tier 2 MolPath; Targeted sequence analysis), while AMP and the majority (7) of the Advisory Panel members recommended a crosswalk of 81215 (BRCA1, gene analysis; known familial variant). CMS's rationale to maintain a crosswalk to 81326 is that they did not see ample justification to change the previously recommended crosswalk.

AMP, along with multiple other societies, continues to advocate that 81215 most closely approximates the work and resources required for 81326. A known familial variant can manifest in various forms including a SNP, duplication, or deletion. In both 81215 and 81326, the most common known familial variant of interest may be a duplication or a deletion. The work involved in duplication and deletion analysis is far more complex than SNP identification and often uses an expensive technology called multiplex ligation dependent probe amplification (MLPA). Thus, to reflect the increase in work and resources needed, AMP and the other professional societies believe the crosswalk to 81215 is the most appropriate.

81334 – RUNX1 (runt related transcription factor 1) (eg, acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (eg, exons 3-8).

AMP, other commenters, and the majority of the Advisory Panel (nine votes) recommended a crosswalk to 81259 (HBA1/HBA2 (alpha globin 1 and alpha globin 2)). However, CMS proposes a crosswalk of 81404 ((Tier 2 MolPath); targeted sequence analysis) stating that both 81334 and 81404 appear to describe a similar sequencing technology for targeted sequence analysis and that the descriptor of 81259 is for a full gene sequence.

AMP thanks CMS for soliciting public feedback on their recommendation. We wish to seek clarification on your recommendation as there appears to be a discrepancy in the descriptor for 81404 listed within the CMS preliminary determination document. The actual descriptor for 81404 is "molecular pathology procedure, level 5" and codes for procedures that analyze nucleic acid for abnormalities that may be indicative of a variety of disorders and for a variety of mutation types, including full gene sequence, duplication/deletion analysis and targeted sequence analysis. Thus, the descriptor of 81404 does not align as directly with 81334 as described in the rationale CMS provided in the preliminary determinations. AMP continues to support its crosswalk recommendation for 81334, which is based on a comprehensive analysis of the procedure and is in alignment across amount of DNA content analyzed, test purpose, and method. AMP recommends CMS adopt AMP's recommendation of 81259, which is supported by other laboratory organizations as the majority of the Panel.

2019 New Procedures

0022U - Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence/absence of variants and associated therapy(ies) to consider.

To date, AMP has not provided CMS with any recommendations for 0022U. However, given the proposed crosswalk recommendation we feel it is imperative to comment at this time. 0022U codes for the Oncomine Dx Target Test, which is a qualitative in vitro diagnostic test that uses targeted high-throughput, parallel-sequencing technology to detect sequence variations in 23 genes in DNA and RNA isolated from formalin-fixed, paraffin-embedded tumor (FFPE) tissue samples from patients with non-small cell lung cancer (NSCLC) using the Ion PGM Dx System. This IVD test is used by a number of AMP member laboratories to provide testing to Medicare patients.

The preliminary determination proposed by CMS is a direct crosswalk to 81445. We recognize that CMS was tasked with a number of pricing options for this code and it appears that in this case, CMS chose to use one of their guiding themes (justification for use of multipliers) to arrive at this preliminary determination. Direct crosswalk of 81445 for 0022U as a preliminary determination is evidence for AMP's concern about the use of the themes to price tests as it has resulted in an inappropriate pricing determination. Crosswalk of 81445, which has a national limitation amount of \$597.91, for 0022U does not cover the cost of the resources required to run this test. For example, simply the test kit for this test (not including the upfront costs of instrumentation, training, and validation) costs \$750, with total cost to run this test ranging from \$1,400-\$1,900 per sample. With the preliminary determination of 81445, clinical laboratories will only be reimbursed for one third, or less, of the cost of running the test, forcing providers to no longer offer 0022U. A likely consequence of and only other option for laboratories in place of 0022U would be to use the less efficient method of testing for crucial biomarkers in NSCLC patient samples; laboratories would be forced to offer individual biomarker testing of each analyte, which has been shown to reduce the number of biomarkers than can successfully be performed, and will ultimately result in suboptimal care for Medicare cancer patients as well as increased costs to the Medicare system.

AMP analyzed this code with the goal of providing a more appropriate crosswalk recommendation to CMS as finalizing the preliminary determination will significantly and negatively impact patient access and AMP member laboratories. To do this, AMP compared a number of factors to determine the most appropriate recommendation but was unable to find an existing code on the CLFS that compares to 0022U. Thus, in this case, AMP concluded that gapfill is the only suitable option and recommends that CMS adjust this determination to gapfill.

80X00 - TERT (telomerase reverse transcriptase) (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region).

CMS proposes a crosswalk of 81403 (Tier 2 MoIPath; level 4) while AMP and the majority (10 members) of the Advisory Panel recommended a crosswalk of 81121 (IDH2, common variants (eg, R140W, R172M)). CMS's rationale for this crosswalk is that the code descriptions for 81403 and 80X00 appear to describe a similar sequencing methodology for targeted sequence analysis. AMP reiterates that in order to develop the most appropriate crosswalk, one must look at other factors of the test beyond the similarities in language amongst the descriptors. Both 80X00 and 81121 utilize very similar methodologies and resources. The work required to assess common variants within two distant codons in the *IDH2* gene is similar to that required to assess targeted sequence analysis with the promoter region of the *TERT* gene. Thus, AMP recommends CMS reconsider the crosswalk for 80X00 and adopt a crosswalk 81121.

81X07 - EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence.

