Personalized Medicine Coalition

Issue Brief

The Adverse Impact of the US Reimbursement System on the Development and Adoption of Personalized Medicine Diagnostics

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BOSTON HEALTHCARE

Dear Colleague,

This Issue Brief reflects the output of a series of guided discussions held over the summer of 2010 with the members of the Personalized Medicine Coalition Medicare Reimbursement Workgroup. The Workgroup comprises representatives of more than 30 diverse PMC member organizations ranging from development stage diagnostic test companies, to large multinational biopharmaceutical companies, to industry trade organizations. We thank each member for their insightful observations and comments throughout the process, and Boston Healthcare Associates for their facilitation of the discussions and preparation of this brief.

The discussion of reimbursement in health care is challenging, as it is the nexus of patients', payers', providers', and innovators' sometimes competing interests in developing, providing, and accessing health care services. The majority of the Workgroup members expressed a common belief that there are significant problems with the Medicare reimbursement system as applied to personalized medicine, especially personalized medicine diagnostics, and that these problems will continue to inhibit the realization of the benefits of personalized medicine if unresolved. However, some Workgroup participants disagreed with a number of the majority viewpoints, and wherever possible we have endeavored to note those alternative views in the brief.

This document is intended to lay out the scope and nature of the problems that the Workgroup identified, as a necessary prelude to proposing rational solutions. The subsequent proposal of possible solutions will require considerable additional thought and debate, as they are likely to require a fresh look at core concepts underlying reimbursement, such as evidence and its evaluation, and value determination. Nevertheless, we hope that this brief will serve to inform and spark a productive dialog with decision makers in the health care industry, especially in the Administration at the Centers for Medicare and Medicaid Services, and on Capitol Hill.

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December 2010

Introduction and Summary of the Problem

The Personalized Medicine Coalition (PMC) is an independent, not-for-profit educational and advocacy organization formed to advance the understanding and adoption of personalized medicine as a viable solution to the challenges of efficacy, safety and cost in health care, for the ultimate benefit of patients. The PMC educates federal and state policymakers and private sector health care leaders about personalized medicine, helping them understand the science, the issues, and what is needed for the positive evolution of personalized medicine. In this mission, the PMC is keenly interested in addressing structural and systematic aspects of the US health care system that tend to inhibit the evolution and adoption of personalized medicine. One such critical aspect of our health care system is reimbursement for personalized medicine diagnostics (PMDs).

As medicine and our understanding of human biology and genetics have become more sophisticated in recent decades, it has become increasingly clear that individualized aspects of patients cause them to manifest diseases differently and to respond differently – in terms of both efficacy and safety – to medical treatments, especially pharmacotherapies. The resulting uncertainty about who might respond positively or negatively to a particular treatment regimen has significant adverse consequences for the quality and cost of health care: quality is degraded for those patients who do not exhibit net positive treatment responses, while the cost of the failed treatments themselves is wasted, and the overall cost of successful treatment often is increased by the delay in getting to the right therapy. Clearly then, the personalization of medicine offers the potential for increasing quality while decreasing cost, by better defining an individual's disease process and permitting more appropriate targeting of treatment.

By their nature, diagnostic tests play the central role in the personalization of medicine: one can only better characterize a disease process, or predict who might respond well or poorly to a treatment, by measuring some biological characteristic of the patient. In fact, the explosion of human genetic information and advances in diagnostic technology platforms over the past decade have at last permitted real progress in personalized medicine. During this time, we have seen the development and validation of diagnostic tests that examine individualized differences in each of protein expression, gene expression, and the genome, and correlate the results with meaningful differences in disease likelihood and course, as well as treatment suitability. For example, just a few of the tests that have been put into actual clinical practice enable:

- improved surveillance and preventive treatment based on susceptibility risk for breast and ovarian cancer [*BRCA 1,2*];
- identification of colon cancer patients likely to be unresponsive to certain specific anti-cancer agents [*KRAS*];
- targeting of a specific anti-cancer agent to lung cancer patients most likely to respond [*EGFR* expression]; and
- identification of patients likely to respond differently to a variety of drugs because of variation in their metabolism of those drugs [CYP P450 allele identification].

The same biological understanding that has permitted the development of these PMDs has enabled the development of increasingly-targeted small molecule drugs and biopharmaceuticals, often intentionally aimed at altering the function of a specific disease-related biochemical pathway. These new pharmacotherapies often exhibit greater efficacy and fewer side effects than the untargeted drugs that preceded them just a few years before.

However, despite the dramatic growth in the number and power of advanced diagnostic technologies, the increasing clinical utility and economic value of the tests derived from them, and the therapeutic power of the drugs whose use can and should be guided by those tests, the US reimbursement system for diagnostic tests has not evolved to accommodate the development and adoption of PMDs. US reimbursement for diagnostic tests remains grounded in decisions made and systems developed decades ago, reflecting the technologies and tests then in use and the way they were used. The reimbursement framework relies on timelines that progress far slower than the pace of PMD development, evidence requirements that are mismatched with the clinical and economic realities of PMD development, and payment methodologies that do not reflect the clinical utility and economic value of PMDs.

Among the stumbling blocks posed by this system for advanced PMDs are:

- a system of descriptive test codes designed to report methods or individual analytes, but with no mechanisms to reflect differences in clinical results or utilities, or to describe complex tests with advanced methodologies and often multiple analytes;
- a process for coverage determination that has few standards, varies widely from test to test, and may depend on robust outcomes evidence that for PMDs, can be prohibitively expensive and impractical or impossible to gather; and
- a payment system anchored in the costs of tests developed and performed decades ago, and applied variably to novel diagnostic assays.

Consequently, many PMDs, particularly complex predictive tests requiring prospective clinical trials, are not reimbursed appropriately. Such inappropriate reimbursement inevitably tends to inhibit access, as laboratories are incentivized to offer tests that are better reimbursed and reluctant to offer tests that are potentially money-losing, with the unfortunate consequence that some treatment pathways may not be appropriately guided with personalized diagnostic information. Moreover, the opacity of the current reimbursement environment disincentivizes research and development investment in innovative diagnostics and, by extension, diagnostic-therapeutic combinations.

The Centers for Medicare and Medicaid Services (CMS) plays a lead role in determining reimbursement for PMDs in the US. In addition to directly setting coverage policy for over 46 million Medicare beneficiaries, all private payers benchmark CMS coverage decisions in establishing their own policies. Moreover, the Medicare Clinical Laboratory Fee Schedule (CLFS) and Physician Fee Schedule (PFS) set the standard for laboratory test payment, to the extent that new laboratory test codes are not available for use until CMS has finalized payment rates. Therefore, throughout this issue brief we focus attention on CMS's systems for PMD reimbursement as the key to addressing similar issues in the US reimbursement system more broadly. Below we examine in more detail specific issues with the three key aspects of reimbursement – coding, coverage, and payment – that are adversely affecting the adoption of PMDs.

