Initial Public Comments for
Anticancer Chemotherapy for Colorectal Cancer
CAG-00179N
05/02/03 – 11/17/03

Commenter: Abbruzzese, James MD
Organization: The University of Texas, MD Anderson Cancer Center

(Comment on next page)

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

COPY FOR YOUR INFORMATION

James L. Abbruzzese, M.D., F.A.C.P.
Professor of Medicine and Chairman
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July 15, 2003

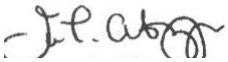
The Honorable Thomas Scully
Administrator
Centers for Medicare and Medicaid
Department of Human Health and Services
200 Independence Avenue SW
Washington DC 20201

Dear Mr. Scully:

As I am sure you are now aware, results presented at the American Society of Clinical Oncology (ASCO) meeting from the MOSAIC trial have supported the role of Eloxatifl administered along with 5-FU *I* leucovorin for the adjuvant management of patients with Stage ill colorectal cancer. The results presented at the ASCO meeting suggested a 5% absolute improvement in three-year disease-free survival, compared with our current standard management using 5-FU and leucovorin alone. While complete five year overall survival data is pending, the use of three-year disease-free survival statistics has been an accepted regulatory and clinical endpoint for adjuvant chemotherapy trials for colorectal cancer, as well as breast and non-small cell lung cancer. Thus, three-year disease free survival is an early indicator of the probable impact on five-year overall survival that could be expected from this trial.

Based on this information, I feel that it is important that Medicare provide coverage that includes Eloxatin for appropriate senior Americans afflicted with Stage ill colon cancer. It appears from these data that an additional two to three thousand patients per year could be cured of their colon cancer through the careful use of Eloxatin in this patient population. Thus, I believe that the Medicare population should have access and coverage for the use of Eloxatin in the management of patients with Stage III colon cancer in the United States.

Sincerely,



James L. Abbruzzese, M.D., F.A.C.P.
Professor of Medicine and Chairman
Annie Laurie Howard Research Distinguished Professor
Department of Gastrointestinal Medical Oncology

JLA/mct

cc: Gay W. Burton
Centers for Medicare and Medicaid
7500 Security Blvd, Mailstop C1-09-06
Baltimore, MD 21244-1850

Commenter: Ajani, Jaffer, MD
Organization: The University of Texas, MD Anderson Cancer Center

(Comment on next page)

THE UNIVERSITY OF TEXAS
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131689

Jaffer A. Ajani, M. D.
Professor of Medicine
Department of Gastrointestinal
Medical Oncology, Unit #426
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March 5, 2003

Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave SW; Room
Washington, DC 20201

Dear Dr. Scully:

I am a medical oncologist who has d alt only with gastrointestinal malignancies for 22+ years. I have firsthand experience with prescribing oxaliplatin to numerous patients. As you well know/ this agent is approved by the FDA for second line therapy of patients with advanced colorectal carcinoma. I would incerely like to see that all patients have free access to this agent. When combined with infusional 5-fluorouracil, it is well tolerated and palliates patients with this dreadful illness. The GI oncology community also believes that patients who receive 5-fluorouracil, CPT-II, and oxaliplatin, sometime during their illness, stand the chance of having a much longer overall survival time than those who receive only CPT-11 and 5-fluorouracil.

I appreciate your consideration in this matter.

Sincerely,

Jaffer Ajani

Jaffer A. Ajani. M. D.

Cc: Jeffrey Shuren
JD Director, Division of Items and Devices
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THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

July 7, 2003

Gay W. Burton
Centers for Medicare and Medicaid
7500 Security Blvd, Mailstop Cl-09-06
Baltimore, MD 21244-1850

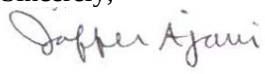
Dear Mr Burton:

Regarding: Adjuvant Therapy for Patients with Node-positive Colon Cancer

At the request of individuals working for Sanofi-Synthelabo, I would like to briefly express my opinion regarding the use of oxaliplatin-based adjuvant chemotherapy in selected patients with node-positive resected colon carcinoma. A multinational European trial called MOSAIC was presented at this year's ASCO. There was a 5% absolute improvement in 3-year disease free survival for patients receiving FOLFOX (oxaliplatin, 5-fluororuadJ, and folinic acid). The survival data is not available at this time. These are impressive r suits and when Dr. Robert Mayer (from the DanaFarber Cancer Center, in Boston) compared these to all previous trials in this setting, the numbers for OLFOX where consistently better than with 5-fluorouracil and folinic acid. Dr. Mayer was conservative in his conclusions. I support him to a great extent. I also believe that not every patients needs to be treated with FOLFOX (not until survival data becomes available), however, selected patients should be offered this combination. One example of a patient would be a 50 year old with T3 N2 cancer or another patient with poorly differentiated histogy.

I eagerly await the survival data from this trial and also on trials using CPT-11 with 5-fIuorouracil and folinic acid.

Sincerely,



Jaffer A. Ajani, MD
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Department of Gastrointestinal Medical Oncology
The University of Texas M. D. Anderson Cancer Center
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713-792-2828

Commenter: Aldige, Carolyn
Organization: Cancer Research and Prevention Foundation

(Comment on next page)

CANCER RESEARCH AND PREVENTION FOUNDATION
www.preventcancer.org

Carolyn R. Aldige
President & Founder

March 12, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW
Room 3140
Washington, DC 20201

Dear Mr. Scully:

I am writing to express my concern regarding a newly announced National Coverage Determination review, and reiterate my opposition to a recently enacted Medicare coverage policy, included in the preamble to the final rule on the Hospital Outpatient Prospective Payment System (HOPPS), 67 Federal Register 66755-56 (November 1, 2002).

In December of 2002, our organization CO-Signed a letter along with 22 other organizations of the Cancer Leadership Council (CLC) expressing our concern with the abrupt policy change in which the Centers for Medicare and Medicaid Services indicated that it would no longer base coverage of new cancer drugs for their labeled indication on approval by the Food and Drug Administration (FDA).

With this policy, CMS gave itself the authority to deny coverage of new drugs for reasons with no basis in the Medicare statute and set forth criteria that represent a severe threat to Medicare cancer patients. Further, the policy undermines the FDA drug approval process, which has long been regarded as the gold standard of safety, effectiveness and clinical benefit.

Today, I reiterate my concerns with this policy, citing the recent CMS action initiated on February 12, 2003 placing Eloxatin under a National Coverage Determination Review. This action will significantly delay patient access to this needed cancer treatments, and potentially others subject to the same process in the future. Further, consistent delay, denial, or restriction in CMS reimbursement decisions regarding novel cancer therapies will erode the quality of care that Medicare cancer patients receive, and could, ultimately, discourage research and drug discovery of drugs that cancer patients of all ages and their families depend upon.

We urge your reconsideration of the CMS policy of conducting a National

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Carolyn R. Aldige
President & Founder

July 7, 2003

The Honorable Thomas Scully
Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Administrator Scully:

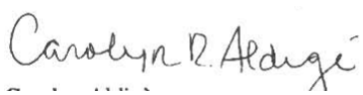
I am writing regarding the Centers for Medicare and Medicaid Services' (CMS) recent action to reverse its call for a National Coverage Determination Review on specific cancer drugs, except in the case of off-label use of those drugs.

While we applaud your decision not to subject novel cancer therapies to a National Coverage Determination Review process, we remain concerned with your decision to review coverage of these drugs when used in the adjuvant setting.

.A significant percentage -of pediatric and adult cancer therapies involve the off label use of approved drugs, and result not only in improved quality of life for cancer patients, but often in potential cures. It is critical that CMS not restrict access to a drug or treatment regimen that a physician determines to be the most effective in treating that patient.

We hope that CMS will reconsider its decision to subject new, lifesaving cancer therapies to National Coverage Determination Reviews.

Sincerely.



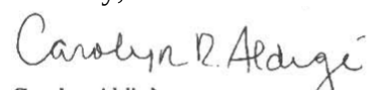
Carolyn Aldige,
President and Founder

cc:

Gay W. Burton
Centers for Medicare and Medicaid Services
7500 Security Boulevard, Mailstop C1-09-06
Baltimore, MD 21244-1850

Coverage Analysis of all new cancer drugs, including your most recent of the drug Eloxatin. I thank you for your attention to these concerns.

Sincerely,



Carolyn Aldige
President and Founder

cc:

Jeffery Shuren
JD Director
Division of Items and Devices
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Commenter: Ansari, Rafat, MD, FACP
Organization: Michiana Hematology Oncology

(Comment on next page)

Michiana Hematology Oncology, PC
The Power of Research-Based Medicine
The Art of Compassionate Care

Thomas A. Troeger, MD, FACP ❦ Rafat H. Ansari, MD, FACP
David A. Taber, MD ❦ Robin T. Zon, MD
Jose A. Bufill, MD, FACP ❦ Michael W. Method, MD, MPH, FACS, FACOG
Michael Rodriguez, MD, FACOG ❦ Rolan A. Pascual, MD
Bilal Ansari, MD ❦ Lowell Smith, MD

July 14 2003

Keith Logie, M. D.
Central Indiana Cancer Center
10212 Lantern Road
Fishers, IN 46038

Dear Keith:

This is to try to get approval from Medicare for Oxaliplatin based chemotherapy as first line for metastatic colon carcinoma.

Keith, you are quite aware of the present Folfox data for metastatic colon carcinoma. This happens to be a better tolerated regimen as well as more effective for metastatic colon carcinoma, but unfortunately we cannot use it, because Medicare approves Oxaliplatin based chemotherapy as a second line rather than first line. I understand that many states, including our neighboring state of Michigan allows Oxaliplatin to be used as a first line therapy for metastatic colon cancer.

I think we as a group should approach Medicare that they should allow Oxaliplatin, not only as a first line therapy for metastatic colon carcinoma, but at the same time also allow in an adjuvant setting.

If we need to have further discussion, I will be available. Thank you for your help.

Sincerely,

Sincerely,

Rafat H. Ansari, M.D. F.A.C.P.

RHN/crh
CC: Carolyn Cunningham, Administar Federal
Gay Burton, CMS

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Call toll-free to any office 1-800-860-8100 ❦ Website: www.mhopc.com

Commenter: Anthony, Lowell, MD
Organization: Louisiana State University Sciences Center

(Comment on next page)

LSU Health Sciences Center
NEW ORLEANS
School of Medicine
Department of Medicine
Section of Hematology/Oncology

School of Medicine
School of Dentistry
School of Nursing
School of Allied Health Professions
School of Graduate Studies

March 10 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW
Room 314 G
Washington, DC 20201

Dear Mr. Scully,

I am writing this letter concerning a matter of utmost concern to me as an oncologist regarding the treatment for patients who suffer from colorectal cancer.

It has been brought to my attention that the drug Eloxatin, (oxaliplatin for injection), is being studied by the Federal Centers for Medicare and Medicaid Services (CMS) for Medicare coverage.

As an oncologist, who specializes in the field of colorectal cancer I would like to give you my past and present experience in using Eloxatin and the drug's favorable impact on my patients' quality of life and extended survival.

Patients who are on a 3-drug regin1en of Eloxatin 5-fluorouracil, and leucovorin for treatment of advanced colorectal cancer have showed an significantly increased response rate and a longer time to radiographic progression. Their appetite is better, symptoms are controlled, disease is stable and they have less pain. Patients feel better and they are able to do more with a decrease in tumor related symptoms. This treatment gives them hope with a much better quality of life. The 3-drug regimen is very well tolerated with low toxicity. Data also suggest that Oxaliplatin, 5-fluorouracil, and leucovorin allows successful resection of initially not optimally resectable liver metastases. The metastatic disease becomes operable after the downsizing of the disease with this 3-drug regimen. Also, the survival of patients on a 3-drug regimen is greater.

Following is some data on survival:

- In the year 2000 there were 4 studies done using the 3-drug regimen, 5% patients with 14.8 % survival, 16% patients with 17.4% survival, 29% patients with 16.2% survival and 60% patients with 19.4% survival.

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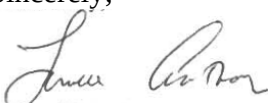
- In the year 2001 68% of patients were on the 3-drug regimen with 21.0% survival.

- In 2002 75% patients had a 21.4% survival

I believe that it is of grave importance for this drug, Eloxatin, to be reimbursed by Medicare so that new treatments that are approved by the Food and Drug Administration may be available to all cancer patients who need them. Patients, oncologist, and the research community would like to see the approval for reimbursement of this drug so that patients can have use of this drug, oncologist can continue to administer this drug to cancer patients to help them survive longer with their cancer and possibly be able to be cured and researchers to continue their research for new agents that the cancer patients will be able to use in their fight against cancer.

Thank you for your consideration on this matter.

Sincerely,



Lowell Anthony, MD
Associate Professor
Director of Gastrointestinal And Neuroendocrine Oncology
Louisiana State University Medical Center
1542 Tulane Avenue
New Orleans, LA 70112-2822

cc: Jeffery Shuren
JD Director
Division of Items and Devices
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Poppy S. Kendall, MRS
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Commenter: Arrowsmith, Edward, MD
Organization: Chattanooga Oncology Hematology Associates

(Comment on next page)

CHATTANOOGA ONCOLOGY & HEMATOLOGY ASSOCIATES, PC
605 Glenwood Drive, Suite 200, Chattanooga, TN 37404
Phone: 423/698-1844 Fax: 423/624-2226
Main Office: Memorial Plaza Satellite Office: North Park Professional Building, Hutcheson Medical Center

March 10, 2003

Thomas A. Scully, Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW, Room 3140
Washington, DC 20201

Dear Mr. Scully:

I am writing to you regarding national coverage determination process regarding oxaliplatin for injection (Eloxatin). I am a practicing medical oncologist who is also an investigator on several of the trials of oxaliplatin for patients with relapsed metastatic colorectal cancer. These trials show that in combination with 5-FU and leucovorin, oxaliplatin is effective at relieving symptoms in patients who would otherwise have no other treatment options. The strength of this data led to the fastest FDA approval of any antineoplastic agent last summer.

However these data do not adequately demonstrate the profound benefit that individual patients have experienced with this drug. Patients are relieved of severe pain or have their lives extended to live to another Christmas or see the birth of a first grandchild. A decision by CMS to not reimburse for oxaliplatin would be a tremendous blow to patients with colorectal cancer.

