



December 23, 2004

Steve E. Phurrough, MD, MPA  
Director  
Coverage and Analysis Group  
Centers for Medicare & Medicaid Services  
Mail Stop C1-09-06  
7500 Security Boulevard  
Baltimore, MD 21244-1849

**Re: Draft Decision Memorandum for Anticancer Chemotherapy for  
Colorectal Cancer (CAG-00179N)**

Dear Dr. Phurrough:

The Biotechnology Industry Organization (BIO) appreciates this opportunity to comment on the Centers for Medicare and Medicaid Services' (CMS) draft coverage decision memorandum for anticancer chemotherapy for colorectal cancer (CAG-00179N). BIO is the largest trade organization to serve and represent the biotechnology industry in the United States and around the globe. BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers, and related organizations in the United States. BIO members are involved in the research and development of health-care, agricultural, industrial and environmental biotechnology products.

Representing an industry that is devoted to discovering new cures and ensuring patient access to them, BIO supports expanded Medicare coverage for drug and biological therapies. We commend Medicare's current local coverage rules for helping to ensure that Medicare coverage keeps pace with advances in standards of care, and we applaud CMS' desire to encourage

seniors to participate in clinical trials by expanding Medicare coverage for certain drugs and biologicals. We note, however, that the draft decision memorandum raises numerous legal, practical, and policy questions that must be answered before we can fully support the effects of the proposed coverage decision. BIO is committed to working with CMS to resolve these issues in a manner that will best protect patient access to innovative therapies.

**BIO supports Medicare’s current coverage rules<sup>1</sup> and procedures for off-label uses of drugs and biologicals, and we urge CMS to clarify that these policies are not altered and should be applied as they are today.**

Medicare’s current coverage policies for off-label uses of drugs and biologicals work well to ensure beneficiary access to critical therapies. The practice of medicine, especially oncology, constantly evolves (approximately every six months) through the incorporation of clinical evidence into improved standards of care. Current Medicare coverage policies support this evolution by allowing carriers to respond quickly to advances in care and new research thereby reducing beneficiaries’ wait for access to innovative therapies. Under these policies, carriers enjoy the flexibility to cover off-label uses of therapies that are listed in selected compendia, supported by clinical research that appears in peer-reviewed medical literature, or are “determined by the carrier to be medically accepted generally as safe and effective for the particular use.”<sup>2</sup> The current off-label policies also allow physicians to exercise their professional judgment in choosing the best treatment options for their patients. We urge CMS to continue to apply these policies and leave the current local coverage process intact.

In the draft decision memorandum, CMS respects the importance of Medicare’s current local coverage policies, but further clarification that the proposed national coverage determination (NCD) would not upset these policies would help ensure beneficiary access to the current standards of care. However CMS decides to proceed, the agency should clarify that it does not intend to effect coverage for off-label uses of these four therapies outside the nine selected trials. Specifically, we urge CMS to reiterate that

---

<sup>1</sup> As described in depth below, we support CMS’ current policy regarding off-label use of anti-cancer drugs as expressed in the Medicare Benefit Policy Manual (CMS Pub. 100-02), ch. 15, § 50.4.5 and applied by contractors today.

<sup>2</sup> Medicare Benefit Policy Manual (CMS Pub. 100-02), ch. 15, § 50.4.5.

local carriers are permitted to cover these therapies outside the context of the NCD. Although the draft NCD states that it “makes no change in coverage for any off-label uses of these drugs not provided in the selected clinical trials,” it also says, “contractors would continue to provide coverage for medically accepted uses of off-label indications when such uses are supported by evidence appearing in CMS-approved peer-reviewed medical literature.”<sup>3</sup> This statement omits an important element of the current off-label coverage policy, local carriers’ discretion to cover uses they determine to be “medically accepted generally as safe and effective for the particular use.” BIO urges CMS to include this statement in any final NCD to ensure that local carriers continue to provide access to innovative therapies.

To prevent confusion among carriers and the public about the NCD’s scope, we also recommend that CMS change the NCD’s title to accurately reflect its contents. The title, “Anticancer Chemotherapy for Colorectal Cancer,” suggests that the NCD applies only to colorectal cancer, when the trials to be covered would study six kinds of cancer. Renaming the NCD with a more appropriate title, such as “Expanded Coverage of Clinical Trial-Based Uses of Oxaliplatin (Eloxatin®), Irinotecan (Camptosar®), Cetuximab (Erbix™), and Bevacizumab (Avastin™),” would help beneficiaries, providers, and contractors to better understand its purpose.