Coding

Test coding and diagnostics reimbursement

The American Medical Association (AMA) has provided a concise history of Current Procedural Terminology (CPT®), including its evolution over time.[1] Briefly, the CPT code system was first developed and published in 1966 and was designed for documentation of physician-performed medical procedures. Between 1966 and the late 1970s second, third, and fourth editions of CPT were published, expanding the range of specialties and procedures included and recognizing advancements in medical technologies. In 1983 the Health Care Financing Administration (HCFA – now CMS) adopted CPT as part of its Healthcare Common Procedural Coding System, thereby establishing it as the *de facto* US standard for reporting non-inpatient medical services. On August 17, 2000, the US Department of Health and Human Services published a final rule adopting the fourth edition of CPT as a mandatory code set for use by covered entities in covered standard electronic transactions (including claims submitted to health plans for non-inpatient medical services) under the Health Insurance Portability and Accountability Act of 1996 ("HIPAA").[2]

Similar to other medical services, laboratory diagnostic tests are described by CPT codes for the purposes of billing, claims adjudication and health services research. According to the AMA, "The purpose of CPT is to provide a uniform language that accurately describes medical, surgical, and diagnostic services…,"[3] and these codes are used to enable the essential standardization required to efficiently process the millions of claims that flow through the US health insurance system annually. By consistently describing services, they allow payers to consistently apply standardized coverage policies and payment amounts to those services.

CPT coding for laboratory diagnostic tests can be analyte- and/or methodology-driven, and the specificity of existing codes determines their applicability to a particular test. Analyte-specific codes are methodology-insensitive and usually describe routine assays with well-established methodologies. An example of such a code is *CPT 83880 – Natriuretic peptide*. Methodology-specific codes describe procedures or steps and are analyte-insensitive. These codes tend to be used for low-volume analytes and "matrixed" multi-step procedures. Examples of methodology-specific codes are *CPT 83902 – Molecular diagnostics; reverse transcription*, and *CPT 88380 – Microdissection; laser capture*. Of particular importance for PMDs are the molecular diagnostics methodology CPT codes, which were created with the intention of being "stacked" in various combinations to describe, as a group, complex molecular diagnostic laboratory tests. The use of these stacking codes has allowed a variety of PMDs to become available without the need either to employ a miscellaneous code as described below, or to apply for a new, unique CPT code.

When neither the analyte nor all of the methodological steps of a test can be described by existing specific CPT codes, a "miscellaneous," "unlisted," or "not otherwise classified (NOC)" code may be required to describe a test until a new CPT code or codes can be applied for and approved. In

1 American Medical Association Physician Resources. Accessed on September 1, 2010 at http://www.ama-assn.org/ama/no-index/physician-resources/3882.shtml.

2 65 FR 50312.

3 American Medical Association Physician Resources, op.cit..

such cases, the insurance claim must be manually examined to determine what service was provided, whether the service was appropriate and medically necessary, and how much (if anything) should be paid for it. These codes also have played an important role in permitting some new PMDs to become accessible to patients before specific codes could be applied for and obtained.

Clearly then, test coding is an essential component of appropriate and timely reimbursement, and therefore access. However, various aspects of the CPT coding system pose significant challenges for PMDs, as described below.

CPT coding often is insufficiently specific, granular, and flexible to adequately differentiate among PMDs.[4]

There are approximately 1250 individual codes currently in the Pathology and Laboratory section of CPT, yet this code set is often insufficient to distinguish adequately among various PMDs that should be separately identifiable.

Consider the application of analyte-specific coding to the range of tests that determine the susceptibility of a tumor to anti-HER2 therapy. Susceptibility could be assessed by measuring HER2 protein levels, RNA levels, or gene amplification. In turn, each of these measurements could be made through different technical methods (e.g., assessment of gene amplification by quantitative PCR vs. fluorescent in situ hybridization (FISH)). A single "HER2" analyte-specific CPT code would fail to differentiate among the various tests that may well have different sensitivities, specificities, applications, clinical utilities, and costs.

Conversely, the application of methodology-specific codes also does not adequately distinguish among PMD tests, as such codes do not describe what is being tested for, and even these step-specific codes often do not capture critical distinctions among tests. For example, while four separate codes[5] describe different methods of mutation identification, none of them provide an opportunity to identify the specific mutation being identified, or the disease or treatment for which the mutation might be tested. As another example, even when two tests have the same steps, their performance characteristics and impact on outcome may be different; the two tests should therefore be separately identifiable for clinical, reimbursement, and health services research purposes.

A further shortcoming of the CPT coding system as applied to PMDs is that, by design, CPT codes are not usually assigned to individual tests. The AMA appropriately endeavors to avoid allowing coding to create competitive advantage for unique medical technologies by not creating "product specific" CPT codes. As a result, the CPT system assumes that all tests described by a code or set of codes are equivalent or interchangeable. As some Workgroup members have highlighted, this can at times work to the advantage of a new PMD for the purpose of establishing reimbursement. The new test may be sufficiently similar to an existing test that it can appropriately use the existing CPT code, thereby giving the test developer the option of accepting the coverage and payment established for the predecessor test or seeking new, unique coding and establishing its own coverage and payment.

4 The AMA has convened the Molecular Pathology Coding Workgroup to consider possible changes to coding for molecular diagnostic PMDs. Please see Appendix 1 for more detail and an analysis of what is reported about this effort.

5 CPT 83904; CPT 83905; CPT 83906; CPT 83914.

However, in too many cases "capture" by existing coding instead results in inappropriate grouping of varied tests. Each PMD has unique performance characteristics and clinical value in which the test's innovator has invested; as a result, grouping it with other tests under the same code(s) may result in inappropriate coverage or underpayment for the innovation represented by the new PMD. Moreover, clinicians, payers, and health service researchers alike may need to distinguish among the different tests, and the current CPT system is a barrier to that distinction. Nevertheless, because at present there often is an inverse relationship between coding specificity and the likelihood of coverage for a PMD, any solution to the current lack of specificity in CPT coding will need to be carefully designed to avoid unintended consequences.

Finally, the CPT system lacks the flexibility to accurately code for tests that could provide one or many analytical and clinical results from the same procedure (e.g., multiplex analyses or whole genome sequencing), or which might provide varying clinical value depending on the disease being tested (e.g., the same multi-gene panel for different cancers). One common characteristic of current and future advanced PMDs is their ability to provide a wealth of analytic and clinically-useful information from a single assay. For example, a whole genome sequencing PMD might be clinically useful for guiding treatment of ten different tumor types based on current information, while two years hence, the same technical assay might guide treatment of twice the number of tumor types simply by drawing on subsequent advances in tumor genetics.

Laboratory test CPT coding is not well suited to coding for information services (e.g., as manifested in algorithms) that may be required to derive clinical information from the results of laboratory procedures.

