News and Notes From the 2009 Carrier Advisory Committee Meeting: Medical Necessity, Off-Label Chemotherapy, and More

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It was a packed house for the 2009 Hematology-Oncology Carrier Advisory Committee (CAC) Network Meeting on July 24, 2009. With health reform and Medicare administrative contractor (MAC) transitions receiving plenty of attention in this year's agenda, tensions ran high at times among the 97 ASCO members in attendance. Two of the most compelling discussions of the day were coverage for off-label uses of anticancer drugs and the medical necessity of oral versus intravenous (IV) antiemetics. Here, we take these discussions to the next level and offer some insight and suggestions to inform decision making among practicing oncologists.

Off Label . . . Out of Luck?

According to the National Cancer Institute (NCI), "frequently the standard of care for a particular type or stage of cancer involves the off-label use of one or more drugs."¹ The US Food and Drug Administration (FDA) has also acknowledged the potential benefits of off-label uses, stating that "under certain circumstances, off-label uses of approved products are appropriate, rational, and accepted medical practice."² This recognition by the NCI and FDA that off-label use of anticancer drugs is both appropriate and widespread lends great support to the oncology community, in which approximately half of drugs prescribed are for indications not listed on drug package inserts.³

The four compendia recognized by Medicare (Table 1) were developed as tools to help insurers and Medicare carriers understand which indications are appropriate for payment without denying patients access to the most current therapy. It would be prohibitively expensive for pharmaceutical companies and the FDA to add to drug labels all of the indications for diseases other than those published in original trials. In addition, the FDA would not be able to keep up with the volume of new indications from the more than two dozen peer-reviewed journals recognized by Medicare for off-label coverage for anticancer therapies alone.⁴

Staying abreast of the current indications in the literature for chemotherapy is a difficult enough task for oncologists, but it is proving so difficult for MACs that they are inadvertently erecting barriers to payment for off-label therapies. Oncologists would do patients a disservice by using only on-label indications. However, when prescribing chemotherapy drugs for off-label indications, oncologists face the dilemma of proving to the carrier that payment should not be denied for the treatment of a specific disease with a given drug.

In the current system, if a drug is listed in the compendia as appropriate treatment for a certain type of cancer, payment is approved for the therapy; this process is designed to accelerate payment decision making by a carrier. If, however, the therapy is not listed, coverage is denied. In that situation, the oncologist can submit phase II (or greater) studies from an approved list of journals (Table 2) and successfully appeal the determination. Appeals are costly and time consuming, and they delay payment.

The four currently approved compendia are: *American Hospital Formulary Service Drug Information*, *National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium*, *Thomson Micromedex DrugDex*, and *Clinical Pharmacology* (Table 1). The Centers for Medicare and Medicaid Services (CMS) requires coverage of an indication if it is listed in one of the compendia; denial of coverage is required if it is listed as "not recommended" in any of the four compendia (despite what the others may say concerning the same indication).

TrailBlazer Health Enterprises (Dallas, TX) is the MAC for the J4 and J7 regions (the J7 contract is in dispute as of this writing). Currently, TrailBlazer is interpreting the CMS requirement to mean that oncologists wishing to obtain payment for off-label use must submit all four compendia. First Coast Service Options (St Augustine, FL) has also asked for all four compendia plus references in peer-reviewed journals. This is a problem, because it is expensive to subscribe to all four compendia, and it is quite time consuming to submit all of them for all of the off-label therapies oncologists use, not to mention sending additional documentation from the literature. *Clinical Pharmacology* costs \$495 per person per year (institutional and group purchasing organization prices vary); *Thomson Micromedex DrugDex* costs \$1,285 for six to 10 users (more for larger groups); *American Hospital Formulary Service Drug Information* carries a list price of \$269 per subscription (discount for five or more subscriptions); finally, *NCCN Drugs and Biologics Compendium* costs \$499 per person per year (bulk discounts start at four subscriptions). The NCCN rate is relatively new; before April 1, 2009, access to the compendium, chemotherapy templates, and guidelines were free to the public with site registration. According to Bill McGivney, PhD, chief executive officer of NCCN, the reason for the change was multifaceted. However, he stressed that recommendations are still available free of charge through the guidelines. United Healthcare (Minnetonka, MN) customers also get free access to the compendium and templates in

Table 1. Medicare-Recognized Drug Compendia

Compendium	Effective Date of Recognition	Covered Uses	Noncovered Uses
<i>American Hospital Formulary Service Drug Information</i>	1993	Narrative text is supportive	Narrative text is not supportive
<i>National Comprehensive Cancer Network Drugs and Biologics Compendium</i>	June 5, 2008	Category 1 or 2A	Category 3
<i>Thomson Micromedex DrugDex</i>	June 10, 2008	Class I, IIa, or IIb	Class III
<i>Clinical Pharmacology</i>	July 2, 2008	Narrative text is supportive	Narrative text is not supportive

NOTE. Table adapted.⁴

addition to the guidelines, thanks to the company's contributions to offset cost.

The development of compendia has become a profitable business, and as customers of this business, we have options.

