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Marc Hartstein
Director, Hospital and Ambulatory Policy Group
Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244

Compromise Crosswalk Proposal for Codes G0464 and 81528

Dear Director Hartstein:

Thank you for your continued deliberations regarding payment for new and reconsidered codes on the clinical lab fee schedule. I very much appreciate the time you and your colleagues took to explain the rationale for your preliminary determinations during our October 7, 2015 conference call.

Cable Car understands your position that the authority to consider factors other than test methodology in establishing a crosswalk is uncertain. Irrespective of your regulatory discretion, you have determined that considering cost-benefit data and test purpose would represent a departure from policy precedent. Therefore, the advisory panel also did not consider these factors. Additionally, you communicated your preference for using tier 1 codes in the crosswalk and your inability to unilaterally introduce potential crosswalk codes that were not proposed by commenters.

Cable Car respectfully notes that had these policy determinations been communicated earlier in the reconsideration process, there might have been opportunity for a more robust discussion of the methodological shortcomings of the current crosswalk. However, even at this late date, there remains an opportunity to consider a significantly more equitable crosswalk. Prior to finalizing your reconsideration determination, Cable Car hereby requests that you consider a compromise crosswalk proposal, which is based solely on test methodology.

Please crosswalk codes G0464 and 81528 to the sum of 82274 PLUS 81275 PLUS 81288.

For the avoidance of confusion, please note that Cable Car supports CMS' proposal to delete code G0464 and replace it with code 81528. Codes G0464 and 81528 reference the same test and should have the same payment level. Accordingly, this compromise proposal is intended for both the reconsidered G0464 crosswalk and the new 81528 crosswalk.

The proposed crosswalk is identical to the current crosswalk except for the substitution of newly gapfilled code 81288 (MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) gene analysis; promoter methylation analysis) for the current methylation code 81315 (Pml/raralpha com breakpoints).



Cable Car notes that one panel member expressed concern about the high cost and potential inapplicability of code 81315 at the August 26, 2015 panel meeting, but Mr. Phurrough could not suggest an alternative code absent suggestions from commenters. Following the policy clarifications in our discussion, Cable Car consulted with a practicing molecular pathologist who identified code 81288 as the most methodologically similar tier 1 code.

Cable Car reiterates the detailed analysis of why KRAS should not be included in the crosswalk advanced at the public meeting and in the previous comment letter. KRAS contributes only 3% of Cologuard's sensitivity and appears to have been included in the assay with the express aim of increasing the eventual payment level of the test. Code 81275 is emphatically not reimbursable for screening purposes; the OIG and statutory authorities cited in the previous commentary are clear on the point. However, from a purely methodological standpoint, it is inarguable that Cologuard contains a KRAS assay. If your policy is to consider only test methodology at the expense of all other considerations, Cable Car suggests a compromise. Code 81275 is retained in the crosswalk, and a lower-priced comparator for the one Cologuard component that is not a pre-existing test is proposed. See Appendix A.

There are several reasons why code 81288 is more methodologically similar to the methylation component of Cologuard and the compromise crosswalk proposal is superior to the current crosswalk. Both the Cologuard methylation and code 81288 are methylation analyses of the promoter regions of genes associated with colon cancer. MLH1 methylation analysis is used in the detection of Lynch syndrome, the most common cause of hereditary colon cancer. Although typically administered subsequent to a colon cancer diagnosis, MLH1 methylation assays of tumor analytes are used to screen patients for further genetic testing. (Pérez-Carbonell, L. et al., "Methylation Analysis of MLH1 Improves the Selection of Patients for Genetic Testing in Lynch Syndrome" J Mol Diagn. 2010 Jul; 12(4): 498–504). If test purpose has any bearing on the crosswalk, code 81288 is thus much closer to a colon cancer screening test than a confirmatory diagnostic for acute promyelocytic leukemia.

Like Cologuard, code 81288 targets a DNA biomarker and includes the DNA bisulfite conversion and purification steps omitted from code 81315. See Appendix B. Both 81288 and the Cologuard methylation test are promoter methylation assays. The primary difference between code 81288 and Cologuard is that 81288 is a qualitative test for a single gene, MLH1, rather than a quantitative assessment of two biomarkers. Although Cologuard is a quantitative assay, as previously discussed at the meeting and in public comments, the Cologuard algorithm returns a qualitative result. Sufficiently high concentrations of individual epigenetic markers result in a positive reading. Not shown in the chart in Appendix B is the fact that the full description of code 81315 applies to both qualitative and quantitative versions of the assay. Therefore, if 81315 were similar to Cologuard, it would not be primarily because of its quantitative component. Code 81288 is the better comparator due to its added gene methylation steps.

Code 81288 is a new code in 2015 which was gapfilled after last year's determinations. It was not suitable for a crosswalk previously as it did not yet have a price at the time of last year's determination or the reconsideration request submission. Now that code 81288 is priced, it should be evaluated as a potential component of the crosswalk.



Finally, please note that as of the date of this letter, Cable Car and its affiliates no longer hold a position in the shares of Exact Sciences. Consistent with its fiduciary duties to clients, Cable Car may change its positioning at any time, but the firm presently has no financial interest in the reconsideration process. Cable Car believes commenters' financial interests should be disclosed without impacting your assessment of the merits.

Thank you once again for your consideration and for providing the opportunity for the public to offer input into the Clinical Lab Fee Schedule.

Sincerely,

Jacob Ma-Weaver, CFA



Appendix A: Updated crosswalk recommendation slide

Recommended crosswalk



Cologuard Component	CY2015 Crosswalk	CY2016 Crosswalk (Proposed)	Reconsideration Rationale	Current Payment (CLFS 2015 NLA)	Proposed Payment
Fecal Hemoglobin	82274 <i>FIT</i>	82274 <i>FIT</i>	Code directly describes test method and purpose	\$21.65	\$21.65
2 DNA Methylation Markers	81315 <i>ML/RARalpha</i>	81288 <i>MLH1 methylation</i>	<u>More similar</u> based on steps involved in promoter methylation and use in colon cancer diagnostics	\$282.12	\$159.48
7 DNA Mutation Markers (KRAS)	81275 <i>KRAS</i>	81275 <i>KRAS</i>	Included due to <u>inarguable methodology as a compromise measure</u>	\$196.99	\$196.99
DNA Normalization Markers	N/A	N/A	Quality assurance marker not separately paid by CMS	N/A	N/A
Collection Kit, Algorithm, Compliance	N/A	N/A	Not separately reimbursable	-1.7% adjustment	N/A
Total				\$492.72	\$378.12

2

Appendix B: Comparison between Cologuard methylation, 81315, and 81288 (Modified from Exact Sciences 2014 presentation to CMS)