Reflecting the growing understanding that the individual manifestation of most diseases results from individualized patterns of gene expression, critical information from PMDs increasingly is derived from comparison of a signal array with a database of comparable arrays derived from a patient population, and that comparison must be accomplished through the use of a bioinformatic algorithm. Because current laboratory test CPT coding is analyte- or methodology-driven, it does not provide a means to describe such critical components of many PMDs. While a single code (CPT 87900) has been developed to describe the application of genotypic bioinformatics to the prediction of infectious agent drug susceptibility, this code is far too specific to apply to the vast majority of PMDs that involve bioinformatic algorithms. Moreover, it is difficult to see how even a family of such codes could succeed in describing the wide variety of algorithms and underlying datasets, given the differences in the number and types of biomarkers, as well as the variations in patient databases. As a result, many PMDs require the use of a miscellaneous (NOC) code to appropriately report this essential aspect of their performance.

The need to code many PMDs using miscellaneous (NOC) codes creates operational inefficiencies for payers, test providers, and health services researchers.

As noted above, by their nature miscellaneous codes do not describe a specific service; therefore payers must manually adjudicate claims involving such codes to determine what service was provided and whether it should be covered and paid. As a result, despite the advantage conferred by miscellaneous codes in permitting some new PMDs to come to market before obtaining new specific CPT codes, the need they create to manually review claims requires that the payers maintain a staff of

skilled claims processors, and inevitably delays the processing of the claims. In turn, the laboratories filing the claims must compile and submit additional documentation to describe and justify the tests, and must accept the uncertainty of the payment level to be received as well as the delay in collection of the associated receivable. The lack of specific test identification that results from the need for miscellaneous codes and code stacking, also limits the ability of payers and health services researchers to track test utilization for healthcare management and public health surveillance purposes.

The minimum time required to obtain a new CPT code and have it available for use is incompatible with the rapid pace of advancement in personalized medicine.

The CPT code application process is managed by the AMA according to a calendar published several years in advance. Applications may be submitted for consideration three times a year – generally in March, July, and November. The following summer, CMS considers the valuation for payment of each new clinical laboratory code approved from all of the prior year's submissions, and a process with similar timelines takes place for the newly approved pathology codes. After the valuation process has concluded, the preliminary code values are published later in the summer, and subsequently, final code values are published in the fall for use in January of the next year. Thus, the minimum time in which a new CPT code can be requested and available for billing is 14 months – November of Year 1 to January of Year 3. During this period, if a new PMD is to be used in clinical practice, reimbursement must be obtained by billing with a miscellaneous code, incurring the operational and administrative burden described above and inhibiting adoption that otherwise might be clinically justified. Moreover, this extended timeframe would be problematic even if the granularity issue raised above were addressed: if a granular system of codes is adopted and miscellaneous coding is lost, but the lengthy time needed to get a new code is not shortened, new PMDs would not be able to be coded and paid for months after introduction – making commercial launch of many new tests untenable.

The effective length of this process is further increased by the new code requirement "that the clinical efficacy of the service/procedure is well-established and documented in US peer review literature."[6] The time required to conduct and publish even one such study adds at least an additional year to the new code process. This situation is further exacerbated by the fact that the AMA has not established firm criteria for the quantity of evidence or number of publications that document the clinical efficacy of a new test, so multiple published studies may be required.

Finally, the process for obtaining new CPT codes requires that the test be "performed by many physicians/practitioners across the United States"[7] before a new code is authorized. However, because billing for the test during the initial diffusion period requires use of a miscellaneous code with its attendant burdens, dissemination to many practitioners may be considerably delayed or entirely thwarted. Several years ago, the AMA created a separate class of CPT codes ("Category III" codes) for emerging technologies, which were intended to address this problem in general by permitting the coding of infrequently performed services so that their diffusion could be tracked. In practice, however, payers often use these codes to identify services as "investigational" for non-coverage.

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6 AMA: Criteria for development and evaluation of CPT® Category I and Category III Codes; Accessed on August 29, 2010 at http://www.ama-assn.org/ama/pub/physician-resources/solutions-managing-your-practice/coding-billing-insurance/cpt/applying-cpt-codes.shtml.

7 Ibid.

The use of CPT codes to serve both the purposes of test identification for claims adjudication and specification of payment (per a fee schedule) is problematic for PMDs.

The US reimbursement system generally provides payment for PMDs through fee schedules, in which individual codes are directly linked to specified payments for the corresponding services. Clinical laboratory tests are reimbursed by Medicare through the CLFS, and PMDs performed and interpreted by anatomic pathologists are paid through the PFS. Most US private payers use the Medicare schedules either directly or as a benchmark for their own rate-setting or contracting processes. We discuss the issues for PMDs created by the fee schedule payment system more extensively below, but note here that this one-to-one correspondence between a CPT code and a payment amount is an impediment to the adoption of PMDs.

The assignment of a single payment level to a particular code implies that all tests described by that code *should* be reimbursed the same amount. However, we have seen above that an analyte-specific code may capture a range of different PMDs and methodologies, some of which may be more informational and have greater clinical utility for a particular disease and patient than others. Moreover, the range of tests and methodologies that might be captured by an individual analyte-specific code virtually guarantees that the costs to perform these different tests will vary widely. Therefore, reimbursing all of these tests at the same rate likely favors some and disadvantages others, but under the current reimbursement system there is no certainty that the relatively favored tests also would be the most clinically useful either for a particular patient, or in general.

Coverage and Evidence Standards

Coverage, evidence standards, and diagnostics reimbursement

"Coverage" by a payer is simply the decision to pay some amount for provision of a medical service or item to an insurance plan beneficiary. A coverage decision, whether for an individual claim or as the foundation for a general policy, requires an understanding of what specifically would be paid for (hence the role of CPT procedure coding in providing standardized service descriptions) and the clinical circumstances under which payment would be justified. At its core, a coverage decision reflects a payer's value judgment – incorporating explicit or implicit inputs from clinical science, health economics, and the imperatives of the payer organization – that the item or service is worth paying for. As such, establishment of positive coverage is critical for patients to gain access to advanced medical technology.

For most diagnostic tests, these coverage decisions are implicit – that is, made without development of or reference to a specific policy. In these cases, the circumstances of coverage are non-controversial: such tests often involve well-established technology and well-understood analytes; their appropriate use is often supported by years of clinical experience and commonly accepted; their specific clinical impact may be minor; and/or their cost may be low, posing little financial risk to the payer. These diagnostic tests do not require explicit review for the payer to decide to cover them, and most such claims are reimbursed without review or challenge when they are received.

However, virtually all PMDs do not have these characteristics. In many cases the technology is cutting-edge and the analytes (or analyte combinations) newly-discovered. As new diagnostic tests, clinical experience is not extensive and clinical utility may be determined primarily by the known biology and the initial specific studies that have been conducted. Their clinical impact is high, as many guide high-stakes therapeutic decision making involving costly treatments for diseases with significant morbidity and mortality. Finally, the cost to perform these tests often is high, reflecting their technology content and development investment. These attributes generally lead both public and commercial payers to deny reimbursement for PMDs until they have had the opportunity to conduct specific technology reviews and develop explicit policies addressing coverage. As a result, PMDs are especially vulnerable to the uncertainties of the Medicare coverage determination process, which pose significant challenges for access and adoption as described below.