Table 2. Medicare-Recognized Peer-Reviewed Journals for Off-Label Coverage Decisions for Anticancer Therapies

Journal
<i>American Journal of Medicine</i>
<i>Annals of Internal Medicine</i>
<i>Annals of Oncology</i>
<i>Annals of Surgical Oncology</i>
<i>Biology of Blood and Marrow Transplantation</i>
<i>Blood</i>
<i>Bone Marrow Transplantation</i>
<i>British Journal of Cancer</i>
<i>British Journal of Hematology</i>
<i>British Medical Journal</i>
<i>Cancer</i>
<i>Clinical Cancer Research</i>
<i>Drugs</i>
<i>European Journal of Cancer</i> (formerly <i>European Journal of Cancer and Clinical Oncology</i>)
<i>Gynecologic Oncology</i>
<i>International Journal of Radiation, Oncology, Biology, and Physics</i>
<i>Journal of the American Medical Association</i>
<i>Journal of Clinical Oncology</i>
<i>Journal of the National Cancer Institute</i>
<i>Journal of the National Comprehensive Cancer Network</i>
<i>Journal of Urology</i>
<i>Lancet</i>
<i>Lancet Oncology</i>
<i>Leukemia</i>
<i>New England Journal of Medicine</i>
<i>Radiation Oncology</i>

NOTE. Table adapted.⁴

The first concerns the current status quo: Every practice purchases the compendia every year at considerable expense and then must appeal at least half of all the chemotherapy administered in the office or infusion center. When every office or center continues to independently appeal every off-label indication, oncology practice becomes far more expensive, and payment is more delayed than is necessary, without adding benefit to patients or providers. The second is to find an alternative, and we propose three possibilities:

- Oncologists could form a clearinghouse that maintains a database of successful appeals for a given indication so that other practices using the same drug for the same disease can submit the same information without duplicating efforts. ASCO would be the ideal organization to provide this resource.
- Oncologists could demand that the developers of the four Medicare-approved compendia hold a consensus conference whenever one of the four lists as "not recommended" a drug approved by the other three. In doing so, we could compel them to eliminate the need for appeals resulting from a single nay despite three approvals.
- Oncologists could promote the requirement that any compendium viewed as authoritative by CMS be made available to the public online, free of charge.

Interestingly, CMS remarks in 2008 suggested that our third idea would be an appealing change: "We believe the public should have access to such materials as necessary to determine if a compendium's actions are indeed consistent with its stated policies. As Medicare beneficiaries who have cancer have the greatest personal stake in this issue, indeed their lives may hang in balance, we believe that public access is less meaningful if it is not provided broadly. Thus, as provided in regulation, we will consider broad access of the compendia to the general public as an additional reasonable factor."⁵ In the same document, CMS praised the *NCCN Drugs and Biologics Compendium* for its free online access, calling it "a significant positive attribute" that "supports public transparency and facilitates...independent review." There are clear advantages to making compendia contents publicly available at no cost, and CMS recognizes them—a powerful step toward mandating this change.

Regardless of which, if any, of these suggestions are implemented, we must examine ways to control costs while

reducing the undue burden that keeps us from devoting the lion's share of our time to patient care. As Medicare payment remains at or below the cost of providing care, the economy continues to founder, and health reform looms on the horizon (as of this writing), any unfunded administrative requirement is an unacceptable burden and could threaten access to appropriate cancer care for Medicare beneficiaries, who number close to 40 million.⁶

In the Eye of the Beholder?

Medical necessity, like beauty, can often be a matter of taste or personal opinion. But as the discussion indicated at the 2009 CAC meeting, the idea of “to each his own” does not work for medical necessity. This conclusion was prompted by a 2008 National Government Services (NGS; Indianapolis, IN) local coverage determination (LCD) update for L25820, entitled “LCD for Drugs and Biologicals, Coverage of, for Label and Off-Label Uses (L25820),” which deals with medical necessity of IV versus oral administration.⁷ An excerpt from the Limitations section of this document summarizing the takeaway from the LCD update is provided here.

This LCD update essentially requires that if oral antiemetics are available, the treating physician must use multiple oral formulations before IV drugs will be covered. NGS is not the only MAC to take this position on oral versus IV antiemetics. Also in late 2008, First Coast made a similar statement about coverage of oral versus IV Emend (aprepitant [oral] and fosaprepitant dimeglumine [IV]; Merck, Whitehouse Station, NJ).⁸ It stated, in part, that “for Medicare Part B to cover the intravenous (IV) product, the IV route of administration

must meet the criteria for what is considered ‘reasonable and necessary’...which indicates medication given by injection is not covered if standard medical practice indicates that the oral administration of the medication is effective and is an accepted or preferred method of administration.” Because there is no national coverage determination on this matter, First Coast will review claims for IV fosaprepitant dimeglumine on a case-by-case basis to determine whether they meet the medical necessity criteria contained in the Medicare Benefit Policy Manual.⁹ Palmetto Government Benefits Administrators (Columbia, SC) followed suit with its 2008 article “Clarification for Billing Part B versus Part D for the Anti-emetic Aprepitant (Emend).”¹⁰

CAC meeting attendees expressed concern that this policy could potentially be applied to all medications, not just oral antiemetics. (The debacle over coverage for subcutaneous growth factors several years ago comes to mind; former director of First Coast Medical, Sid Sewell, MD, FAAFP, posited that they were comparable to insulin, should be self-administered, and should not be covered.) If this were the case, drugs such as iron, dexamethasone, diphenhydramine, and even potentially some chemotherapeutic drugs would require oral administration before IV administration; otherwise, those medications would not be covered.