Further, a decision by CMS to not reimburse for oxaliplatin would send an extremely negative message to all patients with cancer, their loved ones, and caregivers. While controlling government health care spending is an extremely important societal goal, it does not seem reasonable to those of us who deal with cancer each day to start this process by denying coverage for an extremely effective therapy for one of the most common cancers in America. Furthermore, denying Medicare coverage would make the drug available to younger Americans but deny this important therapeutic agent to older Americans.

CMS's action would also have a chilling effect on the desire of the pharmaceutical industry to develop new cancer therapeutics. We are living in the age where President Nixon's war on cancer, started in the 1970s, is beginning to pay dividends. Many new agents are coming to market. If CMS decided to not reimburse for a drug that had been determined by the Food and Drug Administration to be safe and effective for the treatment of cancer, then further research might be substantially curtailed.

Each year more than 150,000 Americans are diagnosed with colorectal cancer and 56,000 die from this disease. Just today, I saw several patients whose lives are profoundly better by the benefit that oxaliplatin has given them in terms of controlling their symptoms and extending their life. It would be a terrible mistake for CMS to deny Medicare coverage for oxaliplatin.

Please feel free to contact me if I can be of any assistance to you in this matter.

Edward R. Arrowsmith, M.D.

cc: Jeffery Shuren, JD Director
Division of Items and Devices
Centers for Medicare & Medicaid Services
7500 Security Boulevard
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Baltimore MD 21244-1850

Poppy S. Kendall, MHS
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Commenter: Baxter International, Inc
Organization: Baxter Healthcare Corporation

(Comment on next page)

Baxter International Inc.
One Baxter Parkway
Deerfield, Illinois 60015-4633

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Fax: 847.948.3948

Baxter

July 1, 2003

Gay Burton
Health Insurance Specialist Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Boulevard
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Baltimore, MD 21244-1850

RE: CMS National Coverage Analysis of Oxaliplatin (Eloxatin) for Colorectal Cancer (#CAG-00179N)

Dear Ms. Burton:

Baxter Healthcare Corporation appreciates the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) regarding Medicare national coverage of oxaliplatin for colorectal cancer patients. Our comments focus on the benefit of this drug when used in combination with infusional 5-fluorouracil (5-FU) and leucovorin (LV) for patients with recurrent colorectal cancer. We also raise for your consideration the need to revise Medicare's policy to allow for coverage of infusion technologies and related services that clinically enhance chemotherapeutic regimen.

Baxter Healthcare Corporation (Baxter) is a global biotechnology and medical products/services company that provides critical therapies for people with life-threatening conditions. Baxter's Medication Delivery business manufactures a range of products that deliver fluids, drugs and medications to patients. Baxter is a recognized leader in developing innovative solutions that improve the quality of life for patients around the world.

Our comments are summarized below and detailed in the sections that follow.

- **Published clinical evidence supports the benefits of oxaliplatin**. Administered in combination with infusional 5-FU and leucovorin, oxaliplatin improves health outcomes for patients with advanced stage colorectal cancer.

- **Published studies demonstrate the clinical benefits of the infusional administration of these chemotherapeutic agents in accordance with the de Gramont regimen.** De GraTIlont is a chemotherapy administration technique in which the drugs are infused over a specified period of time, rather than by bolus injection.

• **The disposable infusion system represents an important technological advance for delivering infusional therapy**. Baxter has developed an innovative alternative to traditional mechanical, battery-operated pumps for use in infusional therapy.

• **Despite the many benefits of the disposable infusion system, Medicare does not currently provide reimbursement for-this technology**. Medicare provides coverage under the durable medical equipment (DME) benefit for mechanical, reusable infusion pumps, supplies, and intravenous drugs for home infusion therapy. However, the program does not cover the disposable infusion system (or the supplies or drugs used with this system) because the system does not meet Medicare's definition of DME.

• **We strongly urge CMS to consider alternative mechanisms for coverage and reimbursement of the disposable infusion system**. Medicare beneficiaries should be provided access to the full range of continuous infusion technologies for chemotherapeutic drug administration, based on their unique medical needs.

Clinical Benefits of Oxaliplatin Combination Therapy and the de Gramont Regimen

For over four decades, systemic chemotherapy with intravenous fluorouracil (5-FU) has represented a well-established first line treatment for patients with metastatic colorectal cancer. During this period, this agent has been therapeutically modulated in various administration regimens and combinations in order to optimize effectiveness. More recently, oxaliplatin was approved by the U.S. Food and Drug Administration for use in combination with in fusional 5·FU for the treatment of patients with metastatic cancer of the colon or rectum whose disease has recurred or progressed within six month of completion of first-line therapy.

Two general methods of intravenous chemotherapeutic administration are prevalent in medical practice. In *bolus administration,* the drug is injected directly into the vein by syringe. In *jnfusional administration* (also referred to as continuous infusion), the drug is infused into the vein over a specified period of time.

A widely used method of infusional administration for the treatment of patients with metastatic cancer is the de Gramont regimen. In this regimen, chemotherapeutic drugs are infused continuously over a period of time, based on specific administration guidelines. Table 1 presents the de Gramont administration schedule for mono- and combination infusional 5-FU therapy, as well as the bolus administration schedule, based on protocols developed by the Mayo Clinic.[1]

Table 1: Overview of Iluoroureil (S-FU) based treatment regimens.

Regimen	Schedule
Bolus 5-FU Mayo	5-FU (425 mg/m²/day)+ FA (20 mg/m²/day) for 5 consecutive days every 4 weeks.
Infusional 5-FU de Gramont	2 hour infusion of FA (200 mg/m²) +bolus 5-FU (400mg/m²) followed by 22-hour infusion of 5-FU (600mg/m²) on days I and 2 of each fortnightly.
Modified de Gramant	FA (200mg/m²) + bolus 5-FU (400mg/m²) followed by a 46 hour infusion of 5-FU (2400-3000mg/m²) fortnightly.
Infusional S·FU combination therapy De GramontiOxalinlatin	As for de Gramont plus oxaliplatin 85mg/m² combined with the initial 2 hour infusion of FA.

Published studies demonstrate that the de Gramont infusional regimen is clinically more effective than bolus administration of5~FU therapies, yielding improved response rate, longer patient survival, and lower toxicity. For example, a study published in the *Journal of Clinical Oncology* in 1997 compared patient health outcomes for bolus 5-FU and de Gramont infusionaI5-FU.[2] This randomized trial compared the effectiveness of monthly low dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus, plus in fusional 5-FU, for advanced colorectal cancer patients. The results of this study are summarized in the Table 2 below.

Table 2. Infusional 5-FU/folinic acid via the de Gramont regimen versus bolus 5-FU/folinic acid via the Mayo regimen.

	Bolus 5-FU (Mayo)	de Gramont 5-FU
Response rate (% of patients)	14.4	32.6
Progression free survival (months)	5.6	7.1
Median survival *(months)*	14.2	15.5
Overall grade 3-4 toxicity (% of patients)	23.9	11

As shown above, the de Gramont regimen for infusion of leucovorin and fluorouracil resulted in improved health outcomes, compared to the bolus method of administration based on the Mayo regimen. Specifically, the de Gramont regimen resulted in the following: 126% increase in the number of patients responding to therapy; 27% increase

in the length of progression free survival; 9% increase in median survival' and 54% reduction in toxicity.

In another study published in the *Journal of Clinical Oncology* in 2000, researchers evaluated leucovorin and fluorouracil without oxaliplatin ("monotherapy") and with oxaliplatin (' combination therapy") as a first-line treatment for patients with advanced colorectal canceLJ Both drug therapies were administered via the de Gramont infusional regimen. The results of the study are summarized in the Table 3 below.

Table 3. Infusional 5-FU/folinic acid via the de Gramont regimen as monotherapy versus infusional 5-FU/folinic acid via the de Gramont regimen with oxaliplatin as combination therapy (RCT)

	de Gramont monotherapy	de Gramont/oxaliplatin
Response rate (% of Patients)	22.3	50.7
Progression free survival (months)	6.2	9.0
Median survival *(months)*	14.7	16.2

As shown in the table above, the combination therapy consisting of infusional 5-FU with oxaliplatin and leucovorin, administered using the de Gramont infusional regimen resulted in the following: 127% increase in the number of patient responding to treatment; 45% increase in progression free survival; and 10% increase in median survival rates when compared to monotherapy.

Considered together, these findings highlight two important points. First combination therapy of 5-FU with oxaliplatin results in improved health outcomes for patients with advanced colorectal cancer compared to 5-FU monotherapy. Second, .infusional administration of this combination therapy, based on the de Gramont regimen, results in improved health outcomes when compared to bolus administration.

Results of more recent studies further validate the benefits of combination infusional 5FU therapy with oxaliplatin for colorectal cancer patients. For example, results from the MOSAIC trial for the use of oxaliplatin, presented by de Gramont at the 2003 annual meeting of the American Society of linical Oncology, demonstrate that the addition of oxaliplatin to infusional 5-FU/leucovorin (5-FUILV) for colon cancer reduces the risk of recurrence by 23 percent, compared to cunent standard treatment alone. Another study published recently highlights the superiority of infusional oxaliplatin with 5-FUILV compared with altemative therapies.[4] This study by Rothenberg et al demonstrated that the combination ofinfusionaI5-FU/LV and oxaliplation provided superior outcomes to either bolus and infusional 5-FU/LV or single-agent oxaliplatin for patients with metastatic colorectal cancer who progress after first-line therapy.

Disposable Syslem for Delivery of Infusional Therapy

There are two types of pumps used to administer in fusional intravenous drugs - *durable* pumps and *disposable* pumps. Durable infusion pumps include electronic and mechanical devices. These pumps include small battery-operated devices, as well as large electric-powered stationary devices.

The disposable infusion system offers a lightweight alternative to durable pumps for continuous medication infusion in the home and alternative sites of care. The system consists of an elastometric reservoir (similar to a balloon) which moves the medication into delivery tubing and through the catheter to the patient's vein. A flow restrictor controls the flow rate of medication infusion. (For more information. refer to enclosed literature regarding Baxter's disposable infusion system, the Infusor™ System.)

The system is designed to make medication delivery as simple and convenient as possible for the patient. It is small, lightweight and compact, allowing patients to be truly ambulatory. The system docs not require a power source for operation, is completely silent and discrete, and is simple for patients to learn and use. The system may be pinned to the patient's clothing, or put in their pocket for easy transportability.

The disposable infusion system offers patients maximum freedom and mobility during home infusion therapy. Several clinical studies have documented the benefits of tile system for both patients and clinicians. For example, a trial conducted by Zahnd et al studied patients who received infusional fluorouracil treatment with the disposable infusion system, as well as an electronically controlled pump.[5] Study participants preferred the disposable infusion system because it weighed less, was smaller, interfered less with daily activities, and was more user friendly.

Another study by Sawaki et 31 of patient and nurse preferences found that mechanical problems were less frequent with the disposable infusion system than with alternative delivery systems in the administration of patient-controlled analgesia. [6] Patients found the disposable system easier to use, especially at night, and the least likely to interfere with ambulation. Eighty percent of nurses in the study preferred the disposable infusion system over other widely used electronic devices.

Medicare Non-Coverage of the Disposable Infusion System

The published studies referenced above document the benefits of the disposable infusion system for both patients and clinicians. Unfortunately, however, Medicare policies and limitations provide no mechanism whereby the program will provide for coverage and reimbursement for the disposable system, or the drugs and supplies used with the system. As a result, Medicare beneficiaries are frequently denied access to this important technology that provides for greater ambulation, less interference with daily activities, and overall improvement in quality of life.

Because they are reusable, durable pumps are covered under Medicare's durable medical equipment (DME) benefit. In addition, CMS provides for reimbursement of the intravenous drugs that must be administered with the durable pump. Covered home infusion drugs include some chemotherapy, pain, and antiviral medications. Supplies used with durable pumps are also covered by the program.

In contrast, disposable infusion pumps are used by a single patient. When the patient receives the disposable pump, it is pre-filled with the medication, and when infusion of the dose is complete, the patient discards the pump. Because the disposable pump is not durable, it is not covered under the Medicare DME benefit. In addition, because the pump is not covered, the supplies and intravenous drugs used with the disposable pump are also not covered.

Current Medicare coverage policies create strong incentives for home infusion therapy providers to restrict the use of the disposable pump, regardless of its clinical benefits. Furthermore, Medicare's policy is in sharp contrast to the growing trend among private payers to reimburse providers an all-inclusive per diem rate that is intended to cover the total costs of infusion therapy services. This rate does not vary based on method of infusion (i.e.,

by durable or disposable pump). Because of this less restrictive policy, many home infusion therapy providers select the disposable pump for patients covered by private insurance. Medicare beneficiaries should be afforded similar access to the full range of infusion pumps available for their therapy.

More generally, legislation is currently being considered by the United States Congress to revise the method of Medicare reimbursement for outpatient drugs. This action will further undermine the provision of in fusional drug therapy for Medicare patients. It is widely believed that Medicare reimbursement of outpatient drugs helps providers to offset underpayment for associated drug administration costs. In fact, a study published by the General Accounting Office in September 2001 notes that providers contend that the excess payment for covered drugs are necessary to offset the lack of Medicare payment for some services related to the administration or delivery of the drugs. Congressional legislation to reduce outpatient drug reimbursement has the potential to further constrain the ability of hospitals and physicians to provide the optimal method of infusional therapy.

Medicare beneficiaries should be provided access to the full range of infusion systems for chemotherapeutic infusional drug administration, based on their unique medical needs. The Medicare program needs to ensure that neutral reimbursement incentives exist for providers to select most appropriate infusion delivery system for these patients.

Modifications to Medicare's Policy Are Needed

Baxter strongly urges CMS to seek changes to its coverage policy for the disposable infusion system, as well as the intravenous drugs and supplies used with the system. CMS should establish an alternative mechanism to provide for reimbursement of the disposable system. CMS should consider the opportunities across the full range of its payment systems to secure adequate reimbursement for this important technology advance. Baxter welcomes the opportunity to work with CMS as it explores modifications to these systems to ensure that Medicare patients have access to the clinical and quality of life benefits of the disposable infusion system.

In conclusion, we appreciate the opportunity to comment on this important issue. Should you have any questions or wish to discuss our comments further, please contact Julie Reed, Director of Health Economics and Reimbursement, at (847) 270-4187.

Sincerely,

Enclosure

[1] Baxter Healthcare. Capecitabine and tegafur with uracil for metastatic colorectal cancer. Submission to NICE, National Institute for Clinical Excellence, London; July 2002, Appendix 1.Table 1.1.