CMS's coverage determination process lacks sufficient predictability in its evidence requirements.[8]

The Medicare program has two types of explicit coverage policies: Local Coverage Determinations (LCDs), which are developed by Medicare contractors for use within the contractors' jurisdictions, and National Coverage Determinations (NCDs), which are developed by CMS itself and supersede local policies and implicit coverage decisions. Both types of policies are meant to specify services and products considered by CMS to be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."[9] Notably, there is no explicit definition of "reasonable and necessary" specified either in the statute or the Code of Federal Regulations. Nevertheless, both CMS and its contractors ground the determination of "reasonable and necessary" in the available clinical evidence. CMS has stated the following regarding evidence review in making NCDs:

> "When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether the evidence is of sufficient quality to support a finding that an item or service that falls within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. This critical appraisal of the evidence enables us to determine whether: 1) assessment questions specific to the process of the evidence evaluation can be answered conclusively; and 2) the investigational item or service will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.
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> When CMS assesses the clinical evidence of an item or service, we take the following three factors into account: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence about the direction and magnitude of the risks and benefits of the item or service under investigation."[10]

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8 Please see Appendix 2 for an example of how one Medicare contractor has attempted to address coding, coverage, and payment uncertainty.

9 SSA §1862(a)(1)(A).

10 Guidance for the Public, Industry, and CMS Staff: National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development. Document Issued on July 12, 2006.

However, CMS provides little specific guidance about the type and strength of evidence that would suffice, and therefore the means by which CMS and its regional contractors make coverage determinations lacks evidence standards that can be clearly understood by PMD innovators. The agency has developed coverage review steps and bodies with guidance documents describing them,[11] and has made statements in final rules,[12] through MEDCAC process documents[13] and proceedings,[14,15] and in NCDs about its criteria for evidence review, rankings of evidence types, and desire for evidence of impact on clinical outcomes. Review of this information provides some insight into the evidence required for Medicare coverage. Nevertheless, in none of these has CMS promulgated coverage policy criteria that clarify the definitions of critical terms like "reasonable" and "necessary,"[16] the specific role of evidence vs. other criteria, or practical standards for its type,[17] quality, and quantity.

As some in the Workgroup noted, the absence of specific evidence criteria permits CMS and its contractors to exercise flexibility and judgment in the type and quantity of evidence that the agency will accept to justify coverage. This flexibility can and has led to coverage of technologies whose positive clinical impact was apparent, but which might not have met evidence standards set at a level that would ensure clinical utility and improved outcomes. However, an unavoidable corollary of using flexible judgment in determining the adequacy of evidence is uncertainty that any particular body of evidence will suffice. Whereas one coverage decision may seem "lenient" relative to the available evidence, another may seem "strict." Therefore, while some PMDs may benefit from flexibility in evidence standards, others may suffer.

Examination of the positive coverage policy developed for a particular PMD, OncoType DX®, illustrates the lack of clarity in evidence standards. This PMD is a test intended to predict the likelihood of disease recurrence for patients with node-negative, estrogen receptor (ER)-positive breast cancer, and therefore aid in the decision to pursue adjuvant chemotherapy. The following language appears in the contractor LCD for OncoType DX.

> "Based on analysis of peer-reviewed publications, local guidance from Oncology Associations (ANCO, MOASC) as to clinic practice standards of care, extensive national comments from our LCD, and guidance from our Contractor Advisory Committee [CAC] oncologists, Palmetto GBA has determined that the OncoType DX test is considered safe and effective and reasonable and necessary…"[18]

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11 CMS Medicare Coverage Center: Coverage Guidance Documents; Accessed on September 1, 2010 at http://www.cms.gov/center/coverage.asp.

12 68FR 63700.

13 MEDCAC Process For Evaluation of Effectiveness And Committee Operations; Accessed on September 24, 2010 at http://www.cms.gov/FACA/Downloads/recommendations.pdf.

14 Transcript of MEDCAC Meeting on Genetic (Genomic) Testing, 2/25/2009; Accessed on September 21, 2010 at http://www.cms.gov/faca/downloads/id47b.pdf.

15 Transcript of MEDCAC Meeting on Pharmacogenomic Testing in Cancer, 1/27/2010; Accessed on September 21, 2010 at http://www.cms.gov/faca/downloads/id53c.pdf.

16 In 2003, CMS formally abandoned its efforts to develop criteria for Medicare coverage through notice and rule making. See 68FR 55634 – 55635.

17 Note that at present, CMS may not consider the cost of an item or service in determining whether it is reason able or necessary.

18 LCD for OncoType DX Test - Breast Cancer Prognosis. LCD #L28287. Palmetto GBA.

However, neither in the LCD nor elsewhere in its publicly available documents does the contractor state the criteria by which safety and effectiveness were determined, or the relationship of evidence required to establish that the PMD was "safe and effective" to that used to judge it "reasonable and necessary." The innovator of another PMD facing a similar coverage review might reasonably be left to ask questions such as: How were the peer-reviewed publications analyzed? Which aspects of the studies described were viewed positively or negatively? Which publications spoke to safety and effectiveness, and which to reasonableness and necessity? Which comments were impactful, and why? What guidance was received from the CAC oncologists? These questions and others like them remain unaddressed by CMS and its contractors, and therefore even a review of benchmark coverage decisions does not provide much useful guidance for a PMD innovator shaping a clinical development plan.

Knowing that coverage is a necessary condition of commercial success, but unsure of the magnitude of investment in clinical research required to achieve coverage, potential test developers and investors may hesitate to move forward with any but the lowest-risk, highest-payoff PMD candidates. On balance, the resulting uncertainty for PMD innovators has a chilling effect on investment in and development of new PMD tests that may outweigh the ability of some tests to benefit from evidence flexibility. Moreover, it must be noted that addressing this issue by establishing high standards that cannot be met for most PMDs (see below) is not a practical solution, as that would merely substitute one chilling influence for another.

CMS and its contractors are also unclear about the evidence needed to support and establish the amount of "value-based" payment, above and beyond the evidence required simply to support coverage. Value-based payment becomes a possibility when a PMD cannot be adequately described by one or a combination of specific CPT codes, and therefore requires the use of a miscellaneous code.

Despite the many administrative drawbacks of using miscellaneous codes (detailed earlier), one aspect of this type of coding that may be beneficial to PMD developers is that it permits the PMD to escape fee schedule-based payment. Because the Medicare contractor must make a local decision on how much to pay for the test, the test provider has the opportunity to negotiate for a payment based on the value of the test. As PMDs can guide the appropriate use of expensive biopharmaceuticals and, by directing patients into the most efficacious treatment pathways, can add considerably to patients' quality and duration of life, they can have considerable clinical utility and health economic value.

In a few instances, Medicare contractors have been willing to reimburse for this value by setting "value-based" payment rates for certain PMDs. While evidence certainly must be required for CMS and its contractors to make these decisions, innovators needing to achieve reimbursement commensurate with the value provided by their PMD innovations have no guidance from CMS on the number of studies to perform, the preferred design and clinical endpoints, the role of health economic endpoints, or other aspects of their clinical development plans.