### **CMS proposes significant policy changes in the draft that are inappropriate for a NCD.**

CMS is using this draft decision memorandum to request comments on a significant new policy that reaches far beyond coverage for four anticancer chemotherapeutic drugs and biologicals. As CMS recently acknowledged, the agency is developing a new role for Medicare by using its coverage decisions to expand clinical research of drugs and biologicals.<sup>4</sup> CMS has chosen to use this draft decision memorandum to seek comments on how to fulfill this role for all therapies, not just the four chemotherapeutic agents named on the NCD tracking sheet. BIO understands the importance of valid clinical data in making patient care decisions, and we appreciate CMS’ desire to rely on clinical evidence to support coverage decisions. We also believe CMS’ plans to collect, analyze, and use data for coverage

---

<sup>3</sup> Draft Decision Memo for Anticancer Chemotherapy for Colorectal Cancer (CAG-00178N), Nov. 1, 2004, available at <http://www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?id=90>.

<sup>4</sup> Gina Kolata, Medicare Covers New Treatments With a Catch, New York Times, Nov. 5, 2004 (quoting Dr. Sean Tunis on a “whole new role for Medicare”).

decisions merit serious discussion with all of Medicare’s stakeholders in an appropriate forum. However, the NCD process is not the appropriate forum for a policy discussion of this scope and significance.

CMS’ longstanding practice is to use the NCD process to determine whether specific items or services are “reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.”<sup>5</sup> Historically, CMS has used this process to evaluate scientific and clinical evidence to address narrow coverage issues for “a particular item or service,”<sup>6</sup> not to develop expansive new Medicare policies as presented here. The NCD development process, reiterated in section 731 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, was designed to enable timely review of the scientific evidence measuring the medical benefits of a particular item or service and to allow public notice and comment on coverage decisions.<sup>7</sup> The process’s short drafting period and informal means of announcing proposed decisions are appropriate because each NCD is intended to affect only a limited portion of the Medicare benefit. This process would not be sufficient, however, for a proposal to fundamentally change CMS’ coverage decision-making process or the requirements for coverage.

This draft decision memorandum departs from CMS’ well-established practice and the statutory requirements for NCDs. In this memorandum, CMS uses a different approach to making coverage decisions. Instead of being based on available evidence measuring the medical benefits of a therapy, their new approach would base a coverage decision on the need to collect more data. Additionally, CMS proposes to apply this policy not to a specific item or service, but to four distinctly different drugs and biologicals, used in combination with each other and with five other therapies. This departure from CMS’ standard coverage decision process does not belong in a NCD draft decision memorandum.

CMS’ additional requests for input in the draft decision memorandum further demonstrate the agency’s misguided use of the NCD process to

---

<sup>5</sup> Social Security Act (SSA) § 1862(a)(1).

<sup>6</sup> The Medicare statute defines an NCD as “a determination by the Secretary with respect to whether or not a particular item or service is covered nationally” by Medicare. SSA §§ 1862(l)(6)(A), 1869(f)(1)(B). CMS has interpreted this to mean “a national policy statement granting, limiting, or excluding Medicare coverage for a specific medical item or service.” CMS, Medicare Program; Revised Process for Making Medicare National Coverage Determinations, 68 Fed. Reg. 55634, 55635 (Sept. 26, 2003).

<sup>7</sup> See SSA § 1862(l)(3).

announce major changes in coverage requirements. CMS attempts to use the NCD comment period to solicit ideas and strategies on wide-ranging policy matters that affect far more than the four therapies named in the NCD, including:

- incorporating input from patient groups, medical professional organizations and other stakeholders into the clinical trial selection process;
- soliciting and facilitating the participation of beneficiaries in selected clinical trials;
- implementing programs that allow both coverage of the off-label use of anti-cancer chemotherapeutic agents and collection of data to advance knowledge in the appropriate use of these agents outside of a clinical trial setting, e.g., drug registration programs;
- enabling more timely contractor determinations of medically accepted off-label indications on a local level; and,
- potential improvements in the guidance provided to contractors regarding coverage of off-label uses of these and other anti-cancer drugs.<sup>8</sup>

These questions are directed toward CMS' efforts to establish a new role for itself in evaluating innovative technology. The questions do not serve the purpose of a draft decision memorandum for a specific national coverage analysis, which is to "lay out and describe the analytic framework for [a] decision under NCD review."<sup>9</sup> These topics do not belong in a draft decision memorandum, but rather are addressed appropriately in a forum that allows for broader notice to the public and fuller opportunity to comment. If the agency wishes to establish new rules and procedures for all Medicare coverage decisions, it should reissue these questions in a more appropriate forum.