[2] de Gramont A, Bosset JF, Milan C *et al.* Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. *Journal of Clinical Oncology* 1997; 15(2): 808-15.

[3] de Gramont A, Figer A, Seymour M *et al.* Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. *Journal of Clinical Oncology* 2000; 18(16): 2938-47.

[4] Rothenberg, M. *et al.* Superiority of oxaliplatin and fluorouracil-leucovorin compared with either therapy alone in patients with progressive colorectal cancer after irinotecan and fluorouracil-leucovorin: interim results of a phase III trial. *Journal of Clinical Oncology* 2003; 21(11): 2059-2069.

[5] Zahnd, D. *et al.* A randomized crossover trial assessing patient preference for two different types of portable infusion-pump devices. *Annals of Oncology* 1999; 10(6): 727-29.

[6] Sawaki, Y. *et al.* Patient and nurse evaluation of patient-controlled analgesia delivery systems for postoperative pain management. *Journal of Pain & Symptom Management* 1992; 7(8): 443-53.

Commenter: Becarra, Carlos, MD
Organization: The University of Texas, Southwestern Medical Center

(Comment on next page)

THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER
AT DALLAS

Harold C. Simmons Comprehensive Cancer Center

March 10 2003

Mr. Thomas A. Scully, Administrator
Centers for Medicare and Medicaid Services
200 Independence Avenue, SW, Room 314G
Washington, DC 20201

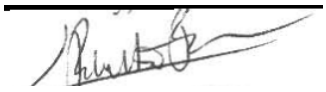
Dear Mr. Scully,
Subject: Oxaliplatin in colorectal cancer

Colorectal cancer is the 4th cause of cancer and second leading cause of death in the United States. After many decades of clinical research in the past 3 years we have been able to incorporate 2 new drugs, lrinotecan and Oxaliplatin into our therapeutic armamentarium for patients with metastatic colorectal cancer. Both drugs have proven clinical benefit in our patients with metastatic colorectal cancer.

In particular Oxaliplatin represents an important second line regimen that prolongs survival and improves quality of life as proven in well-designed phase III clinical trials. Denying access of Medicare patients to Oxaliplatin would constitute substandard care for this patient population.

I urge you to consider incorporating Oxaliplatin for our Medicare patients.

Sincerely,



Carlos Becerra MD
Assistant Professor
UT Southwestern Medical Center
2201 Inwood Road
Dallas, Texas 75390-8852

Cc: Jeffery Shuren, JD Director
Division of Items and Devices
Centers for Medicare & Medicaid Services
7500 Security Blvd., Mailstop C1-09-06
Baltimore, MD 21244-1850

Poppy Kendall, MHS
Centers for Medicare & Medicaid Services
7500 Security Blvd., Mailstop CI-09-06
Room C1-12-06
Baltimore, MD 21244-1850

Commenter: Begas, Albert, MD
Organization: The Center for Hematology-Oncology

(Comment on next page)

THE CENTER FOR
HEMATOLOGY-ONCOLOGY

March 11, 2003

Mr. Thomas A. Scully
Administrator
Center for Medicare and Medicaid Services
200 Independence Avenue, SW
Room#314G
Washington, D.C. 20201

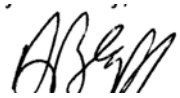
Dear Mr. Scully:

I am writing in support of Eloxatin. Our group has treated over 100 patients with Eloxatin and we find that the drug does have good activity in colorectal cancer. Its side effect profile is favorable as compared to CPT-11 and we believe that the drug does offer a benefit to patients suffering from a terminal illness.

We hope that CMS will have a favorable review process concerning Eloxatin and we are confident if appropriate attention is given to the matter, you will consider it a reasonable and necessary drug for Medicare coverage.

I am available to speak with you at any time concerning our patients treated and the favorable responses obtained.

Very sincerely,



Albert Begas, M.D.

AB:GT/wja

cc: Jeffrey Shuren, JD Director
Poppy S. Kendall, MHS

Commenter: Bhatia, Andres, MD
Organization: Gainesville Hematology-Oncology Associates

(Comment on next page)

GAINESVILLE HEMATOLOGY-ONCOLOGY ASSOCIATES

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BRUCE K. STECHMILLER, M.D., P.A.
Diplomate: American Board of Internal Medicine
American Board of Oncology

MANUEL DE LA PUERTA, M.D.
Diplomate: American Board of Internal Medicine
American Board of Oncology

HEATHER G. LEWIN, A.R.N.P.

VERNON P. MONTOYA, M.D.

ANDRES W. BHATIA, M.D.
Diplomate: American Board of Internal Medicine
American Board of Oncology
American Board of Hematology

JENNIFER S. TONEY, A.R.N.P.

April 3, 2003

To Whom It May Concern

RE: Oxaliplatin (eloxatin)

Dear Sirs:

I have been practicing oncology in the Gainesville area since 1993, and am board certified in oncology. I am writing this letter to see if the above-mentioned drug could be covered as first-line treatment for metastatic colorectal cancer. Oxaliplatin has already been approved by the FDA as second-line treatment for metastatic colon cancer.

There are 2 trials that have compared Oxaliplatin to 5 FU and leucovorin and a third trial that has compared Oxaliplatin-based chemotherapy to irinotecan, showing on all 3 occasions that patients on the Oxaliplatin chemotherapy did statistically significantly better. The trials comparing Oxaliplatin to 5 FU and leucovorin were published in the year 2000, both in the *Journal of Clinical Oncology.* One authored by Decramont and the other by Giachetti.

The third trial that I mentioned above was a phase III trial which has been completed and is known as N9741, which compares Oxaliplatin plus 5 FU and leucovorin (Folfox 4) against the Saltz regimen, which is irinotecan, 5 FU and leucovorin. This trial also showed statistically significant improvement in survival in patients taking Folfox.

Based on the above-mentioned information, I believe that Oxaliplatin should be available to physicians if they want to use it as first-line chemotherapy in metastatic colon cancer.

Please do not hesitate to contact me with any questions regarding this matter.

With kindest regards

Andres W. Bhatia, MD
AWB/vwg

PRACTICE LIMITED TO HEMATOLOGY, ONCOLOGY

Commenter: Blanke, Charles, MD
Organization: Oregon Health and Science University, School of Medicine

(Comment on next page)

SCHOOL OF MEDICINE

OREGON HEALTH & SCIENCE UNIVERSITY
DIVISION OF HEMATOLOGY AND MEDICAL ONCOLOGY
3181 S.W. SAM JACKSON PARK ROAD
MAIL CODE: L586
PORTLAND, OREGON 97239-3098
TEL: 503 494-8534
FAX: 503 494-4285

March 12, 2003

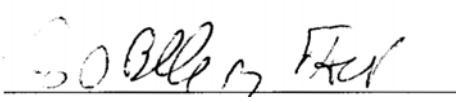
Thomas Scully
Centers for Medicare and Medicaid Services
200 Independence Avenue SW, Room 314G
Washington, D.C. 20201

Dear Administrator Scully,

I understand that the Centers for Medicare and Medicaid Services has recently taken actions which I think will dramatically restrict patient access to new Oncologic therapies that would potentially be of benefit. From elements published in the Federal Register, November 1, 2002, it was stated that FDA approval was necessary but insufficient to gain reimbursement status for a drug. It was also stated that determination of clinical effectiveness by CNS is outside the scope of the determination of safety and efficacy by the FDA. In other words, FDA approval is no longer the default status for Medicare patients. Finally CNS will assess whether a new treatment is reasonable and necessary for the Medicare population and that reimbursement may be denied if the drug represents a complex therapy that could be costly to Medicare.

I was specifically concerned about lack of reimbursement for Oxaliplatin. Oxaliplatin in combination with other chemotherapy an extremely active regimen in colorectal malignancy and it is clearly superior to the standard IFL regimen. In my experience, which in total sums over 1,000 patients with colorectal cancer, this is the most active regimen in existence. I can tell you that denying Medicare coverage has caused personal hardship to patients who have gone into remission on that drug but had to stop it when they could no longer afford to pay for it out of pocket.

I also have concerns that reimbursement for any Oncology drug could be denied under your new guidelines. I hope you will reconsider your position and I appreciate your attention to this letter.



Charles D. Blanke, M.D., F.A.C.P.
Associate Professor of Medicine
Hematology and Medical Oncology

CDB:wer

Cc:
Jeffrey Shuren
J D Director Division of Items and Devices
Center for Medicare and Medicaid Services
Mail Stop C1-09-06
7500 Security Blvd.
Baltimore, Maryland 21244-1850

Poppy Kendall, MHS
Mail Stop C1-09-06
7500 Security Blvd.
Baltimore, Maryland 21244-1850

Commenter: Brandt, Debra
Organization: Northwestern Connecticut Oncology/Hematology Associates, LLP

(Comment on next page)

Northwestern Connecticut Oncology/Hematology Associates, LLP

Debra S. Brandt, DO
Susan DiStasio, APRN
Catherine Hosterman, APRN
Orion Howard, MD

Gerard Kruger, MD
Jedd F. Levine, MD
Ivan S. Lowenthal, MD
Michael C. Magnifico, MD

March 7, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW
Room 314G
Washington, DC 20201

Dear Mr. Scully:

This letter is in reference to determination of whether Eloxatin is to be covered by Medicare and Medicaid.

I have significant personal experience in treating patients with metastatic colon and rectal carcinoma with Eloxatin, as I was a principal investigator with three studies testing Eloxatin in those patients in the second, third, and fourth line settings. As you are well aware, more than 150,000 Americans are diagnosed with colorectal carcinoma each year and 56,000 die of the disease. Of these individuals, 27% are treated in a hospital setting and would be affected by the CMS policy. Eloxatin was recently approved by the FDA in the United States in second line treatment of metastatic colon carcinoma when given in combination with infusional 5-FU and Leucovorin. Phase II trials of Oxaliplatin in combination with 5-FU and Leucovorin, demonstrated response rates ranging from 23 to 58% and survivals ranging from 12 to 17 months. There is a significant improvement in time to progression when Eloxatin is given in combination with 5-FU and Leucovorin when compared to 5-FU and Leucovorin in combination with Camptosar. Eloxatin is an example of a new cancer therapy that addresses an unmet need in patients with advanced colorectal carcinoma. I have clearly seen promising responses in patients treated with Eloxatin and 5-FU. I have a number of patient who I am sure would not be alive today if it was not for Eloxatin. One patient in particular comes to mind; she has tolerated over 22 cycles of Oxaliplatin, 5-FU and Leucovorin, is very active, continues to work and take aerobic classes. I am certain that she would not be able to do this if it was not for the availability of Eloxatin. Denying Medicare coverage for Eloxatin would adversely affect older Americans who are most likely to have a diagnosis of colorectal carcinoma. Restricting patient access would come at a time when the best chances for survival depend on a range of treatment options that are available. In addition, patients tolerate varying regimens differently and having an option allows better patient selection and helps manage toxicities. In this case, Eloxatin is an effective regimen for patients with very few treatment options. These patients need a range of therapies to improve their chances of survival.

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19 West Main Street • P.O. Box 1707 • Sharon, CT 06069 • Tel.: 860-364-0531 • Fax: 860-364-2148
17 Poplar Street • New Milford, CT 06776 • Tel.: 860-354-5656 • Fax: 860-354-6868

An adverse decision by CMS resulting in the denial of Medicare coverage for Eloxatin would be the first time in United States history that an FDA approved cytotoxic agent was not covered by the Medicare program. This, I believe, would set a dangerous precedent.

Please, for the benefit of all patients with colorectal carcinoma, strongly consider the approval of Eloxatin.

Sincerely,

DSB:jr

cc: Jeffery Shuren
JD Director
Division of Items and Devices
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Mailstop C1-09-06
Baltimore, MD 21244-1850

Poppy S. Kendall, MHS
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Mailstop C1-09-06
Room C1-12-06
Baltimore, MD 21244-1850

Commenter: Buckner, Jan, MD
Organization: Mayo Clinic

(Comment on next page)

Mayo Clinic
200 First Street SW
Rochester, Minnesota 55905
507-284-2511

J. C. Buckner, M.D.
Medical Oncology
& Internal Medicine

March 11, 2003

Jeffrey Shuren, M.D.
JD Director Division of Items and Devices/Center for
Medicare/Medicaid Service
Mail Stop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Doctor Shuren:

I am writing as the chairmen of the NCCTO regarding the experience that the group has had with a large clinical trial testing oxaliplatin against several other drugs in the treatment of advanced colon cancer. This clinical trial known as, N974l was run through the NCCTO 01 committee. It is a phase III study funded by the National Cancer Institute in which all cooperative groups in the U.S. and Canada that focus on medical oncology trials participated. The study was monitored by our NCCTO external data monitoring committee as is required for all phase III studies conducted by cooperative groups.

In April of 2002, the external data monitoring committee chose to release the data from this study to the investigator team early. As you know clinical trials have early stopping rules written in to them according to work done by O'Brien and Fleming. These early stopping rules can allow a study to be interrupted, modified, or released early in the event that toxicity issues or activity issues meet certain end points. The NCCTO external data monitoring committee released the data early on this study for two reasons. One was that the activity of the so-called FOLFOX regimen, which contains oxaliplatin, crossed the O'Brien/Fleming early stopping rule for improvement in activity over the standard regimen. In other words, there was statistically significant improvement in outcomes for patients receiving FOLFOX

compared with other treatments. The standard regimen in this case was irinotecan, 5-FU, and leucovorin or the so-called IFL regimen. The FDA had approved this regimen for the indication of treatment of patients with previously untreated metastatic colorectal cancer in April of 2000. The clinical trial that our group conducted found that the standard IFL regimen was too toxic. They observed an excess of early deaths in patients enrolled on that arm of the study. Because of that the doses of IFL were reduced from those of standard in April 2001. In addition, in April of 2002 the improvement in time to progression, response rate, and median survival for patients enrolled on the FOLFOX arm was statically significant at a P.002 level favoring FOLFOX over IFL. On the basis of these findings, data were released as specified by protocol to the investigative team.

Only compelling data prompt an external data monitoring committee to intervene in a phase III trial. In this circumstance the group intervened with respect to toxicity in April of 200 1 and with respect to activity in April of2002. This is an indication of the advantages of the FOLFOX regimen over the IFL regimen. The advantages were both in major improvement in all measures of outcome as well as a major improvement in measures of severe toxicity. Based on the results of the trial we certainly believe that the Center for Medicare and Medicaid Services needs to permit patients with metastatic colorectal cancer to have access to oxaliplatin and particularly to the FOLFOX regimen. If you would require further information on this, please feel free to contact me.