Meeting an evidence standard reasonably sure to achieve PMD coverage is often impractical and too costly.

Basing PMD coverage decisions on the rigorous evaluation of evidence speaking to analytical validity, clinical validity, and clinical utility is both good science and sound health care policy, as such a

process should allocate health care dollars only to those tests that enable real improvement in health outcomes. Nevertheless, for several reasons, it is difficult to develop the quantity and type of such evidence for PMDs that clearly has satisfied CMS's evidence needs for coverage in the past. First, as noted above, CMS has not established evidence criteria for coverage. Therefore, to be reasonably certain of success a PMD innovator must anticipate meeting a very high standard, which likely means multiple prospective trials, each requiring numerous sites and a large number of subjects at or above 65 years of age (the Medicare eligibility age). Executing such robust trials for a test that is personalized or applied to a small population is inherently difficult to do. By their nature, PMDs are used for relatively small populations, as they generally are intended to indicate the suitability of a particular course of treatment. As a result, many potential clinical trial sites may have insufficient patient volume, and even for those that do, patient recruitment is slower than for more broadly indicated diagnostic tests.

Second, it is difficult to construct a viable business model for independent (i.e., not sponsored by a pharmaceutical company) development of high levels of evidence to support PMD coverage, especially for PMDs addressing a small clinical population. Development of the type and quantity of evidence that would afford reasonable certainty of coverage costs several million dollars, but the small market for many PMDs and the low payment rates resulting from the current payment setting process (see below) makes it difficult, if not impossible, to recoup that investment. Thus, requiring high levels of evidence for coverage of PMDs effectively orphans many such tests, because the markets are too small to justify the investment.

An example of this conundrum is KRAS mutation testing, which is performed to assess the suitability of patients with advanced colorectal cancer for treatment with certain anti-cancer agents. KRAS testing is covered by Medicare, as described in this excerpt from a Local Coverage Determination:

> "[The contractor] has determined that sufficient literature support now exists to allow coverage for KRAS testing. Its coverage is limited to use in patients with metastatic colorectal cancer for whom either cetuximab (Erbitux) or panitumumab (Vectibix) therapy is contemplated as being appropriate. Although there remain some unanswered questions concerning the role of "personalized medicine," it appears that there is sufficient sensitivity and specificity in the KRAS testing to allow the decision to be made that use of either of the two drugs noted above would be inappropriate if the KRAS mutation is identified."[19]

Examination of the KRAS literature available at the time the LCD was issued reveals that the policy decision appears to have been based primarily (if not exclusively) on clinical literature addressing trials of the drugs whose efficacy is affected by KRAS mutation, and on technology assessment and clinical guideline publications summarizing and effectively endorsing the conclusions of that literature.[20,21] Publications describing independent trials of the KRAS test(s), sponsored by independent test developers, were not cited. In effect, the cost of the evidence development needed

19 LCD for Genetic Testing. LCD #L24308. Noridian Administrative Services.

20 American Society of Clinical Oncology Provisional Clinical Opinion: Testing for KRAS Gene Mutations in Patients With Metastatic Colorectal Carcinoma to Predict Response to Anti–Epidermal Growth Factor Receptor Monoclonal Antibody Therapy. Allegra CJ, et al. J Clin Oncol April 20, 2009:27(12) 2091-2096.

21 KRAS Mutations and Epidermal Growth Factor Receptor Inhibitor Therapy in Metastatic Colorectal Cancer. Blue Cross Blue Shield Technology Evaluation Center Tec Assessment Program January 2009: 23(6).

to establish coverage for KRAS PMDs was borne by the pharmaceutical companies developing the associated drugs.

KRAS testing has a small population (at most approximately 85,000 US patients/year[22]), modest reimbursement at fee schedule rates (approximately $300),[23] and multiple competing tests. The total annual revenue for the entire KRAS testing market therefore is estimated to be approximately $25 million, which then is divided among the various competing test offerings. Thus, it is not surprising that KRAS test innovators did not take the lead in developing evidence for coverage: each would need to rely on the profits from a fraction of $25 million in sales to recoup the millions of dollars of invested in clinical studies for coverage purposes. While the pharmaceutical industry-funded model of coverage evidence development may work economically for a PMD required for the appropriate use of a specific drug, it does not work for independently-developed PMDs, or for those not specifically tied to a particular drug.

Human factors confound PMD coverage review, especially gaps in technical expertise and the availability of CMS and contractor "bandwidth" to address a wide variety of tests.

By their nature, PMDs are technically complex and often involve cutting-edge science, and understanding their clinical utility and appropriate use sufficiently to make informed coverage decisions requires expertise in human genetics, genomics, molecular biology, and cellular biochemistry, among other scientific and clinical disciplines. However, such expertise is in relatively short supply in the medical community, and this shortage is reflected among coverage decision makers at CMS and its contractors. As a result, appropriate and consistent coverage decisions may not be made, or made in a timely manner, as outside expertise from third party technology assessment organizations or the MEDCAC is sought.

Moreover, because under current coding practices many PMDs must be coded with miscellaneous CPT codes for claims processing, often PMDs require explicit review before a claim-specific coverage decision is made. As the number of individual PMD claims requiring coverage decisions increases, the risk of delays and incorrect coverage decisions also increases.

Payment

Payment and diagnostics reimbursement

By itself, coverage of a PMD specifically identified through coding is insufficient for adequate reimbursement, because an appropriate payment level must be applied to the test. The most common method of payment for laboratory diagnostic tests is through a fee schedule, wherein each code used to describe a test is paid at a separate fixed rate. CMS pays for clinical laboratory tests through its CLFS, which is updated, primarily for the addition of new tests, once each year.[24] A few

[22] Estimated from National Cancer Institute SEER data for colorectal cancer stage-specific incidence. http://seer.cancer.gov/.

[23] Estimated from Boston Healthcare Associates primary research, 2010.

[24] A useful concise summary of the history and method of Medicare payment for laboratory tests, including refer ences to relevant statute and regulation, can be found in the introduction to the OIG report "Variation in the Clinical Laboratory Fee Schedule," July 2009; OEI-05-08-00400.

laboratory tests[25] are currently paid under the PFS, but this fee schedule has increasing importance because of proposed changes to coding for molecular diagnostics, which would move these tests to the PFS for payment.

Briefly, the CLFS was established by amendment of the Social Security statute in 1984 for Medicare payment of outpatient laboratory services.[26] At the same time, the initial payment rate for each test was set at 60% of the prevailing charge level for similar clinical diagnostic laboratory tests for the applicable carrier coverage area, and provision was made for the payment rates to be adjusted annually to reflect the Consumer Price Index.[27] Notably, to date, CMS has not established standards or guidelines for carrier use in determining payment for miscellaneous (NOC) codes.