**BIO supports coverage expansions, but the draft decision memorandum leaves too many questions unanswered for us to fully endorse it.**

CMS described this draft NCD as a "coverage expansion,"<sup>10</sup> providing Medicare payment for oxaliplatin (Eloxatin®), irinotecan

---

<sup>8</sup> Draft Decision Memo for Anticancer Chemotherapy for Colorectal Cancer (CAG-00178N), Nov. 1, 2004, available at <http://www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?id=90>.

<sup>9</sup> 68 Fed. Reg. at 55635.

<sup>10</sup> CMS Press Release, Medicare Launches Efforts to Improve Patient Care for Cancer Patients, Nov. 1, 2004, available at <http://www.cms.hhs.gov/media/press/release.asp?Counter-1244>.

(Camptosar®), cetuximab (Erbix™), and bevacizumab (Avastin™) when used in selected clinical trials. At this point, however, we are unable to assess whether this NCD would actually improve beneficiary access to these therapies or other innovative drugs and biologicals. The effects of the coverage proposal cannot be determined until its many unanswered questions are addressed.

Our primary concern is to provide beneficiaries access to these innovative drugs and biologicals in the nine selected trials – as well as access to other cutting-edge therapies in the future. We have not been able, through repeated attempts, to answer many of the basic questions that CMS and the National Cancer Institute (NCI) recommend patients ask before participating in clinical trials. These questions include:

- Who is eligible to enroll in the study?
- What is the purpose of the study?
- How do the possible risks and benefits of the trial compare with those of other options?
- What kinds of treatment, medical tests, or procedures will the participants have during the study? How much will patients have to pay for these services?
- Where will participants receive their medical care? Will participants be able to see their own doctor?
- How long will participants need to stay in the study? Will beneficiaries who must drop out of a trial prematurely still receive Medicare reimbursement for their course of therapy?
- How will the results be shared?<sup>11</sup>

The answers to these questions will determine what effect, if any, the NCD would have on beneficiary access to advanced cancer therapies through these trials. For example, the trials' entry criteria are critical for estimating the number of Medicare beneficiaries who could participate in these trials. The cost to beneficiaries of participating in these trials also will affect access. If beneficiaries are liable for 20 percent coinsurance on the drugs and biologicals provided in these trials, but could enroll in other trials where all costs are paid by the manufacturers, beneficiaries will not choose to enroll in CMS' selected trials and access under Medicare will not be

---

<sup>11</sup> See NCI, Clinical Trials: Questions and Answers, Cancer Facts 2.11, [available at http://cis.nci.nih.gov/fact/2\\_11.htm](http://cis.nci.nih.gov/fact/2_11.htm); CMS, Medicare and Clinical Trials, [available at http://www.medicare.gov/Publications/Pubs/pdf/ct.pdf](http://www.medicare.gov/Publications/Pubs/pdf/ct.pdf).

expanded. Additionally, patients may not want to enroll in these trials if they would be required to change physicians or travel to receive care. CMS must answer these essential questions about the trials' designs before Medicare's stakeholders can provide meaningful comment on this proposal.

Expanding beneficiary access also requires giving patients a choice of therapies and sites of care. This NCD could have consequences for beneficiary access to care in other trials or in non-clinical-trial settings. As we discussed above, the draft decision memorandum appears to protect carriers' ability to make local coverage decisions, although some clarification is still needed. Unless CMS takes care to ensure beneficiary access to these therapies outside these nine clinical trials, the agency's proposal could fail to expand coverage significantly. This is why we believe it is critical for CMS to clarify that local coverage policies remain unchanged. We also ask that the agency respond to the following questions, carefully considering this NCD's potential effects on patient access to care:

- How and why were these trials selected? How will other trials be added, and what criteria will be applied? Will non-NCI trials be eligible?
- Will beneficiaries in all areas of the country have access to these clinical trials? If not, can they still obtain Medicare coverage for these treatments if their use is consistent with an approved trial protocol?
- Will beneficiaries who do not meet the requirements of the protocols and thus are unable to enroll because of comorbidities, use of other drugs, or other circumstances still be able to obtain Medicare coverage for these treatments?