Sincerely,

Jan C. Buckner, M.D.
Chair, North Central Cancer Treatment Group

JCB:dmh

cc: Thomas A. Scully

Commenter: Bunn, Paul, MD
Organization: American Society of Clinical Oncology

(Comment on next page)

AMERICAN SOCIETY OF CLINICAL ONCOLOGY

March 6, 2003

Poppy S. Kendall, MHS
Centers for Medicare & Medicaid Services
Mailstop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244

Dear Ms. Kendall:

These comments are submitted by the American Society of Clinical Oncology (ASCO) in response to the notice, published on the CMS website, stating that CMS has internally generated a national coverage determination to evaluate when the newly approved anticancer drug oxaliplatin is reasonable and necessary in the Medicare population. The notice states that this review is being undertaken because of "the potential impact of this treatment on the Medicare program." ASCO is the national organization representing physicians who specialize in the treatment of cancer. We are very concerned about how the potential restrictions on oxaliplatin apparently contemplated by CMS may adversely affect our patients.

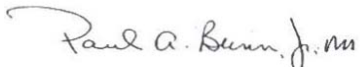
For most types of items and services, the Medicare statute confers broad authority on CMS to determine whether the item or service is reasonable and necessary and hence whether it is covered by Medicare. That is not the case, however, for drugs and biologicals used in anticancer chemotherapy regimens. Under section 1861 (t)(2) of the Social Security Act, there is mandatory coverage of drugs and biologicals in such regimens when used for purposes approved by the Food and Drug Administration, supported by citations in specified compendia, or determined by carriers to be medically accepted based on clinical evidence published in certain journals.

This provision was added to the statute in 1993 to stop the practice, employed by some carriers, of denying Medicare coverage for medically accepted indications on the ground that they were not included in the FDA-approved labeling. Congress amended the statute to deny any discretion to the Medicare program to deny coverage of medically accepted indications of drugs used in anticancer therapy.

1900 Duke Street, Suite 200 Alexandria, VA 22314 Telephone: (703) 299-0150 Fax: (703) 299-1044 E-mail: asco@asco.org Website: www.asco.org

Accordingly, ASCO sees no legally permissible function of a national coverage determination on oxaliplatin. All indications approved by FDA or listed in the compendia must be covered. Other indications are covered if carriers determine that they are supported by the medical literature. In light of the special statutory rules applicable to drugs used in anticancer chemotherapy regimens, CMS lacks the authority to restrict coverage of oxaliplatin. We therefore request that the proposed national coverage determination be withdrawn.

Sincerely,



Paul Bunn, MD
President, American Society of Clinical Oncology

Commenter: Burroughs, Frank
Organization: Abigaill Alliance for Better Access to Developmental Drugs

(Comment on next page)

Abigail Alliance for Better Access to Developmental Drugs
www.abigail-alliance.org
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1518 North Buchanan Street Arlington, VA 22205
703-525-9266 cell:703-963-2518 frankburroughs@hotmail.com
Board of Directors: Jeffrey Irving Grauer: Senior Partner, Grauer Global Partners, LLC
Doug Bauer: David's Father, Cancer Advocate
Gene Krueger: Abigail's Step Father, Cancer Advocate
Anne Agnew: Booz Allen Hamilton
Prince Agarwal, University of Virginia
Jo Grauer, Cancer Advocate
Cynthia Small, Charter One Mortgage

March 10, 2003

Thomas Scully
Administrator, Centers for Medicare and Medicaid Services
200 Independence Avenue. S.W.
Hubert Humphrey Building - Room 422-G
Washington, D.C. 20201

Dear Thomas Scully,
It is with profound concern that I have learned that the Centers for Medicare and Medicaid Services are considering not to cover the life saving cancer drug EIoxatln, even though the FDA approved Eloxatin! If this decision were implemented, it would be a tragedy!

A negative decision by CMS would cost people their lives! Our U.S. Government is primarily responsible for the protection of the people of the United States of America. Billions of dollars are spent on defense, airline safety, life saving research, and other life saving efforts.
CMS's notice is already causing uproar in the patient advocacy community, among oncologists, and is spreading very rapidly elsewhere. If CMS decides to withhold Medicare reimbursement for Eloxatin, this action will go against the FDA and President Bush's expressed concern for the poor and the elderly!
I have copied some of the key friends of the Abigall Alliance. These people are also friends of the people who deserve a right to live! The list is long!
Again, a negative decision would be tragic and could lead to more tragic decisions.
I expect a very prompt reply to the Abigail Alliance.
With deep concern for special people in need,

Frank Burroughs. President

Frank Burroughs

Abigail Alliance for Better Access to Developmental Drugs

cc:
The Honorable W.J. Tauzin
Chairman
House Committee on Energy and Commerce

United States House of Representatives

The Honorable James C. Greenwood
Chairman.
House Subcommittee on Oversight and Investigations
United States House of Representatives

The Honorable Peter Deutsch
Ranking Minority Member.
House Subcommittee on Oversight and Investigations
United States House of Representatives

The Honorable John D. Dingell
Ranking Minority Member,
House Committee on Energy and Commerce
United States House of Representatives

The Honorable Dan Burton
United States House of Representatives

The Honorable Jo Ann Davis
United States House of Representatives

The Honorable Tom Davis
United States House of Representatives

The Honorable Deborah Price
United States House of Representatives

The Honorable Sherrod Brown
United States House of Representatives

Alan Slobodin
House Committee on Energy and Commerce
United States House of Representatives

Dr. Mark McClellan
FDA Commissioner
Food and Drug Administration

Linda Arey Skladany
FDA Senior Associate Commissioner

Bill Hubbard
FDA Deputy Commissioner

TerryToigo
Patty Delaney
JoAnn Minor
FDA Office of Special Health Issues

Commenter: Campos, Luis, MD
Organization: Oncology Consultants, PA

(Comment on next page)

ONCOLOGY CONSULTANTS, P.A.

LUIS T. CAMPOS, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

CHARLES E. MANNER, M.D.
American Board of Internal Medicine

DAVID B. SANFORD, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

MIGUEL MIRO-QUESADA, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

PAUL Y. HOLOYE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

HARRY R. PRICE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

July 7, 2003

Gay Burton
Centers for Medicare & Medicaid Services
Mailstop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244

Dear Mr. Burton,

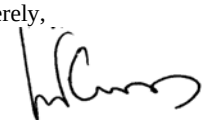
I would like to submitted comments in response to the notice, published on the CMS website, stating that CMS has internally generated a national coverage determination to evaluate when the newly approved anticancer drug oxaliplatin is reasonable and necessary in the Medicare population. The notice states that this review is being undertaken because of "the potential impact of this treatment on the Medicare program." our physicians at Oncology Consultants, P.A. who specialize in the treatment of cancer are very concerned about how the potential restrictions on oxaliplatin apparently contemplated by CMS may adversely affect our patients.

For most types of items and services, the Medicare statute confers broad authority on CMS to determine whether the item or service is reasonable and necessary and hence whether it is covered by Medicare. That is not the case, however, for drugs and biological used in anticancer chemotherapy regimens. Under section 1861 (t)(2) of the Social Security Act, there is mandatory coverage of drugs and biological in such regiments when used for purposes approved by the Food and Drug Administration, supported by citations in specified compendia, or determined by carriers to be medically accepted based on clinical evidence published in certain journals.

This provision was added to the statute in 1993 to stop the practice, employed by some carriers, of denying Medicare coverage for medically accepted indications on the ground that they were not included in the FDA-approved labeling. Congress amended the statute to deny any discretion to the Medicare program to deny coverage of medically accepted indications of drugs used in anticancer therapy.

Accordingly, Oncology Consultants sees no legally permissible function of a national coverage determination on oxaliplatia. All indications approved by FDA or listed in the compendia must be covered. Other indications are covered if carriers determine that they are supported by the medical literature. In light of the special statutory rules applicable to drugs used in anticancer chemotherapy regimens, CMS lacks the authority to restrict coverage of oxaliplatin. We therefore request that the proposed national coverage determination be withdrawn.

Sincerely,



Luis T. Campos, M.D.
President
Oncology Consultants,
P.A.

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(713) 797-6323
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ST. JOSEPH
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SUGAR LAND
15200 Southwest Frwy., Ste. 292
Sugar Land, Texas 77478
(281) 491-5511
Fax (281) 491-5513

Commenter: Cancer Leadership Council
Organization:

(Comment on next page)

CANCER LEADERSHIP COUNCIL

A PATIENT-CENTERED FORUM OF NATIONAL ADVOCACY ORGANIZATIONS ADDRESSING PUBLIC POLICY ISSUES IN CANCER

March 14, 2003

Poppy S. Kendall, MHS
Lead Analyst
Centers for Medicare and Medicaid Services
200 Independence Avenue, S.W.
Hubert Humphrey Building - Room 433-G
Washington, D.C. 20201

Dear Ms. Kendall:

The Cancer Leadership Council (CLC), representing cancer patients, providers, and research institutions, is submitting these comments in response to the initiation of a National Coverage Analysis of oxaliplatin. We understand that this review process was commenced by the Centers for Medicare and Medicaid Services on February 12, 2003, with an expected completion date of May 13, 2003.

In the attached letter, dated December 16, 2002, the CLC outlined its objections to the coverage policy announced by the agency in the preamble to the Hospital Outpatient Prospective Payment System, 67 Federal Register 66755-56 (Nov. 1, 2002). It is the position ofthe CLC that the new CMS coverage policy is inconsistent with the Medicare statute, which defines "drugs" to include "any drugs or biologicals used in an anticancer chemotherapeutic regimen for a medically indicated indication," including "any use which has been approved by the Food and Drug Administration." 42 U.S.C. §1395(t)(2)(A and B).

We urge the agency to abandon its efforts to conduct a National Coverage Analysis of all new cancer drugs, as these efforts are inconsistent with the Medicare statute.

Sincerely,

Cancer Leadership Council

Alliance for Lung Cancer
American Cancer Society
American Society of Clinical Oncology
Association of American Cancer Institutes
Cancer Care, Inc.
Cancer Research and Prevention Foundation
The Children's Cause, lnc.
Coalition of National Cancer Cooperative Groups, Inc.
Colorectal Cancer Network
National Patient Advocate Foundation
International Myeloma Foundation
The Leukemia & Lymphoma Society
Lymphoma Research Foundation
Multiple Myeloma Research Foundation
National Coalition for Cancer Survivorship
North American Brain Tumor Coalition
Pancreatic Cancer Action Network (PanCAN)
US TOO International, Inc.
The Wellness Community
Y-ME National Breast Cancer Organization

Contact: 1301 K Street N.W. • Suite 800 East • Washington, D.C. 20005
Phone: 202-626-3970 • Fax: 202-626-3961 • www.cancerleadership.org

CANCER LEADERSHIP COUNCIL

A PATIENT-CENTERED FORUM OF NATIONAL ADVOCACY ORGANIZATIONS ADDRESSING PUBLIC POLICY ISSUES IN CANCER

Enclosure - December 16, 2002, letter to Poppy S. Kendall, MHS

cc: The Honorable Tommy Thompson, Secretary, HHS
Mark McClellan, Commissioner, FDA
The Honorable Charles Grassley
The Honorable Max Baucus
The Honorable Deborah Pryce
The Honorable William Thomas
The Honorable Charles Rangel
The Honorable Nancy Johnson
The Honorable Pete Stark
The Honorable Billy Tauzin
The Honorable John Dingell
The Honorable Michael Bilirakis
The Honorable Sherrod Brown
Alex Azar, General Counsel, DHHS
Sheree Kanner. Associate General Counsel,
Health Care Financing Division, DHHS
Troy Daniel. Chief Counsel, FDA

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Contact: 1301 K Street N.W. • Suite 800 East • Washington, D.C. 20005
Phone: 202-626-3970 • Fax: 202-626-3961 • www.cancerleadership.org

CANCER LEADERSHIP COUNCIL

A PATIENT-CENTERED FORUM OF NATIONAL ADVOCACY ORGANIZATIONS ADDRESSING PUBLIC POLICY ISSUES IN CANCER

December 16, 2002

Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Avenue, S.W.
Hubert Humphrey Building - Room 433-G
Washington, D.C. 20201

Dear Mr. Scully:

The undersigned organizations, representing cancer patients, providers and researchers, are writing to express their serious concern about a new Medicare coverage policy announced in the preamble to the final role on the Hospital Outpatient Prospective Payment System (HOPPS), 67 Federal Register 66755-56 (Nov. 1, 2002). In an abrupt and unjustified change of policy, the Centers for Medicare & Medicaid Services (CMS) indicated it would no longer defer to the expertise of the Food and Drug Administration (FDA) in determining whether to cover drugs for their labeled indications. This change is inconsistent with longstanding administrative interpretations of the Medicare statute, as well as the terms of the statute itself, and should not be implemented.

Under the new policy announced by CMS without benefit of prior notice or opportunity for public comment, CMS may deny coverage of new drugs for a number of reasons that have no basis in the Medicare statute, including characterization of the drug as "novel, complex., or controversial," "costly to the Medicare prograrn," or "receiv[ing] marketing approval based on the use of surrogate outcomes." These non-statutory criteria represent a severe threat to cancer treatment for Medicare beneficiaries.

If coverage can be denied because a new drug is "novel" or "complex." cancer patients will likely be refused access to cutting-edge therapy. Even if there were a basis in the statute for such denials of coverage, it would represent bad public policy given our Nation's investment in biomedical research funding that supports development of "novel" and "complex" new drugs.

Similarly, the fact that a new therapy may be "costly to the Medicare program" is not a reason for non-coverage under the Medicare statute. Indeed, cancer care generally is more costly that many other diseases because it involves patients who are very ill and require aggressive treatment for their condition. Congress has never authorized CMS to deny coverage based on the cost of therapy, and it has not been the practice of the Medicare program to do so.

Contact: 1301 K Street N.W. • Suite 800 East • Washington, D.C. 20005
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Further, many new cancer drugs are approved on the basis of surrogate endpoints like "response rates" or "time to progression.," rather than the more difficult and time-consuming endpoint of survival. These surrogates have been identified by medical experts at FDA as indicative of clinical benefit. In fact, it is not correct to suggest, as CMS does, that FDA does not make- its decisions based on "clinical effectiveness," FDA is widely regarded as one of the premier health regulatory bodies in the world, and CMS has no basis upon which to challenge the thoroughness or correctness of its decision-making.