Rate-setting for new tests added to the CLFS takes place through one of two methods specified in regulation: crosswalking and gap-filling.[28] In crosswalking, CMS determines that a new test is comparable to an existing test in terms of analyte or methodology (including, possibly, several different or multiples of existing codes grouped together, or a fraction of an existing code), and then assigns the new test the same payment as the comparable test. Thus, most crosswalked payment rates have their ultimate basis, either directly or through several generations of crosswalking, in the prevailing charges for the lab tests that existed in 1984, as adjusted irregularly for inflation. The gap-filling process is used when CMS determines that a test is not comparable to any existing test in the CLFS, including through the combination or fractionation of codes. In the first year of this process, each carrier determines a carrier-specific reimbursement amount, specifically referencing the following information:

- charges for the test and routine discounts to charges;
- resources required to perform the test;
- payment amounts determined by other payers; and
- charges, payment amounts, and resources required for other tests that may be comparable or otherwise relevant.[29]

In the second year, CMS establishes a National Limitation Amount for the test based on the median of the carrier-specific reimbursement amounts.

The PFS and its underlying conceptual base, the Resource-Based Relative Value Scale (RBRVS) were established by the Omnibus Budget Reconciliation Act (OBRA) of 1989, and its phase-in began in 1992.[30] The PFS is based on the concept that physician services have relative values based on the amount of physician work and the cost of practice expenses and other resources required to deliver them. For pricing purposes, each physician service is divided into the three components: physician work, practice expense, and malpractice expense. Each component is assigned a calculated number

25 Generally speaking, these are tests performed and/or require interpretation by laboratory professionals other than clinical pathologists, and include a number of anatomic pathology procedures such as immunohistochem istry and fluorescence in situ hybridization.

26 SSA §1833(h)(1).

27 SSA §1833(h)(2). Note that the statute provided that the initial payment rates for certain qualified hospital laboratories would be set at 62% of the prevailing charge level. Also, while provision was made for adjusting the CLFS annually for inflation, in practice this adjustment has often been amended or skipped entirely, as occurred most recently from 2004-2008.

28 42 CFR 414.508.

29 42 CFR 414.508(b)(1).

30 SSA §1848(a)(1).

of Relative Value Units (RVUs), which then are summed and converted into a payment amount by the application of a conversion factor. The resource inputs to set RVUs are determined by surveying physicians about the amount of work and the cost of materials and ancillary labor resources used involved in delivering the service. Thus, despite the use of the term "Relative Value" to describe the units used to set payments, the PFS is fundamentally a cost-based fee schedule.

Through the CLFS and the PFS, CMS plays the central role in setting payment for clinical laboratory tests for the entire US health care system. Most private payers also pay for laboratory testing through a fee schedule and commonly either use CMS's fee schedules directly, or as a benchmark, in setting and negotiating their own payment rates. Therefore, the payment decisions made by CMS have wide-ranging consequences for PMDs provided to all types of patients.

Fundamental characteristics of the CLFS and PFS make their application to payment of PMDs problematic.

As noted above, many PMDs are complex with multiple analytes and methodological steps, and, as a result, their coding may not be straightforward. This coding uncertainty has an implication for payment because under these fee schedules, each code has a fixed payment. Therefore, if the coding is uncertain, payment under the fee schedule also will be uncertain, and the actual payment made for the PMD will vary depending on the interpretation of appropriate coding. In practice, some Medicare carrier contractors may not acknowledge a particular code stack, or they may force a test into a code stack or a miscellaneous code depending on which is considered more appropriate by the contractor for payment.

A further shortcoming of the CLFS as it applies to PMDs is that as PMDs become more complex, a professional interpretive component becomes required for some tests performed in the clinical laboratory. This interpretive component is a real clinical service that should be reimbursed, but with the exception of a single molecular diagnostics "interpretation and report" code[31] paying between $5 and $18 (depending on how it is billed) CLFS-based payment of PMDs does not provide for this. Further, while interpretive services performed by physicians are reimbursable under the PFS, qualified Ph.D. scientists who often perform such services in clinical laboratories are not currently authorized to bill Medicare for their services under the PFS.

As discussed above, value-based payment for a PMD sometimes is achievable through negotiation with one or more contractors for laboratory developed tests (LDTs) that require a miscellaneous (NOC) code. However, this pricing model does not work well in practice for test kit manufacturers that distribute their tests as products to many laboratories. While Medicare pricing of laboratory services indirectly affects the price at which test kits can be sold, Medicare does not directly pay for or establish the price of test kits. Further, while one or more laboratories may want to work with a test kit manufacturer in negotiating payment rates with contractors for a particular test, any such negotiations must be carefully conducted to avoid anti-trust issues, and laboratories typically do not want reimbursement for their services negotiated by a third party in their absence. These differences in the pricing models for products that Medicare does not pay for and services that Medicare does pay for help to explain why many PMD developers have elected to launch their tests as LDTs.

[31] CPT 83912.

Finally, with the exception of the few PMDs paid on the basis of negotiated value, the payment available by stacking codes in the CLFS often is insufficient to permit a commercially-viable return on the investment necessary for test development, and to further develop the evidence needed to achieve any necessary regulatory approvals and Medicare coverage. The National Limitation Amounts for the 21 individual molecular diagnostic codes in the 2010 CLFS range from $5.74 to $48.02; all but four pay either $5.74 (8 codes) or $24.01 (9 codes).[32] Clearly, even with numerous steps it is difficult to achieve a total payment of even several hundred dollars. With the costs of discovery, development, regulatory approval, and evidence development for payer coverage totaling in the tens of millions of dollars for many advanced PMDs, and markets for individual tests being relatively small, it is very difficult to establish an attractive return on investment for a test reimbursed in the low hundreds of dollars per test.

The payment-setting process for new PMDs fails to recognize their clinical utility and economic value.

The current crosswalking, gap-filling, and RVU setting methods of establishing payment for new codes have no mechanism for incorporating or reflecting the clinical utilities, or economic and patient values of PMDs. As noted earlier, many PMDs guide treatment decisions that effectively reduce the waste of expensive therapeutics on patients who will not benefit, while reducing downstream costs of treatment by increasing the success rates of immediate treatment. Often these avoided costs can run into the tens of thousands of dollars per patient, while patient gains in additional and higher-quality lifespan add additional value.

Yet, crosswalking PMDs to existing codes picks up only the value assigned to those older codes when they were created – value that in some cases is rooted in prevailing charges from the 1980s. Gap-filling is only slightly better at reflecting the value of a PMD, but because gap-filling for new tests often relies on cost analysis, the resulting payment amount is cost-based rather than value-based. The same shortcoming applies to the RVU setting process; surveying physicians for the amount and cost of resources used also generates a payment that is cost-based.

Implications for Personalized Medicine

Reimbursement in general, and for PMDs in particular, is a complex interplay of codes, coverage decisions and policies, and payment amounts. For reimbursement to be adequate, coding must be clearly understood, appropriate to the service and technology, and consistently and rationally applied. The path to coverage must be apparent, and the standards of evidence clear and appropriately set to be feasible both scientifically and economically. Payment must be sufficient, rationally determined, and grounded in the utility or value of the service being provided. Nevertheless, we have seen that for PMDs, these things generally are not certain today. Left unaddressed, the implications for the evolution and adoption of personalized medicine are serious. We briefly discuss below several of the more important implications.