CMS proposes a crosswalk of 81406 (Tier 2 MoIPath, level 7), while AMP and the majority of the Advisory Panel members recommended a crosswalk of 81175 (ASXL1, gene analysis; full gene sequence). CMS's

rationale for 81406 is that it appears to use similar sequencing methodology for full gene sequencing. AMP continues to advocate a crosswalk of 81175 for 81X07. While the methodology described for 81X07 is similar to 81406, it does not take into consideration the amount of genetic material assessed and the technical difficulties of sequencing *EZH2*. The recommendation for a crosswalk to 81175 is the result of a comprehensive assessment of the work and resources required to perform this test. *EZH2* has 25 exons with one large exon requiring multiple amplicons for performing sequencing – similar to the *ASXL1* full gene sequencing which has 18 exons and one very large exon. Also, both tests are primarily used in hematologic diseases including leukemia and myelodysplastic syndrome. Given this strong evidence, AMP recommends CMS reconsider the crosswalk for 81X07 and adopt a crosswalk of 81175.

81X10 - PLCG2 (phospholipase C gamma 2) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F).

CMS proposes a crosswalk of 81210 (BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s)), while AMP and the majority (10) of the Advisory Panel members recommended a crosswalk of 81225 (CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17); common variant(s)). CMS's rationale for 81210 is that it appears to use similar resources to analyze specific variants. While the methodologies described for both 81X10 and 81210 appear similar, they do not take into account that *PLCG2* consists of 3 distant codons. For this reason, when AMP developed the crosswalk recommendation for this code, they identified 81225 as the most direct crosswalk due to similar methodologies and the resources utilized for the assessment with 81X10. For these reasons, AMP recommends CMS reconsider the crosswalk for 81X10 and adopt a crosswalk of 81225.

81X78 - BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis.

CMS proposes a crosswalk of 81406 (Tier 2 MolPath, level 7) + 81216 (BRCA2 gene analysis' full sequence analysis). AMP recommended crosswalk of 81408, which was also recommended by a number of other stakeholders. Additionally, this crosswalk received the most votes by the Advisory Panel. 81X78 is one code in the *BRCA* code set, which also encompasses 81162 as well as new codes 81X78, 81X79, 81X81, and 81X82. 81162 is the comprehensive code, encompassing full gene sequencing of *BRCA1*, *BRCA2* as well as full duplication and deletion analysis of each gene.

AMP continues to advocate that crosswalk to 81408 makes the most sense due to the amount of DNA content analyzed. Full sequence analysis of *BRCA1* involves sequencing of 24 exons and full sequence analysis of *BRCA2* involves sequencing of 27 exons, with a total exon content for this code amounting to 51 exons. Procedures categorized under 81408 involve analysis of greater than 50 exons. The combined sequencing analysis of *BRCA1* and *BRCA2* across 51 exons is performed utilizing the same method and resources and is more comparable to the analysis of a 51-exon gene than it is to two separate analyses of a 24- and a 27-exon gene. Performing 81X78 is a single procedure done by bi-directional sequencing of coding regions and well as exon-intron junctions by Sanger or next generation sequencing. Laboratories analyzing for sequence variations in the *BRCA1* and *BRCA2* genes do so at the same time rather than in separate single gene analyses. Thus, the most direct crosswalk is the 81408 which assesses 50 or more exons as the methodology and the amount of DNA sequencing of the large genes, such as DMD, is most similar to new code, 81X78.

81X81 - BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis.

CMS proposes a crosswalk of 81406 (Tier 2 MolPath, level 7). AMP recommended a crosswalk to code 81408 (Tier 2 MolPath, level 9) x 50%, which was supported by three members of the Panel and a significant number of other stakeholders. Similar to 81X78, 81X81 is one code in the *BRCA* code set, which also encompasses 81162 as well as new codes 81X78, 81X79, 81X81, and 81X82. Thus, AMP retains support for its crosswalk recommendation of 81408 X 50%. 81X81 codes for the full sequence analysis of *BRCA1*, and involves sequencing of approximately half the work than what is required for 81408.

8X033 - SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence.

CMS proposes a crosswalk of 81405 (Tier 2 MolPath; level 6) while AMP and four members of the Advisory Panel recommended a crosswalk of 81317 (PMS2 gene analysis; full sequence analysis). CMS's rationale for 81405 is that the description of 8X033 is identical to that listed under 81405. AMP used multiple factors to determine the most appropriate crosswalk for 8X033. It is important to note that for sequencing of *SMN1* extra work is required to differentiate the pseudogene from *SMN1* and correctly identify the location of the mutations that need to be reported. A direct crosswalk to the Tier 2 code of 81405 does not adequately address the amount of work involved to perform the testing to detect mutations within this gene *and* also distinguish that sequence from the *SMN* pseudogene. Further, it is worth noting that when *SMN1* was originally placed in the Tier 2 structure there was concern that it had indeed been misplaced in the incorrect subcategory of Tier 2 codes, which was 81405. AMP recommend CMS reconsider the crosswalk for 8X033 and adopt a crosswalk of 81317.

We thank you for the opportunity to submit these comments on the CY 2019 CLFS preliminary pricing determinations. We believe that the rationale, data, and recommendations provided above will result in more accurate pricing for these laboratory tests. We are happy to answer any questions about our recommendations and provide follow up information. Please direct your correspondence to Tara Burke, Senior Director of Public Policy and Advocacy, at tburke@amp.org.

Sincerely,

Samuel K. Caughron, MD
Chair, Economic Affairs Committee
Association for Molecular Pathology