The potential refusal of CMS to cover new drugs consistently with the indications approved by FDA is particularly unsupportable with respect to cancer drugs. Motivated by excessive denials of coverage for medically appropriate uses of cancer drugs, Congress in 1993 restricted the discretion of CMS and its contractors to deny coverage for such uses. Specifically, for purposes of coverage, the term "drugs" is defined to include "any drugs or biologicals used in an anticancer chemotherapeutic regimen for a medically accepted indication," including "any use which has been approved by the Food and Drug Administration." 42 U.S.C. §1395x (t)(2)(A and B).

FDA approval is viewed as the gold standard of safety, effectiveness and clinical benefit. We question wbether CMS has the medical expertise to second-guess the science-based decisions of FDA. Moreover, if the policy is implemented by CMS, many beneficiaries with cancer may be denied access to life-extending therapies. We urge CMS not to implement the newly articulated coverage policy in the absence of specific authorization by Congress.

Sincerely,

Cancer Leadership Council

Alliance for Lung Cancer Advocacy, Support, and Education
American Cancer Society
American Society of Clinical Oncology
American Society for Therapeutic Radiology & Oncology, Inc.
Association of American Cancer Institutes
Cancer Care, Inc
Cancer Research Foundation of America
The Children's Cause. Inc.
Coalition of National Cancer Cooperative Groups
Colorectal Cancer Network
International Myeloma Foundation
Kidney Cancer Association
The Leukemia & Lymphoma Society
Lymphoma Research Foundation
Multiple Myeloma Research Foundation
National Childhood Cancer Foundation
National Coalition for Cancer Survivorship
National Patient Advocate Foundation
National Prostate Cancer Coalition
North American Brain Tumor Coalition
Pancreatic Cancer Action Network
Us Too! International- Prostate Cancer Education and Support
Y-ME National Breast Cancer Organization

cc: The Honorable Tommy Thompson, Secretary, DHHS
Mark McClellan, Commissioner, FDA
The Honorable Charles Grassley
The Honorable Max Baucus
The Honorable Deborah Pryce
The Honorable William Thomas
The Honorable ChArles Rangel
The Honorable Nancy Johnson
The Honorable Pete Stark
The Honorable Billy Tauzin
The Honorable John Dingell
The Honorable Michael Bilirakis
The Honorable Sherrod Brown
Alex Azar, General Counsel, DHHS
Sheree Kanner, Chief Counsel, DHHS
Troy Daniel, Chief Counsel, FDA

Commenter: Comis, Robert, MD
Organization: Coalition of National Cancer Cooperative Groups, Inc.

(Comment on next page)

COALITION
OF NATIONAL CANCER COOPERATIVE GROUPS, INC.
SAVING LIVES... ADVANCING SCIENCE... THROUGH CLINICAL RESEARCH

1818 Market Street, Suite 1100 ➤ Philadelphia, PA 19103 ➤ Phone: 215-789-3600 ➤ Fax: 215-789-3655

March 13, 2003

Thomas A. Scully
Administrator
Medicare and Medicaid Services
200 Independence Ave, S.W.
Room 314G
Washington, DC 20201

Dear Mr. Scully,

I am writing in my capacity as President of the Coalition of National Cancer Cooperative Groups, a not-for-profit organization representing the major NCI-supported Cooperative Groups involved in clinical trials in the United States. We are concerned that The Centers for Medicare and Medicaid Services has taken several actions that could have broad - ranging implications with respect to patient access to oncology drugs and the ability of publicly sponsored research organizations to successfully serve our patients and complete cancer clinical trials.

The key elements from the CMS guidance published in the Federal Register on November 1, 2002 are:

- FDA approval is necessary but insufficient to gain reimbursement status for a drug, and that the determination of "clinical effectiveness" by CMS is outside the scope of the FDA's "safe and effective" determination. Moreover, CMS will assess whether or not a compound or therapeutic modality is "reasonable and necessary" (or "inherently reasonable"} *for* the Medicare population.

- Reimbursement may be denied when the drug or biological represents a novel, complex, or controversial treatment; would be to costly to Medicare, or received marketing approval based on surrogate outcomes.

This broad policy could, in effect, prevent access to many novel agents currently both in development or recently approved for use in cancer by FDA.

After years of stagnation, the availability of research from well-designed clinical trials of newer agents has changed the entire landscape for patients with advanced colorectal cancer. The most recent advance being the development of oxaliplatin (Eloxatin). Eloxatin fills an *unmet medical need:* as an efficacious therapy for patients with advanced

colorectal carcinoma that has progressed after front-line treatment with irinotecan/5-FU/leucovorin (IFL). This was demonstrated in a randomized, controlled trial in which treatment with Eloxatin in combination with infusional 5-FU (FOLFOX4) was compared to infusional 5-FU alone. The results were as follows: 9.9% of the patients on the FOLFOX4 arm had objective responses and 60% of the FOLFOX4 patients experienced disease stabilization (for a total of 70% of FOLFOX4 patients with tumor control) compared to 0% responses and 46% disease stabilization on the infusional 5-FU arm (or 46% of patients with tumor control, $p<0.0001$). There was also a significant difference in time to disease progression (4.6 months on FOLFOX4 versus 2.7 months on infusional 5-FU, $p<0.0001$). As importantly, a difference in reduction of tumor-related symptoms was observed (35.4% on the FOLFOX4 arm versus 14.3% on the infusional 5FU arm, $p<0.001$), which correlated with tumor control.

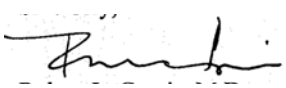
In addition, one of our member Cooperative Groups (North Central Cancer Treatment Group - NCCTG) has completed and presented a study (N9741 , interim results presented at ASCO and ESMO in 2002), involving Eloxatin in combination with infusional 5-FU/leucovorin (FOLFOX4). This study documented significantly higher response rates, times to disease progression and survival, and significantly less toxicity than IFL in the first-line setting.

Both of these results are real and important to patients with colorectal cancer. A decision by CMS to deny reimbursement for this drug will make it inaccessible to thousands of patients who could potentially benefit from its use.

In addition to the tremendous effects a negative coverage decision would have on the lives of individuals with colorectal cancer, it will have a massive, chilling effect on all of the national cancer trials groups attempting to complete accrual to other trials which will refine the role and extend the utility of this important new drug for colorectal cancer.

Our groups treat thousands of colorectal cancer patients who have committed themselves to the clinical trial process in order to lead the way for advances in therapy for the good of all who follow. To interrupt this chain of commitment, courage and progress will do a great harm to both colorectal cancer patients, and the process of medical advancement. On behalf of these truly committed patients, and medical community, which supports and treats them, we urge you to approve the reimbursement of Eloxatin, and revise the proposed policy in order to ensure the availability of new, scientifically proven therapeutic alternatives to Americans with cancer.

Sincerely,



Robert L. Comis, M.D.
President and Chairman

Cc: Jeffrey Shuren, JD
Director, Division of Items and Devices
Center for Medicare and Medicaid Services Mailstop: C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

Commenter: Congressional Delegation (4)
Organization: House of Representatives, Co-Chair House Cancer Caucus

(Comment on next page)

Congress of the United States
Washington, DC 20515

April 11, 2003

Thomas Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Avenue SW
Washington, D.C. 20201

Dear Administrator Scully,

As the Centers for Medicare and Medicaid Services (CMS) considers issuing a final decision regarding the National Coverage Determination process, we would like to share with you our strong support for ensuring any final decision guarantees quality and affordable access to approved medications to Medicare beneficiaries with cancer.

As co-chairs of the House Cancer Caucus, it is our responsibility to educate our colleagues in the House of Representatives about cancer-related issues important to their constituents. From supporting cancer research to initiating screening programs in underserved areas to updating Medicare policy to cover new cancer therapies to ensuring access to care for all Medicare beneficiaries fighting cancer, nearly every constituent in every congressional district across this nation has been touched by cancer in some way, shape or form and cares about these issues. Researchers have invested countless hours and taxpayers have invested billions of dollars into developing life-saving medicines to treat cancer. More than half of all cancer diagnoses are within the Medicare population and 20% of all Medicare beneficiaries have at least one cancer diagnosis. Yet although Medicare does not currently have a comprehensive prescription drug benefit, Medicare does in fact cover therapies to treat cancer.

We would hope that any final decision by CMS regarding Medicare coverage for cancer treatments approved by the Food and Drug Administration (FDA) will continue to ensure patient access. The investments we have made in bringing cancer therapies from bench to bedside have been far too numerous and valuable to implement any changes that could impede patient access.

Thank you for your consideration of our interest in this issue. Please let us know if we can be of any assistance as you continue to move forward in issuing this coverage decision.

Sincerely,

DEBORAH PRYCE
Member of Congress
Co-chair House Cancer Caucus

LOIS CAPPS
Member of Congress
Co-chair House Cancer Caucus

SUE MRYICK
Member of Congress
Co-chair House Cancer Caucus

STEVE ISRAEL
Member of Congress
Co-chair House Cancer Caucus

Commenter: Congressional Delegation (7)
Organization: House of Representatives

(Comment on next page)

Congress of the United States
House of Representatives
Washington, DC 20515

May 8, 2003

Mr. Tom Scully
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Administrator Scully:

It is our understanding that the Centers for Medicare and Medicaid Services (CMS) is currently in the process of determining whether Oxaliplatin is medically necessary for the purposes of allowing for Medicare reimbursement nationwide in both inpatient and outpatient settings.

As you are aware, OXaliplatin -- whose trade name is Eloxatin -- was approved by the Food and Drug Administration last summer for use in patients with colorectal cancer. Specifically, this drug can be used to treat patients with recurring colorectal cancer or patients whose cancer has become worse following the initial therapy.

Currently, seniors in our districts are able to receive Medicare reimbursement if they choose to receive this treatment in a doctor's office, but not in a hospital setting. However, due to the complicated administration of this drug, few doctors are able to offer this treatment. Therefore, Medicare patients all over the state of New Jersey oftentimes are not able to obtain this critical cancer drug.

With approximately 4,800 New Jersey residents who suffer from colorectal cancer, this disease will kill an estimated 1,900 people in New Jersey this year, according to the American Cancer Society (ACS), which also endorses Medicare reimbursements in a hospital setting.

With this in mind, we urge CMS to complete its review of this drug in a timely manner.

Sincerely.

FRANK LOBIONDO JIM SAXTON SCOTT GARRETT

BILL PASCRELL, JR. CHRISTOPHER SMITH STEVEN ROTHMAN FRANK PALLONE

Commenter: Costanzi, John, MD
Organization:

(Comment on next page)

JOHN J. COSTANZI, M.D.
ONCOLOGY & HEMATOLOGY

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MEDICAL OAKS PLAZA #130
2410 ROUND ROCK AVE.
ROUND ROCK, TX 78681
TELEPHONE: (512) 244-1881

March 7, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave., S.W.
Room 3l4-G
Washington, D.C. 20201

SUBJECT: Eloxatin

Dear Ms. Scully,

This letter is to, hopefully, encourage you to allow Eloxatin to be covered by the Medicare program.

Eloxatin (Oxaloplatin for injection) is one of the major break-through drugs for the treatment of colon cancer. I was fortunate enough to use it while it was an experimental drug and the protocol that I had was to use it after patients failed on standard therapy (of which there is not very much). I was extremely surprised by the efficacy of this drug. Of my first ten patients seven of the patients had an excellent response. Normally, no treatment was available to these people and most of them would have to be put on hospice. I was truly excited about the use of this drug. And, I am more excited about even using it up front - as first line treatment for advanced colorectal cancer.

It would be most valuable to have it approved for Medicare coverage.

Because of the prevalence of colorectal cancer in the United States, the potential impact of CMS decision denying or restricting coverage of Eloxatin would be significant. Each year more than 150,000 Americans are diagnosed with colorectal cancer and, unfortunately, 56,000 die of the disease. Of these individuals, 27% are treated in the hospital setting and would be affected by this CMS policy.

CMS's new reimbursement policy will send a negative message to cancer patients, oncologists and the research community that important, new, effective treatments approved by the FDA may not be available to all cancer patients who need them.

An adverse decision by CMS would result in the denial of Medicare coverage for Eloxatin and would be the first time in the United States that an FDA approved cytotoxic agent was not covered by the Medicare program - this is truly a dangerous precedent.

Eloxatin is an example of a new cancer drug that addresses a very important unmet need. Used in combination with other cancer drugs, it is highly effective where no other treatment is available.

Unfortunately, denying Medicare coverage for Eloxatin would adversely affect older Americans who are most likely to be diagnosed with colorectal cancer. These patients need a range of treatments to improve their chances of survival and Eloxatin is definitely one of them.

CMS's action could also discourage research of promising new drugs that would ultimately be effective, but may ultimately be denied coverage and reimbursement.

It is without hesitation that I implore you to help Medicare approve the reimbursement for Eloxatin. This would truly be an impact on mankind.

I thank you for the opportunity of writing this letter. If I can answer any specific questions concerning this topic, please feel free to contact me.

Sincerely,

John J. Costanzi, M.D.

cc: Jeffrey Shuren
JD Director
Division of Items and Devices
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mail Stop C1-09-06
Baltimore MD 21244-1850

JJC:mdp

Commenter: Dakhil, Shaker, MD
Organization: Cancer Center of Kansas, P.A.

(Comment on next page)

Cancer Center of Kansas, P.A.

Shaker R. Dakhil, M.D., F.A.C.P.
Michael W. Cannon, M.D., F.A.C.P.
David B. Johnson, M.D., F.A.C.P.
Bassam I. Mattar, M.D.
Dennis F. Moore, Jr., M.D., F.A.C.P.
Thomas K. Schulz, M.D.

818 North Emporia, #403 • Wichita, KS 67214 • (316) 262-4467 • FAX: (316) 262-3762
www.cancercenterofkansas.com

March 10, 2003

Mr. Thomas A. Scully, Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW, Room 3140
Washington, D.C. 20201

RE: Eloxatin ™ coverage by CMS

Dear Sir:

CMS' new reimbursement policy is sending a negative message to cancer patients, oncologists and the research community that important new treatments approved by the Food and Drug Administration may not be available to all cancer patients who need them. An adverse decision by CMS could result in the denial of Medicare covered for Eloxatin ™ and would be the first time in the U.S. that an FDA-approved cytotoxic agent was not covered by the Medicare program - indeed, a dangerous precedent.