Second, we are concerned about CMS' payment for the drugs, biologicals, and other services provided in these trials. Since September 2000, CMS has paid for the routine costs of care in certain clinical trials, including NCI-sponsored trials. We would appreciate clarification as to how the proposed NCD is an expansion of coverage, not merely an application of the current NCD to the nine listed clinical trials. We also request more information on CMS' plans to pay for the non-routine costs of these trials, such as infusion services and additional laboratory and diagnostic tests. We recognize that NCDs do not address payment issues, but this NCD raises significant payment questions that must be answered before we can fully understand its effects on access to care, providers' willingness to participate, and manufacturers' support of clinical trials. BIO looks forward to talking

with CMS to discuss these concerns. We pose the following questions to encourage these discussions:

- Will manufacturers still be requested to donate drugs and biologicals or non-routine items and services for these clinical trials?
- How are donated or substantially discounted sales for these selected clinical trials reflected in a manufacturer's Medicaid best price? Is this treatment consistent with CMS' objectives?
- We ask for confirmation that donated drugs or drugs sold at a nominal cost are not counted under Average Sales Price methodology.
- How will these rules interface with the Food and Drug Administration's (FDA's) IND process?
- How will the logistics of reimbursement work to ensure that the trials continue to be blinded?
- How will CMS and NCI ensure that reimbursement does not create selection bias, especially when multiple trials are being conducted at the same site and not all trials will be reimbursed by Medicare?

Third, we request more information about CMS' plans to collect, use, and disseminate the information gathered during these trials. The long-term effects of the trials will depend on what data are collected and how the data are gathered and analyzed. We urge CMS to facilitate stakeholder involvement in the coverage process by sharing its plans for the data and by providing timely public access to the trials' findings. BIO looks forward to working with CMS to establish the appropriate data standards in order to accurately make clinical decisions. Before CMS finalizes any coverage decision, we ask CMS to address these concerns with stakeholder input, including the following questions:

- Are these trials intended to collect data CMS will use to make future coverage decisions?
- Will the trials enroll enough Medicare beneficiaries to reach valid conclusions about these therapies' benefits for this population?
- Who will own the data gathered in these trials?
- Who will analyze it?
- When and how will the data be shared with the public?
- Will this coverage remain in effect until all of the studies are completed and analyzed?

We look forward to working with CMS and the NCI in order to resolve the many issues raised by this policy initiative. However, in the



meantime, we urge CMS to reconsider the specifics of this NCD in light of the many yet unanswered questions.

\* \* \*

In conclusion, BIO is committed to ensuring beneficiary access to innovative drug and biological therapies. Until CMS answers the myriad of legal, policy, and practical questions regarding this proposed NCD, however, we are unable to fully assess whether this NCD truly would improve beneficiary access to these four therapies – as well as set an important precedent for ensuring access to other breakthroughs in the future.

Furthermore, we believe that the important, general coverage policy questions CMS asks in this draft decision memorandum would be addressed more appropriately outside the NCD process. The NCD process is not intended or designed to resolve broad questions regarding Medicare coverage and CMS’ role in evaluating innovative technologies. We encourage CMS to seek input from a full array of beneficiaries, providers, manufacturers, and other stakeholders on these issues by presenting its questions in a more appropriate forum.

In any event, we believe it is critical for Medicare’s current coverage policies for off-label drugs and biologicals to remain intact. Continuing to apply these policies as they are today will help ensure Medicare beneficiaries have access to the drugs and biologicals they need in their battle against cancer.

BIO appreciates this opportunity to comment on our concerns about the draft decision memorandum. We look forward to working with CMS to protect Medicare beneficiaries’ access to life-improving drug therapies. Please contact Jayson Slotnik at 202-312-9273 if you have any questions regarding our comments. Thank you for your attention to this very important matter.

Sincerely,

/s/

Michael Werner  
Chief of Policy

cc: Dr. Mark McClellan  
Administrator

Sean Tunis  
Director, Office of Clinical Standards and Quality

James A. Rollins, MD  
Coverage and Analysis Group

Gay W. Burton  
Coverage and Analysis Group