[32] 2010 Medicare Clinical Laboratory Fee Schedule. Available for download at http://www.cms.gov/ClinicalLabFeeSched/02_clinlab.asp#TopOfPage.

Underutilization of PMDs

For any type of medical technology or service to be provided and appropriately utilized in the US, it must be routinely and adequately reimbursed. The same is true of PMDs. If there is uncertainty about the ability to recoup the cost of performing a PMD test, then the laboratory will not offer it. If the physician must provide an elaborate justification of medical necessity, then the test will not be ordered. If the patient is told that Medicare is unlikely to reimburse, then the test will be refused. In all cases, the patient will be denied the benefits of personalized treatment – the right medicine, at the right time, for the right indication.

For PMDs to be appropriately utilized, there need not be financial incentives for their use: clinicians, payers, and patients all acknowledge the inherent logic and potential advantages of personalizing treatment. However, there must not be financial disincentives, or the sheer inertia of medicine as usual will ensure that it remains the standard.

Underinvestment in Development of PMDs and Personalized Therapeutics

The advance of personalized medicine is driven by investment in the companies that develop the targeted therapeutics and the PMDs that target them. Rational investors require a clear path to gaining a return on their investments and a good understanding of the investment risks entailed. The uncertainty imposed by the current reimbursement system makes it difficult for investors to see clearly whether they will gain a return on investment in PMDs and the therapeutics that depend on them, or fully understand what their risks will be. In response, R&D investment in PMDs is now driven by drug manufacturers developing companion diagnostics for their targeted drugs. Investment in development of other PMD types lags behind, again denying patients the full benefits of personalized medicine.

From company inception through the time that Medicare agreed to cover OncoType DX, the test developer, Genomic Health, Inc., amassed an accumulated deficit of $96 million.[33] That was the cost incurred by *one* company to bring *one* valuable PMD from concept to coverage, navigating the current reimbursement system. If the US wants more such PMDs, development costs must be recoverable with appropriate reimbursement, and reimbursement uncertainty must be reduced. As should now be clear, the current reimbursement system is a central contributor to this cost and uncertainty, and therefore an impediment to the development of PMDs. Addressing the issues outlined in this brief will be essential if we are to see personalized medicine continue its evolution and advancement, and enjoy its benefits.

[33] Genomic Health, Inc. Form 10-K (2005).

Appendix 1: A Medicare Contractor Acknowledges and Attempts to Address Coding, Coverage and Payment Issues

Very recently the Medicare contractor for the California/Nevada/Hawaii (J1) jurisdiction, and the Ohio, South Carolina, and West Virginia (J11) jurisdiction, has posted articles describing its "Laboratory and Molecular Diagnostic Services Program."[1] In outlining the program, the contractor states that its responsibility to "determine reasonable and necessary services and apply fair reimbursement to services that are not listed in the current CMS laboratory fee schedule" is complicated by aspects of the current reimbursement system, with the result that the contractor and CMS are exposed to "vulnerabilities." This program provides processes and criteria by which the contractor will determine coverage and payment for molecular diagnostic and certain other tests, and establishes rules for identification of the tests on claims. The program contains a phase-in period from September 1, 2010 to December 1, 2010; after that time claims must be submitted according to the program rules.

Coding

The contractor acknowledges that the lack of specificity and granularity in the current CPT coding system prevents it from specifically identifying some diagnostic services performed and billed to Medicare. Therefore, it has mandated the program for laboratory diagnostic tests that require multiple methodology-based or miscellaneous (NOC) CPT codes (including, specifically, the molecular diagnostics "stacking" codes). To address this lack of specificity, the contractor now requires that the test or assay name be provided in the description field of claims for these tests. In effect, this carrier is establishing its own system of "word codes" to uniquely identify PMDs, and it states that it will subsequently publish coding guidelines for each assay or test reviewed.

This contractor's attempt to circumvent some of the deficiencies of CPT coding for PMDs is an understandable development, although the proposed "descriptor" method of test identification may be difficult in practical implementation. Nevertheless, the use of non-CPT test identifiers, that themselves do not need to be assigned through another administrative process, provides one option for addressing the problem of long lead times for code assignment that would result from trying to achieve more granularity through the CPT process.

Coverage

As another part of the program, the contractor also has implemented a "Coverage Decision Request Process,"[2] which must be followed for the specified tests to gain coverage or to maintain previous implicit coverage. As described in the contractor's document, this process is considerably more

1 Palmetto GBA, Jurisdiction 1 Part B: Palmetto GBA Laboratory and Molecular Diagnostic Services Program; Accessed on September 4, 2010 at http://www.palmettogba.com/palmetto/providers.nsf/DocsCat/Providers~Jurisdiction%201%20Part%20B~Articles~Lab~88UPT28777?open&navmenu=%7C%7C.

2 Palmetto GBA, Coverage Consideration Request Form; Accessed on September 4, 2010 at http://www.palmettogba.com/Palmetto/Providers.Nsf/files/Coverage_Consideration_Request_Form_PartB.pdf/$File/Coverage_Consideration_Request_Form_PartB.pdf.

specific than those for coverage decision-making by CMS and its contractors in general. Overall, such increased specificity and clarity should tend to improve the predictability of the coverage process.

However, two aspects are of particular note and concern for PMDs. The first is the explicit requirement for substantial published evidence documenting both clinical validity and clinical utility (analytical validity may be substantiated with either published or in-house evidence). The contractor is requiring a minimum of four peer-reviewed publications: two each for clinical validity and utility. The contractor further states that only articles cited in the PubMed database can satisfy this requirement, considering but not counting the published opinions and treatment guidelines of respected clinical organizations such as the College of American Pathologists and the American Society of Clinical Oncology. The second concern is the level of evidence specified in the process to establish clinical utility. The contractor states that a satisfactory published study must have "sufficient numbers of subjects to establish clinical significance and includes [the] Medicare population in [the] study group", and "demonstrate[s] change in physician treatment behavior based on the assay results and/or improved patient outcomes."

Elsewhere in this document, we describe in detail the difficulties inherent in developing such quantities and types of clinical evidence for PMDs. To recap briefly, it is problematic to execute such controlled studies for PMDs in a reasonable timeframe because of the relatively small populations involved, which rule out some potential trial sites and extend the time required for study enrollment at others. More importantly, the expense required to execute two clinical validity studies and two more controlled multi-center clinical utility studies in the Medicare population is prohibitive and decreases the likelihood of a reasonable return on investment in PMD development. On balance, then, while the specificity of the contractor's coverage process is welcome, the specified evidence requirements are likely to inhibit the development of useful PMDs and could threaten coverage and availability of some existing, well-established PMDs.