Denying Medicare coverage for Eloxatin ™ would adversely affect older Americans who are most likely to have a diagnosis of colorectal cancer. Restricting patient access would come at a time when the best chances for survival depend upon having a range of treatment options available. In this case, Eloxatin ™ is an effective regimen for patients who have very few treatment options. These patients need a range of therapies to improve their chances of survival.

Eloxatin™ is an example of a new cancer therapy that addresses an unmet need. Used in combination with two other oncology drugs (S-fluorouracil and Leucovorin), Eloxatin ™ is used to treat patients with advanced colorectal cancer who otherwise would have no treatment options.

The availability of more than one effective regimen for advanced colorectal cancer may be the start of a sea change in the treatment of the disease, similar to changes in how breast and ovarian cancers are now treated. CMS policy should support these advances to ensure that all cancer patients under Medicare have the best chance of fighting their cancer. CMS' action could discourage research if promising drugs are ultimately denied coverage and reimbursement.

Because of the prevalence of colorectal cancer in this country, the potential impact of a CMS decision denying or restricting coverage of Eloxatin™ would be significant. Each year, more than 150,000 Americans are diagnosed with colorectal cancer and 56,000 died of the disease.

Of these individuals, 27% are treated in a hospital setting and would be affected by this CMS policy.

Our experience in treating patients with Eloxatin™ at the Cancer Center of Kansas has been very positive.

Thank you for your consideration,

Shaker R. Dakhil, M.D.
President, Cancer Center of Kansas

srd:ks

cc:
Mr. Jeffery Shuren, JD Director
Division of Items and Devices
Centers for Medicare & Medicaid Services
7500 Security Blvd., Mailstop C1-09-06
Baltimore, MD 21244-1850

Commenter: Davis, Walter, MD
Organization: Regional Hematology/Oncology Associates

(Comment on next page)

Regional Hematology/ Oncology Associates
S. Maynard Bronstein MD Edwin B. Cox MD Walter E. Davis MD James W. Hathorn MD
4411 Ben Franklin Blvd., Durham NC 27704
Phone (919) 477-0047 Fax (919) 477-6919

March 10, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Avenue, SW
Washington DC 20201

Dear Mr. Scully,

I am a medical oncologist in private practice and care for both Medicare and Medicaid patients. I am writing to strongly encourage you to approve Oxaliplatin (Eloxatin) for reimbursement with Medicare and Medicaid patients.

This drug alone is probably not the best answer to management of colon cancer that is metastatic, but it adds significantly to the armamentarium that oncologists have to treat patient with advanced metastatic disease. There are few second line agents that are available to use in patients with metastatic disease. Although second line therapy adds little statistically to survival in patients with metastatic colon cancer, this disease in some patients has a rather indolent course and in those patients in particular having second line agents may add many months of relatively good quality oflife. I have recently treated a couple of patients with this drug when they had progressive disease on the other available agents. There has been stabilization for 6 months in one, and regression of disease for 8 months in another patient. They would tell you that the length and quality of life gained is worthwhile to them.

Another issue that seems to me particularly pertinent in this situation, is making this drug not available for reimbursement, makes it quite unlikely that many if any further studies of its use with different combinations and administration formats will be initiated. It is not unheard of for a drug with less than overwhelming activity as frrst available, finds a much more effective use when it is available.

Most patients with metastatic colon cancer will receive 5-FU and leukovorin early in their treatment course. When Oxaliplatin is not available for them, if they have recurrent disease; the only agent that their tumor has not demonstrated resistance to is irinotecan. This certainly is an appropriate agent to use in metastatic disease, but it often is not tolerated well enough by older patients to allow them to continue it regardless of response. In my opinion Oxaliplatin is better tolerated and sometimes the only additional agent that is available to elderly or poor performance status patients with advanced disease.

Walter E. Davis MD

cc:

Jeffery Shuren
JD Director
Division of Items and Devices
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Baltimore MD 21244-1850

Regional Hematology/ Oncology Associates
S. Maynard Bronstein MD Edwin B. Cox MD Walter E. Davis MD James W. Hathorn MD
4411 Ben Franklin Blvd., Durham NC 27704
Phone (919) 477-0047 Fax (919) 477-6919

Poppy S. Kendall, MHS
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Room C1-12-06
Baltimore MD 21244-1850

Commenter: Donley, Susan
Organization: Eyeontheprize.org

(Comment on next page)

EyesOnThePrize.org:
Support for Women with Gynecologic Cancer
www.EyesOnThePrize.org

March 12, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW
Room 314G
Washington, DC 20201

Sent by email and hardcopy

Dear Mr. Scully,

EyesOnThePrize.org: Support for Women with Gynecologic Cancer is one of many cancer organizations representing the 9,000,000+ Americans who have been directly touched by cancer.

We are writing to urge that Medicare reimburse beneficiaries for Eloxatin (oxaliplatin) therapy against advanced colorectal cancer. Eloxatin has shown to provide a very significant benefit to these patients.

Eloxatin is an example of a new cancer therapy that addresses an unmet need. Used in combination with two other oncology drugs (5fluorouracil and leucovorin), Eloxatin is used to treat patients with advanced colorectal cancer who otherwise would have no treatment options. The Food and Drug Administration (FDA) approved Eloxatin in record time, reflecting the obvious benefit to the many patients who have received it.

Prior to now, patients with advanced colorectal cancer have had only one treatment option. The availability of more than one effective regimen for advanced colorectal cancer may be the start of a sea change in the treatment of the disease, similar to the changes in how breast and ovarian cancers are now treated. CMS policy should support these advances to ensure that all cancer patients under Medicare have the best chance of fighting their cancer.

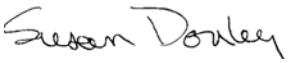
In addition, we are gravely concerned to learn that the Centers for Medicare & Medicaid Services (CMS) will no longer defer to the expertise of the FDA in determining whether to cover drugs for their labeled indications.

FDA approval is viewed as the gold standard of safety, effectiveness and clinical benefit. This was recognized by Congress in 1993 when they

restricted the discretion of CMS and its contractors to deny coverage for drugs use against cancer. Specifically, for purposes of coverage, the term "drugs" was defined to include "any drugs or biologicals used in an anticancer chemotherapeutic regimen for a medically accepted indication," including "any use which has been approved by the Food and Drug Administration." 42 U.S.C. §1395x (t)(2)(A and B).

This policy will come under fire from **all** cancer patients as new, promising cancer therapies are approved and beneficiaries with cancer are denied access to life-extending therapies.

Thank you for your careful consideration of our concerns,



Susan Donley
President
EyesOnThePrize.org: Support for Women with Gynecologic Cancer
412-828-8679
SueD@eyesontheprize.org

cc: *Jeffery* Shuren, JD
Director
Division of Items and Devices
Centers for Medicare & Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Baltimore, MD 21244-1850

Poppy S. Kendall, MHS
Centers for Medicare & Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Room C1-12-06
Baltimore, MD 21244-1850

Commenter: Eisenberg, Peter, MD
Organization: California Cancer Care, Inc.

(Comment on next page)

CALIFORNIA CANCER CARE, Inc.

Mike Turbow, M.D.
Kent Adler, M.D.
John Siebel, M.D.
Brenda Shank, M.D., Ph.D
Douglas A. Kaufman, M.D.

Peter D. Eisenberg, M.D.
Bobbie Head, M.D., Ph.D.
David S. Gullion, M.D.
Jennifer B. Lucas, M.D.

March 11, 2003

Mr. Thomas A. Scully, Administrator
Centers for Medicare and Medicaid Services
Room 314G
200 Independence Avenue, SW
Washington DC 20201

Dear Mr. Scully:

We are doctors who care for patients with cancer. We participate in many clinical trials and have a large experience with Eloxatin (oxaliplatin).

In fact, before it was approved, we treated more than 100 patients with Eloxatin as we were one of only two sites in California to have the drug available for compassionate use.

In our experience, Eloxatin is an active agent for colorectal cancer, and the FDA has agreed by approving it.

That CMS is considering denying Medicare coverage for Eloxatin is of great concern to my colleagues and me for these reasons:

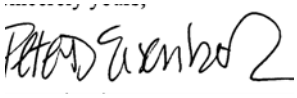
1. It is an effective agent for the treatment of colo-rectal cancer and has been approved by the FDA for such treatment.
2. There are no very effective treatments for colo-rectal cancer, and Eloxatin significantly improves our choices for therapy
3. CMS sends a negative message to cancer patients, oncologists and the research community that important new treatments, approved by the FDA, might not be available to all cancer patients who need them.
4. This would be the first time that an FDA-approved cancer agent was not covered by the Medicare program - - this seems to be a dangerous precedent.

5. The most significant group to suffer would be older Americans who are most likely to have a diagnosis of colorectal cancer. Restricting patient access to this effective drug would come at a time when a wide range of treatment options should be made available.
6. Eloxatin is an example of a new cancer therapy that addresses an unmet need. Used in combination with other oncology drugs it seems to be most effective.
7. CMS's action could discourage research if new and effective drugs are denied coverage.
8. Each year, more than 150,000 Americans are diagnosed with colorectal cancer. Almost 60,000 of them die with their disease. If CMS denies coverage for Eloxatin, a significant number of patients would be so affected.

We hope that CMS will re-consider and cover this FDA-approved drug, one with significant activity in colorectal cancer, for Medicare coverage.

Thank you very much for your consideration.

Sincerely yours,



Peter Eisenberg, M.D.
cc: Jeffrey Shuren, JD Director
Division of Items & Devices
Centers for Medicare and Medicaid Services
Mailstop C1-09-06
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Poppy S. Kendall, MHS
Centers for Medicare and Medicaid Services
Mailstop CI-09-06; Rm C1-12-06
7500 Security Blvd
Baltimore, Maryland 21244-1850

1350 South Eliseo Drive, Suite 200, Greenbrae, California 94904-2011
Phone: (415) 925-5000 Fax: (415) 925-5050

Commenter: Ellison, Russell, MD
Organization: Medical Affairs

(Comment on next page)

March 14, 2003

Ms. Poppy Kendall
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Mailstop CI-09-06, Room *C1-12-06*
Baltimore, Maryland 21244-1850

Reference: Oxaliplatin (Eloxatin®) for Colorectal Cancer
#CAG-00179N

Dear Ms. Kendall:

Sanofi-Synthelabo Inc. (Sanofi) is the manufacturer of Eloxatin® (oxaliplatin by injection), a chemotherapeutic agent that received accelerated approval by the Food and Drug Administration (FDA) last year, as a significant new addition to the treatment of patients with advanced colorectal cancer *(CRC).* Sanofi is a major global research-based pharmaceutical group, headquartered in Paris, France, with 30,000 employees in more than 100 countries. Our U.S. headquarters is in New York, and we have over 3500 employees in the U.S. in facilities and offices in 8 states and Puerto Rico. Our efforts focus on the major public health challenges corresponding to our areas of expertise: cardiovascular disease and thrombosis, diseases of the central nervous system, internal medicine and oncology.

Background

Eloxatin®, our newest oncology product, is undergoing a national coverage determination (NCD) by the Centers for Medicare and Medicaid Services (CMS) to determine whether the drug is suitable for Medicare coverage in the treatment of Medicare beneficiaries suffering from *CRC.* Sanofi is pleased to provide additional comments in support of this significant new addition to the currently very limited therapeutic options for patients with advanced *CRC,* a disease that causes enormous suffering. These comments supplement the detailed presentation made recently to the Agency's coverage staff in Baltimore, MD by noted clinical investigators from Vanderbilt University and the Mayo Health Foundation, joined by company representatives.

Eloxatin® (oxaliplatin by injection), as a new chemotherapy drug, received approval by the FDA following a 46-day priority review. Eloxatin®, in combination with S-fluorouracil (S-FU) and leucovorin (LV), was approved as a so-called 2nd line therapy for an unmet medical need in patients whose advanced colorectal cancer has recurred or progressed following 1st line therapy. At the time

of the approval, noted health leaders, including Secretary Tommy Thompson, voiced strong approval of this significant addition to CRC care.

Since then, Eloxatin®, in the regimen approved by FDA, was rapidly incorporated in the major cancer treatment guidelines promulgated by the National Comprehensive Cancer Network (NCCN), a leading professional health care organization in the U.S. There should be no question of the value of this therapy from the perspective of professionals engaged in oncology care, nor in the improvement in cancer care that this therapy will bring to the Medicare population relative to currently covered therapies.

Sanofi applied last Fall for recognition of Eloxatin® as a pass-through drug in the Medicare hospital outpatient prospective payment system, with expected approval to have been effective with hospital payment updates onJanuary 1,2003. We were surprised and dismayed at the Agency's decision to delay consideration of that application and instead divert this drug for a national coverage determination. Not only does this action delay access for Medicare beneficiaries with CRC to the clearly and demonstrably superior 2nd line therapy for advanced CRC, it places a financial burden on hospitals and major cancer centers that wish to incorporate Eloxatin® into their therapeutic regimens.

Sanofi has provided free treatment in the past few years to over 10,000 CRC patients through our compassionate use programs. However, we expected that those programs could wind down gradually once FDA approval was gained. Our goal, therefore, is to expeditiously secure favorable coverage for Eloxatin® for Medicare beneficiaries consistent with our original application.

Summary

Review of clinical evidence is integral to the NCD process and necessarily complex. Therefore, we will simply summarize in this cover letter the major pertinent points in support of Medicare coverage of Eloxatin®. Attached you will find essential supporting material in the following areas: background on the history and state-of-the-art of treatment for CRC (Attachment A), and a question and answer response to CMS's published matrix of four coverage questions (Attachment B). As noted, these supplement the detailed slide presentation and research findings provided earlier. In brief, at the present time, metastatic, unresectable CRC is not a curable disease. The paradigm, therefore, for the treatment of such non-resectable cancers is to use *combinations* of drugs that have differing mechanisms of action and non-overlapping toxicities. It is in combination with other drugs that oxaliplatin brings genuine advancement in clinical benefit for CRC patients. The main dimensions for evaluating benefits for

patients relate to stabilization of the disease, tumor response, and evaluation of tumor-related symptoms.

FDA approved the combination of oxaliplatin/5-FU/leucovorin (aka FOLFOX4) as a 2nd_line therapy when a significant improvement in response rate and time to disease progression was demonstrated in patients with progressive CRC relative to other therapies. Critical factors in the FDA's decision to approve the regimen were: the trial was a randomized, well-controlled trial; the trial was rigorously monitored, with objective endpoints and toxicities assessed by an independent Data and Safety Monitoring Board and, finally, the differences that were observed both rose to the level of statistical significance and also provided validated and meaningful measures of clinical relevance ('clinical efficacy').