ASCO responded to this change in coverage policy with a letter to Barry Straube, MD, acting CMS chief medical officer, in February 2009,¹¹ which stated that “intravenous antiemetics are to be denied coverage in favor of oral antiemetics only if use of oral antiemetics—rather than intravenous antiemetics—is the established medical practice in the circumstance at issue.” ASCO asserted that the

Excerpt From the NGS LCD Update for L25820

The local coverage determination (LCD) publication by the National Government Services (NGS), entitled “LCD for Drugs and Biologicals, Coverage of, for Label and Off-Label Uses (L25820),”⁷ affects coverage approval for the use of oral and intravenous antiemetics on the basis of medical necessity, much to the concern of the oncology community. The salient portion of the document reads:

“Not only does the indication for the use of the drug need to meet medical necessity requirements, but the route of administration is also subject to medical necessity criteria. *Contractors must continue to apply the policy that not only the drug is medically reasonable and necessary for any individual claim, but also that the route of administration is medically reasonable and necessary. That is, if a drug is available in both oral and injectable forms, the injectable form of the drug must be medically reasonable and necessary as compared to using the oral form.* (Pub 100-02, Medicare Benefit Policy Manual, Chapter 15, Section 50.2—Determining Self-Administration of Drug or Biologic [Rev. 91; Issued: 06 to 20-08; Effective/Implementation Date: 07 to 21-08]). *Medication given by injection (parenterally) is not covered if standard medical practice indicates that the administration of the medication by mouth (orally) is effective and is an accepted or preferred method of administration.* (Pub 100-02, Medicare Benefit Policy Manual, Chapter 15, Section 50.4.3) Specifically, for antiemetic medication, CMS states: *It is recognized that a limited number of patients will fail on oral antiemetic drugs. Intravenous antiemetics may be covered (subject to the rules of medical necessity) when furnished to patients who fail on oral antiemetic therapy.* (Pub 100-02, Medicare Benefit Policy Manual, Chapter 15, Section 50.5.4)

... Medical necessity is not demonstrated in the cases where a patient has not taken the oral medication, for patient or provider convenience purposes, or for financial or emotional reasons; and such claims are subject to denial.”

standard practice of antiemetic administration in conjunction with anticancer chemotherapy was indeed IV administration, and thus the policy announced by NGS and echoed by others was inconsistent with national Medicare policy and would adversely affect Medicare patients. The letter concluded: "ASCO sees no basis for the new NGS policy, which purports to be simply an implementation of longstanding Manual provisions even though no other contractor has interpreted the Manual in this manner. ASCO respectfully requests that CMS direct NGS to rescind its recent policy announcement and to cover medically necessary intravenous antiemetics without requiring a showing that the patient has failed on oral antiemetics." To date, there has been no official response to ASCO's letter; unofficially, CMS has taken the position that determination of coverage on this issue is up to carrier discretion.

The breakout session on oral and IV antiemetics at the CAC meeting was host to enthusiastic debate. The carrier medical directors expressed a need for sufficient medical necessity justifying use of IV drugs, such as documented reasons why a patient could not tolerate oral medications. Such indications could include radiation mucositis, esophageal cancer, bowel obstruction, and severe anticipatory nausea and vomiting. The carrier medical directors present did not agree that patient compliance and convenience were sufficient reasons for use of IV antiemetics. CAC members posited that IV antiemetics have been and continue to be the standard of care nationwide, an argument that echoed ASCO's letter to CMS and that is supported by guidelines from ASCO, the NCCN, and Cancer Care Ontario. They also highlighted the fact that IV administration is routinely the control route of administration in randomized clinical trials, providing additional support for its position as the standard of care. These points yielded no agreement.

Although beauty may certainly be in the eye of the beholder, medical necessity cannot be decided by differing interpretations; the result is inconsistent and inadequate care for our patients. Without additional clarification from CMS, practitioners are at risk for an unfavorable coverage decision after the fact, leading to greater financial uncertainty in an already unstable economy. Mandating oral antiemetics may

also result in more hospital admissions for nausea and vomiting, a cost our system can ill afford. This could send us back to the "bad old days," when chemotherapy had a well-deserved reputation for causing vomiting, and we had to administer many drugs in the hospital. IV antiemetics have made chemotherapy more tolerable for patients, increased compliance with treatment regimens, and turned around the concept of cancer as completely destroying quality of life. It will be to the detriment of our patients and the practice of oncology as a whole if we lose this progress as a result of ill-informed coverage policies.

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