Payment

The payment aspects of the contractor's program are equally adverse for PMD development, because they appear to apply the most harmful aspects of the current CLFS payment system and reject the concept of value-based payment. The published program description does not explicitly address payment of tests that can be fully described by groups or stacks of methodology-specific CPT codes used in accordance with CPT coding rules. Since payment for such tests previously would be made by summing the CLFS payments for the individual codes in the stacks, it would appear that the contractor intends to continue this practice – which often underpays for the costs of test discovery, product and clinical evidence development, manufacturing, distribution, and use.

The articles note that CMS has not to date published any criteria for determining the payment amount for miscellaneous (NOC) tests, and state the carrier's intention to apply the principles of crosswalking and gap-filling to set payment for such tests. As highlighted elsewhere in this brief, crosswalking and gap filling provide no mechanism for incorporating or reflecting the clinical utilities, or economic and patient values of PMDs, and therefore often result in test payments that are low compared with the value provided.

> Compounding this problem are the contractor's statements that it "is not bound to a reimbursement established by another contractor prior to jurisdictional award" and "may decide to continue the previously established reimbursement during a jurisdictional consolidation, but may [choose] to reassess reimbursement following the consolidation." Taken at face value, these statements imply that the contractor may roll back any value-based payment determinations made by predecessor contractors, revaluing those PMDs on the basis of crosswalking or gap filling.

While this contractor's recognition of the problems caused by the application of current Medicare reimbursement to PMDs is welcome, its proposed solutions are far from a complete remedy for many of the issues described in the brief.

Appendix 2: Reforms to Molecular Diagnostic Test Coding Proposed by the AMA Molecular Pathology Coding Workgroup

Recognizing that the current methodology-based CPT coding for molecular diagnostic tests had become inadequate to handle the increased number and diversity of these tests, over the past year, the Molecular Pathology Coding Workgroup of the AMA has been working to develop a revised system of coding for this section of CPT-4. While meetings of the Workgroup are open to the public, their proceedings are confidential, so there is little publicly-available official information about the proposed changes. Nevertheless, the trade press has obtained and reported[1] information about the proposed changes that the PMC believes to be reliable.

As reported, the proposed new coding structure has two tiers of tests. The first tier will contain about 90 tests that are either commonly performed or for specific (though rare) genetic mutations. This tier is likely to encompass tests such as KRAS mutation identification and cystic fibrosis genotyping. It is unclear from reports the extent to which Tier 1 codes will refer to the analyte alone, or specify both the analyte and the methodology by which it is assayed, but it appears that these codes likely will be analyte-specific.

The second tier is intended to code for more complex tests, which presumably are insufficiently common to be in Tier 1. This tier is reported to have nine levels of increasing complexity, which are expected to capture most other molecular diagnostic assays. The lowest level is characterized by assays of a single SNP assayed by simple methodology, while the highest is intended for tests that characterize more than 50 exons in a particular gene. These codes appear to be methodology-driven. Reportedly, the CPT Editorial Panel is contemplating appointing an expert panel to determine the assignment of specific tests to one of the nine groups.

The Workgroup intends to continue enabling the practice of stacking methodology codes to describe tests that fit into neither Tiers 1 nor 2. Perhaps the most significant change to existing molecular diagnostics coding, however, is that the new codes will be part of the Physician Fee Schedule instead of the Clinical Laboratory Fee Schedule, so a different process will be used to assign reimbursement values to the codes.

The extent to which this new coding system may be able to address the PMD coding issues identified elsewhere in this brief is unclear as yet, but specific issues are discussed below.

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[1] PGx Reporter, genomeweb.com; October 20, 2010.

Coding specificity and granularity

The proposed system appears to assign individual CPT codes to at least 90 specific molecular diagnostic tests. However, it remains uncertain whether the new codes will adequately differentiate among, for example, KRAS testing performed by different methodologies. To the extent that the new codes do not differentiate among methodologies that yield different qualities or quantities of information, and therefore have different clinical utilities, the new Tier 1 codes also will be insufficiently granular. The nine Tier 2 codes are non-specific by design, and therefore stakeholders likely will need to rely on some secondary identification system to designate specific tests.

Coding for information services

In a fee-schedule driven payment environment, it is essential that every aspect of a PMD be taken into account, either through fully granular methodology coding, or through specific individual test codes, for at least the full cost of a PMD to be recognized for payment. Thus the difficulty of coding information services such as multi-variable interpretive algorithms is a significant shortcoming of the current CPT structure. Presumably, the proposed new structure would account for these services either as an inseparable component of specific Tier 1 codes or as part of the test complexity determining assignment to one of the Tier 2 codes. However, more details about the proposed new system are needed to determine whether this is in fact the case.

Use of miscellaneous (NOC) codes

The proposed coding revisions clearly seem intended to reduce the number of molecular diagnostic tests requiring the use of a miscellaneous CPT code. In particular, if the expert panel charged with test assignment acts swiftly to assign new tests to specific Tier 2 codes upon test launch, then the need for miscellaneous codes might truly be reduced. However, notwithstanding the administrative burden they carry, such a reduction of miscellaneous coding is not without its disadvantages. As noted elsewhere in this brief, the claim-specific coverage decisions required when NOC codes are used afford the opportunity to escape fee-schedule based payment and negotiate directly with the payer for value-based reimbursement; this opportunity may be lost under the new code structure. Miscellaneous codes also represent the only opportunity to capture reimbursement for completely new aspects of PMDs. It remains to be seen whether the expert panel will "force-fit" such PMDs with new aspects into one of the Tier 2 codes, or whether genuinely needed miscellaneous coding will survive.

Lengthy process for new code development

Notably, none of the trade press reports about the proposed coding changes mention any specific alterations to the process of obtaining a new CPT code. To the extent that a new test is quickly assigned to one of the Tier 2 codes, then the assignment process could be shorter than the new code process. However, any gain in speed of effective code assignment may be offset by a loss of coding specificity, including the risk of assignment to a code with a fee schedule payment adequate for the "average" test at that level, but inadequate for the specific new test.

Tight linkage of CPT codes and fee-schedule payments

> The new molecular diagnostics codes apparently will be part of the PFS instead of the CLFS. This shift means that physician interpretive services may now be part of each molecular diagnostics code, and that the crosswalking and gap-filling processes of setting new code payments would be replaced by determinations of relative value units and practice expenses. These payment-setting practices offer greater opportunities for the full cost of performing a PMD test to be measured and captured. Nevertheless, they still afford little opportunity for the value of a PMD to be represented in its payment. Moreover, the uncertain granularity of the Tier 1 codes, and certain lack of granularity of the Tier 2 codes, makes it likely that multiple tests, each with a unique cost and value, again will be receiving the same fee schedule payment. Thus, the proposed new coding structure appears to do little to alleviate this issue.

Without question, the AMA's recognition of shortcomings in current CPT coding for molecular diagnostics, and the decision to take action, is a welcome development for personalized medicine. However, it is not clear that the actions taken represent the right solutions for many of the coding issues that have been identified.

Notes

Personalized
Medicine Coalition