Conclusion

To summarize, it was found that oxaliplatin, when used in conjunction with 5FU and leucovorin, is the onlyeffective treatment for patients with progressive colorectal cancer following front-line chemotherapy.

The crucial benefits are expressed in the areas of disease stabilization, tumor response, and significant and sustained relief in tumor-related symptoms. The tumor-related symptoms relate to pain and analgesic consumption, performance status, body weight loss and other symptoms that cause great discomfort and difficulty for patients undergoing these life-prolonging therapeutic regimens. Medicare currently covers 5FU and leucovorin. Based on the major improvements for patients shown in clinical trial results due to adding oxaliplatin to the therapeutic regimen, it is clearly essential for patients with advanced CRC that the Medicare program provide rapid coverage of Eloxatin® for inclusion in the older and already covered regimen, in all clinically appropriate settings.

Thank you for the opportunity to provide information on our product, Eloxatin®, which we think represents a major advance in treatment of advanced colorectal cancer. This is an advance that must not be denied to Medicare patients. We would be pleased to answer any other questions that you might have during this process. Please direct any inquiries or requests for further information to our representative, Kathy Means of Patton Boggs LLP in Washington, DC. She can be reached on 202457-6328.

Sincerely,

/s/
Russell Ellison, M.D.
Vice-President, Medical Affairs

Attachment A

Additional Background On Colorectal Cancer, Disease Staging And General Therapeutic Regimens

Colorectal Carcinoma

Approximately 152,000 new cases of colorectal carcinoma are diagnosed in the U.S. each year. At the time of diagnosis, nearly 75% of patients (approximately 114,000 patients) have disease that is restricted to the colon. The treatment for such colon-limited tumors is surgery, with curative intent. Patients considered at high risk for relapse or disease progression, determined by the depth and extent of tumor invasion, the spread into local tissues or lymph nodes, as well as (investigationaily) certain biologic markers, may receive adjuvant (post-operative) chemotherapy, and some patients (such as those with rectal carcinoma) receive radiotherapy. The standard adjuvant chemotherapy regimen is 5-FU/leucovorin.

Disease Staging

Following is a schematic of tumor staging and treatment for colorectal cancer:

Stage 0: Tumor that is non-invasive; limited only to the cells that directly line the intestinal tract.

Stage I: Tumor invading into the submucosa, the layer of cells beneath those directly lining the tract.

Stage II: Tumor beyond the submucosa, into the muscular layer of the intestine.

Stage III: Anyone of the following: tumor invasion through the intestinal tract and into the local tissues; or any involvement of one or more lymph nodes that surround the intestine (even if the rest of the tumor remains relatively localized and non-invasive).

Stage IV: Metastatic disease.

Overview of Therapeutic Regimens

The initial treatment for all patients with non-metastatic (stages I-III) disease is surgery, with curative intent. (patients with rectal carcinoma are generally pretreated with radiotherapy, in order to perform sphincter-sparing procedures, i.e., to

limit the extent of resection so as to preclude the need for a colostomy.) Patients with stage III disease are considered at high risk for relapse or disease progression, and are routinely treated with adjuvant chemotherapy (chemotherapy that is begun almost immediately after surgery). Investigationally, certain subsets of patients with stage II disease may also receive adjuvant chemotherapy, although the prognostic factors that lend to such decision-making are still are a matter of controversy. The standard adjuvant chemotherapy regimen is 5-FU/leucovorin, administered on one of several dosing schedules, over a period of up to 6 months.

Despite all these measures, nearly 50% of patients who initially present with localized disease will relapse with distant metastases, and an additional 25% of the total 152,000 (38,000 patients) are found to have disease that has already metastasized at the time of diagnosis.

At the present time, metastatic, unresectable CRC *is not a curable disease. The paradigm, therefore, for the approach to the treatment of such non-resectable cancers is to use combinations of drugs that have differing mechanisms of action and non-overlapping toxicities.* The rationale for such combinations is that, by using a combination of approaches, the therapy may either literally cause tumors to regress (by virtue of actual tumor cell death) or, at least, result in disease stabilization, with a cessation of tumor growth. In hematologic malignancies, four and five drug regimens are common. However, in the solid tumors (e.g., CRC, breast carcinoma, ovarian carcinoma, etc.), it has become evident over the years that there is greater gain for patients when relatively simple regimens (e.g., two drug combinations) are given sequentially compared to those in which 3 or more drugs given at once.

Until the recent past, the prognosis for patients found to have metastatic CRC was dismal. Despite intensive efforts and myriad clinical trials over a period of more than 25 years (1970-96), the only agents shown to have efficacy was the combination of 5-FU/leucovorin, which yielded a median survival of 11 months. (It should be noted that 5-FU is the active agent; leucovorin is always co-administered with 5-FU, as it serves to "rescue" normal cells from 5-FU's toxic effects; hence, 5-FU/leucovorin is viewed as a single agent.) *Unti11996, there were no therapeutic options for patients who failed front-line 5-FU/ leucovorin.* In 1996, irinotecan was approved as a second-line agent for patients failing front-line 5-FU/leuvovorin. In 2000, on the basis of a randomized clinical trial of first-line therapy that compared the combination of irinotecan/5-FU/leucovorin (IFL) to 5-FU/leucovorin, IFL was approved and became the standard of front-line care, when it was found that the regimen yielded a median survival of 14-16 months, a clear improvement over the 11 month survival obtained with 5-FU/leucovorin alone. However, not all patients were able to benefit from IFL therapy, and even those with optimal benefit had non-durable responses. Moreover, many patients were unable to tolerate the regimen's toxicities which were, in some instances, life threatening.

Prior to August 2002, patients whose disease progressed eifter IFL or who were unable to tolerate IFL *had no approved therapeutic options.* Having failed IFL, there was no rationale to re-dosing them with single agent irinotecan, or even with irinotecan in combination with 5-FU/leucovorin; their tumors, in progressing, had already proved themselves to be resistant to the therapy. Such resistance is called "refractoriness". It may be intrinsic to a particular tumor, i.e., a tumor may be inherently insensitive to a drug or combination., or it may be acquired: a tumor that was initially sensitive to therapy may mutate and develop mechanisms of specific or even multi-drug resistance. While there have been studies treating such tumors with another dosing schedule or even dosage formulation of 5-FU (eg., the oral5-FU pro-drug, capecitabine), there is no evidence that either of these approaches induces anything more than transient responses (at best), and the therapeutic indices are typically unfavorable (more pain than gain).

Introduction of Oxaliplatin as FDA-Approved 2nd_line CRC Therapy

In August 2002, the combination of oxaliplatin/5-FU/leuvorin (FOLFOX4) was approved as 2nd_line therapy when a significant improvement in response rate and time to disease progression was demonstrated in patients with progressive CRC after IFL compared to infusional 5-FU/leucovorin alone (a third arm, single agent oxaliplatin, was also studied). Critical factors in the FDA's decision to approve the regimen were: the trial was a randomized. well-controlled trial; the trial was rigorously monitored. with objective endpoints and toxicities assessed by an independent Data and Safety Monitoring Board and, finally, the differences that were observed both rose to the level of statistical significance and also provided validated and meaningful measures of clinical relevance ('clinical efficacy').

Mechanisms of Action

With the three FDA-approved agents for the treatment of CRC, it is now possible to mount a coordinated approach to the treatment of CRC. We now have different ways to attack tumor cells: we can inhibit two different enzymes, both of which are critical to cell replication: thymidylate synthase (5-FU) and topoisomerase I (irinotecan); and can also directly damage the tumor cell DNA, itself (oxaliplatin). **As noted earlier, it is critical to understand that it is the use of these drugs, including the additional power granted by the introduction of oxaliplatin, in combinations and in sequence that is creating significant recent strides in the treatment of patients with colorectal cancer.**

Attachment B

The Significance of Oxaliplatin in Caring for Medicare Patients with CRC
Study EFC 4584

The Medicare program has published four questions to guide the consideration of value of new therapies for coverage purposes in the Medicare program. These are:

CMS Coverage Questions

1) Is there sufficient evidence that demonstrates that the item or service is medically beneficial to a defined patient population?

2) For the defined patient population, is there a medically beneficial alternative item or service(s) that is the same clinical modality and is currently covered by Medicare?

3) Is the item or service substantially more or substantially less beneficial than the Medicare-covered alternative?

4) Will the item or service result in equivalent or lower total costs for the Medicare population than the Medicare-covered alternative?

Importance of Oxaliplatin to Medicare Beneficiaries

The study design, methodology and results of EFC 4584 were already provided to CMS coverage staff. This is the trial that provided the basis for FDA approval of oxaliplatin/ 5-FU/LV for second-line therapy of metastatic CRC. The results of the study, therefore, may be addressed in the context of *three of the four CMS* matrix questions as follows:

1) Is the item or service substantially more or substantially less beneficial than the Medicare-covered alternative?

In August 2002, the combination of oxaliplatin/5-FU/leuvorin (FOLFOX4) was approved as 2nd-line therapy when a significant improvement in response rate and time to disease progression was demonstrated in patients with progressive CRC after IFL compared to infusional5-FU/leucovorin alone (a third arm, single agent oxaliplatin, was also studied). Critical factors in the FDA's decision to approve the regimen were: the trial was a randomized. well-controlled trial; the trial was rigorously monitored, with objective endpoints and toxicities assessed by an independent Data and Safety monitoring Board and, finally, the differences that were observed both rose to the level of statistical significance and also provided validated and meaningful measures of clinical relevance ('clinical efficacy').

Note that in prior independent studies, infusional 5-FU was shown to have superior efficacy and reduced toxicity compared to bolus 5-FU regimens ("bolus" refers to rapid intravenous administration, as compared to infusion over an extended period.) Patients treated with FOLFOX4 not only had more frank tumor

regression than those on infusional 5-FU/LV (9.9% vs. 0%, p<0.0001) but they had more disease stabilization (60% vs. 46%), which lasted longer than the stable disease seen with infusional 5-FU. Viewed together, this translated into increased (70% vs. 46%); and more sustained tumor control, the ability to keep the tumor in check longer. The fact that there was a significant difference in time to disease progression (4.6 months vs. 2.7 months, p<0.0001), which favored those on the FOLFOX4 arm, provided evidence that this beneficial effect was more sustained on FOLFOX4 than on the infusional 5-FU/LVarm.

It also must be noted that toxicities experienced by patients on the FOLFOX4 arm were at least as manageable as those due to S-FU/LV, and could generally be mitigated or prevented with either prophylactic measures (such as routine antiemetics) or, in the case of neuropathy, by cessation of therapy. The fact that there was a significantly greater reduction in tumor-related symptoms (see below) observed in patients on FOLFOX4 compared to those on the control arms supports a favorable therapeutic ratio (benefit:toxicity) on the FOLFOX4 arm.

Therefore, FOLFOX4 is substantially more beneficial than the Medicare-covered alternative.

2) For the defined patient population, is there a medically beneficial alternative item or service(s) that is the same clinical modality and is currently covered by Medicare?

The answer to the first question also addressed this point. However, it is important to understand that *Study EFC* 4584 *demonstrates not only that the* FOLFOX4 *regimen is superior to the alternative, 5-FU/ leucovorin, but that the combination of the agents is necessary to derive the benefit - neither will suffice as single agents.* And, as noted above, in patients whose tumors had clearly developed resistance - or had been inherently insensitive to irinotecan, there was no rationale to re-dosing with that drug. Note also that none of the other platinum-based chemotherapy drugs is active in colorectal cancer.

3) Is there sufficient evidence that demonstrates that the item or service is medically beneficial to a defined patient population?

There was a relatively novel feature of Study EFC 4584 that permitted a direct and immediate measure of clinical benefit, and that is the assessment of the tumor-related symptoms (TRS). The TRS results (composite score) in Study EFC 4584 demonstrated that 35.4% of patients on FOX4compared to 14.3% of those on infusionaI 5-FU/LV (p<0.001) experienced a measurable and sustained improvement in their tumor-related symptoms. This is discussed below.

A key consideration in assessing the results of a clinical trial is the true clinical relevance of study endpoints. The simplest modality is tumor response rate, which represents objective assessments of measurable tumor burden (as compared, for example, to that which is not directly measurable, such as tumor in bone metastases or body cavity fluids). However, response rate is no longer considered the only meaningful endpoint for trials, as responses may be non-durable, and need not translate into increased disease-free survival (typically called time to disease progression, or TIP). Moreover, measurable tumor may only provide a hint of the true tumor burden.

As stated above, there was a relatively novel feature of Study EFC 4584 that permitted a direct and immediate measure of clinical benefit, and that is the assessment of the tumor-related symptoms (TRS). In order to put this in perspective, it is useful to understand that there was as great a degree of rigor and careful follow-up required for these evaluations as was required for the measurements of the physical parameters of individual tumors. Moreover, in order to be considered evaluable for these assessments, a patient had to have symptomatology, as measured by validated and objective criteria, that had been previously determined (in discussions with the FDA and well-regarded independent investigators, prior to beginning the protocol) as likely to substantially interfere with a patient's life. And, in order to be considered a TRS "responder", the TRS improvement had to be sustained for a minimum of 4 weeks (identical to the requirement for tumor response assessment). Therefore, any therapy that could significantly mitigate this symptomatology could be viewed objectively as being clinically meaningful.

Thus, the TRS evaluations made it possible to more directly assess the true burden of illness as experienced by the patient, which can provide a starting point for further assessing the epiphenomena and costs associated with this illness.

The TRS results (composite score) in Study EFC 4584 demonstrated that 35.4% of patients on FOLFOX4 compared to 14.3% of those on infusiona1 5-FU/LV ($p<0.001$) experienced a measurable and sustained improvement in their tumor-related symptoms. [Note: this result differs slightly from that in the Rothenberg manuscript because this analysis is derived from the NDA, which worked from a slightly more up-dated database than the Rothenberg manuscript, which was submitted for publication a few months earlier.] Statistically, there was a positive correlation between TRS improvement and tumor control. Thus, these clinical evaluations provide a parallel insight into the benefit represented both by increased time to disease progression and the improved control of measurable tumor burden observed with FOLFOX4 compared to infusional 5-FU/LV. Therefore, the results of Study EFC 4584, in their totality, permit a more comprehensive understanding of the burden of illness for patients.

4) Will the item or service result in equivalent or lower total costs for the Medicare population than the Medicare-covered alternative?

Detailed materials on this point were provided to CMS in the company's initial presentation. To summarize, the most useful point of comparison is the estimated total regimen cost for 2nd-line therapy for Medicare beneficiaries suffering from advanced CRe. At present, Medicare covers Camptosar® (irinitecan) for 2nd-line indications. Eloxatin® (oxaliplatin) has a higher per vial price than Camptosar®, but that is highly misleading. After adjusting for dosing, average number of cycles associated with each drug, and cost per cycle based on average wholesale price, the estimated regimen cost for Eloxatin® ($17,892) compares favorably with Camptosar® ($23,016.) We estimate Eloxatin®'s contribution to the care of the Medicare population receiving 2nd-line therapy for CRC to rise gradually from about 9,177 patients (41% share) in 2003 to about 12,758 patients (57% share) in 2005. We believe that Eloxatin® will result in equivalent or lower costs for the Medicare population.

Commenter: Emanuel, David, MD
Organization: Sanofi-Synthelabo, Inc.

(Comment on next page)

sanofi~synthelabo

Wednesday, July 09, 2003

Centers for Medicare and Medicaid SelVices
7500 Security Boulevard
Mailstop C1-09-06, Room C1-12-06
Baltimore, Maryland 21244 -1850
Attention: Gay Burton

Reference: Oxaliplatin (Eloxatin®) **for Colorectal Cancer** (CRC)
CAG00179N

Dear Ms. Burton:

Sanofi-Synthelabo Inc. (Sanofi is the manufacturer of Eloxatin® (oxaliplatin by injection), a chemotherapeutic agent that received accelerated approval by the Food and Drug Administration (FDA) last year, as a new addition to the limited number of active drugs available to treat patients with colorectal cancer (CRC). Sanofi is a major global research-based pharmaceutical group, headquartered in Paris, France, with 30,000 employees in more than 100 countries. Our U.S. headquarters is in New York, and we have over 3500 employees in the U.S. in facilities and offices in 8 states and Puerto Rico. Our efforts focus on the major public health challenges corresponding to our areas of expertise: cardiovascular disease and thrombosis, diseases of the central nervous system, internal medicine and oncology.

CMS recently determined that Eloxatin qualified for pass-through payment under the hospital outpatient prospective payment system (OPPS) as a component of the treatment of advanced metastatic colorectal cancer. It is our understanding that pass-through payment for this indication will be effective for services furnished on or after July 1,2003. Pursuant to this approval Sanofi-Synthelabo has requested a meeting with CMS to discuss the potential use of Eloxatin for the adjuvant treatment of colorectal cancer.

The use of chemotherapy following prior total surgical resection of tumor is known as adjuvant treatment, which, in contrast to the use of chemotherapy in the advanced disease setting, always has curative intent. The primary purpose of this letter is to provide information to support the position that physicians caring for patients with CRC should have the option of prescribing Eloxatin for adjuvant use if and when this is clinically indicated. This decision would always be made in the context of whether the addition of Eloxatin to 5-fluorouracil plus leucovorin, the currently utilized standard of care, would potentially enhance the prospect for cure.

Review of all available clinical evidence is integral to the review process and is necessarily complex. We have not yet had the opponunity of presenting these data to CMS, which will be done at the scheduled July 11th meeting. Therefore, I will only provide a top-line summary of the major pertinent points to be discussed at the upcoming meeting. Patients who are initially diagnosed with colorectal cancer undergo a workup to determine the extent of disease. This process is known as staging. A universally recognized staging process has been developed, which determines how an individual patient will be treated following the initial diagnosis. A simplified

summary of the staging system used in colorectal cancer and the intent of treatment for each stage is graphically presented below in Table 1.

Table 1: Clinical Staging of Colorectal Cancer

Stage	Local Spread of Tumor	Lymph Node Involvement	Presence of Metastases	Treatment Treatment Intent
1	Confined to the superficial layers of the bowel wall	No	No	Surgery *Cure*
2	Extends through the bowel wall	No	No	Surgery +_adjuvant chemotherapy *Cure*
3	Extends through the bowel wall	Yes	No	Surgery +_adjuvant chemotherapy *Cure*
4	Extends through the bowel wall	Yes or No	Yes	Chemotherapy *Prolong survival Tumor-related symptom control*

Approximately 75% of patients with CRC will present at a stage when the tumor can be surgically resected. Nevertheless more than 50% of patients will eventually die of metastatic disease, primarily because residual disease is not noted at the time of surgery. Patients with stage I disease are treated by surgical resection of the tumor and are not candidates for adjuvant chemotherapy. Patients with stage II disease, where the disease is still localized to the colon, have heretofore not routinely been considered candidates for adjuvant chemotherapy. However a significant number of these patients will eventually go on to develop advanced metastatic disease despite surgical resection of their tumor at the time of initial diagnosis and will die as a consequence. After the efficacy and safety of adjuvant chemotherapy was unequivocally demonstrated in patients with Stage III disease, adjuvant chemotherapy studies in patients with stage II disease have been undertaken. A great deal of research is still ongoing to determine how to best identify patients with stage II disease who might benefit from adjuvant chemotherapy. In contrast, most patients with stage III disease, who are able to tolerate chemotherapy, are offered the opportunity for adjuvant treatment. The use of adjuvant chemotherapy in patients with stage III disease has been demonstrated to improve overall survival by reducing the risk of subsequent relapse. The prevailing standard of care in the United States is the use of leucovorin modulated 5-fluorouracil (5-FU) therapy, which is usually given for a period of 6 months following surgery.

Although the clinical stage of disease is the primary determinant of treatment outcome, various additional clinical risk factors have also been identified which significantly impact on an individual patient's chance for cure. These include the number of regional lymph nodes that are infiltrated with tumor, the tumor histology and genetic profile, bowel obstruction and perforation of the involved colon. In practice, the decision to offer adjuvant chemotherapy to an individual patient is a complex one and is dependent on a number of factors, including disease stage, the presence or absence of risk factors, patient age and patient/physician preference. In essence, the decision is always driven by an assessment of risk versus benefit for the individual patient.

Summary of New Clinical Data supporting the Use of Eloxatin for the Adjuvant Treatment of Colorectal Cancer

In October 1998 Sanofi-Synthelabo initiated a large international study called MOSAIC to compare the efficacy and safety of the combination of Eloxatin, 5-FU and Leucovorin (FOLFOX4) to a control arm of 5-FU and Leucovorin alone (de Gramont regimen), as adjuvant therapy for patients with either stage II or stage III colorectal cancer who had a prior complete resection of their tumor. The FOLFOX4 regimen is currently registered in the United States for the second-line therapy of colorectal cancer following failure of a first-line irinotecan-containing chemotherapy regimen. The primary endpoint of the study was the comparative 3-year disease-free survival (DFS), a standard endpoint currently being used in other adjuvant treatment studies currently being conducted in the United States. Secondary endpoints included safety and overall survival. Prior studies using the de Gramont and other 5-FUlLV regimens for the adjuvant treatment of CRC consistently demonstrated a 65-73% 3-year disease-free survival rate. The expectation for the MOSAIC study was that the addition of Eloxatin to 5-FU/LV would improve 3-year DFS to 79%, representing an absolute increase of 6% or a reduction of risk of relapse of 25% compared to 5FUlLValone. In order to have 90% power to detect this difference, 2200 patients were required for the study.

2246 patients (1123 patients into each arm) were enrolled from October 1998 through January 200l. The five highest enrolling countries were France, United Kingdom, Spain, Italy and Belgium.

The 3-year DFS was observed to be 77.8% in the FOLFOX4 arm and 72.9% in the 5-FU/LVcontrol arm representing a 23% risk of relapse reduction in the FOLFOX4 arm of the trial. This highly statistically significant result demonstrates that the use of FOLFOX4 for the adjuvant therapy of CRC is superior to the use of 5-FUlLValone. Importantly, the adjuvant use of the FOLFOX4 regimen was well tolerated and safe, with a toxicity profile very similar to that observed in the pivotal registration trials resulting in 2nd-line CRC approval. The incidence and severity of Eloxatin-induced neurological toxicity, a well described side effect of the use of platinum-containing chemotherapy regimens, was similar to that observed in prior Eloxatin trials. Of great interest was the observation that most neurological toxicity was mild to moderate in severity with only 1% of patients having functionally significant neurological toxicity 1 year after completing treatment.

Sanofi-Synthelabo Inc.

90 Park Avenue, New York, NY 10016 - Tel.: (212) 551-4300 - Fax: (212) 551-4902

To put this result in perspective, this is the first trial to have demonstrated a significant improvement in DFS in colorectal cancer for >10 years. The crucial benefit of Eloxatinl5-FU/LV is expressed in the statistically significant improvement in 3-year DFS compared to the use of 5-FUlLV. Medicare currently covers the combination of 5-FU and leucovorin as adjuvant treatment of colorectal cancer. A 23% reduction of the risk of relapse with the addition of oxaliplatin to the current standard of care will result in thousands of lives saved annually in the United States. Based on these data and the proven demonstration of the safety of the FOLFOX4 regimen in multiple clinical trials, it is vital that patients are not denied access to this therapy for reimbursement reasons if their physician determines that this treatment is clinically indicated and desirable for the patient.

We are most grateful for the July 11th invitation to present information to CMS on Eloxatin as a component of the adjuvant therapy of colorectal cancer treatment. It is quite clear that the oncology community has determined that this new therapy represents a major advance in the treatment of colorectal cancer. You will shortly be receiving further information about the potential impact of this therapy regimen on the adjuvant therapy of colorectal cancer from key oncology opinion leaders in the United States. In addition, we would be pleased to answer any other questions that you might have during this process. Please direct any inquiries or requests for further information to our representative, Kathy Means of Patton Boggs LLP in Washington, DC. She can be reached on 202 457-6328.

Sincerely,

David Emanuel MD
Senior Director, Oncology
Sanofi-Synthelabo Inc.
90 Park Avenue, New York Qty, NY 10016

The Significance of Oxaliplatin as Adjuvant Therapy for Medicare Patients with CRC MOSAIC Study

The Medicare program has published four questions to guide the consideration of value of new therapies for coverage purposes in the Medicare program. These are:

CMS Coverage Questions

1) Is there sufficient evidence that demonstrates that the item or service is medically beneficial to a defined patient population?

2) For the defined patient population, is there a medically beneficial alternative item or service(s) that is the same clinical modality and is currently covered by Medicare?

3) Is the item or service substantially more or substantially less beneficial than the Medicare-covered alternative?

4) Will the item or service result in equivalent or lower total costs for the Medicare population than the Medicare-covered alternative?

Importance of Oxaliplatin to Medicare Beneficiaries

A full presentation of the study design, methodology and results of the MOSAIC study will be provided to CMS coverage staff at the meeting scheduled for July 11th 2003. The results of the study, therefore, will only be addressed in the context of *three of the four* CMS matrix questions as follows:

1) Is the item or service substantially more or substantially less beneficial than the Medicare-covered alternative?

In August 2002, the combination of oxaliplatinl5-FU/leuvorin (FOLFOX4) was approved as 2nd - line therapy when a significant improvement in response rate and time to disease progression was demonstrated in patients with progressive CRC after failure of first-line therapy with the combination of irinotecanl5-FU and leucovorin (IFL) compared to infusional5-FU/leucovorin alone (a third arm, single agent oxaliplatin, was also studied). The same Eloxatin-containing regimen (FOLFOX4) was utilized as the experimental arm of the MOSAIC study.

In October 1998 Sanofi-Synthe1abo initiated a large international study called MOSAIC to compare the efficacy and safety of the combination of Eloxatin, 5-FU and Leucovorin (FOLFOX4) to a control arm of 5-FU and Leucovorin alone (de Gramont regimen) as adjuvant therapy for patients with either stage II or stage III colorectal cancer who had a prior complete resection of their tumor. The primary endpoint of the study was the comparative 3-year disease-free survival (DFS), which is the FDA-sanctioned endpoint currently being used for adjuvant treatment trials in colorectal and breast cancer in the United States. Secondary endpoints included safety and overall survival. Prior studies using the de Gramont and other 5-FUlLV regimens for the adjuvant treatment of CRC consistently demonstrated a 65-73% 3-year disease-free survival rate. The expectation for the MOSAIC study was that the addition of Eloxatin to 5-FU/LV would improve 3-year DFS to 79%, representing an absolute increase of 6% or a reduction of risk of relapse of 25% compared to 5FU/LV alone. In order to have 90% power to detect this difference, 2200 patients were required for the study.

2246 patients (1123 patients into each arm) were enrolled from October 1998 through January 2001. The five highest enrolling countries were France, United Kingdom, Spain, Italy and Belgium.

The 3-year DFS was observed to be 77.8% in the FOLFOX4 arm and 72.9% in the 5-FU/LVcontrol arm representing a 23% risk of relapse reduction in the FOLFOX4 arm of the trial. This highly statistically significant result demonstrates that the use of FOLFOX4 for the adjuvant therapy of CRC is superior to the use of 5-FUlLValone.

The incidence of adverse events $\geq$ grade 3 for the two treatment arms is described in the table below:

NCI ≥ Gr 3 (%)	FOLFOX4(n=1108)	LV5FU2(n=1111)
Thrombocytopenia	1.6	0.4
Neutropenia	41.0 (Gr 4: 12.2)	4.7
Febrile neutropenia	0.7	0.1
Neutropenic sepsis	1.1	0.1
Diarrhea	10.8	6.7
Stomatitis	2.7	2.2
Vomiting	5.9	1.4
Allergy	3.0	0.2
Alopecia (Gr2)	5.0	5.0
All cause mortality	0.5	0.5

The incidence of >grade 3 neutropenia, vomiting and diarrhea were higher in patients treated with FOLFOX4 compared to those receiving 5-FU and leucovorin (LV5FU2 regimen). However, the all cause mortality in the two treatment arms was the same and overall the FOLFOX4 and LV5FU2 regimens were both well tolerated.

The primary oxaliplatin- related toxicity of clinical significance for patients is the development of peripheral sensory neuropathy, similar to that observed with other platinum-containing chemotherapy agents. The incidence and severity of neuropathy in the MOSAIC study is outlined below:

Parasthesia Grade (NCI Version1)	FOLFOX4Arm: On Study	FOLFOX4 Arm: One year follow-up
Grade 0	8%	71%
Grade 1	48.1%	24%
Grade 2	31.5%	4%
Grade 3	12.4%	1%

Grade 3 neuropathy, indicative of functional impairment, occurred in 12.4% of patients on-study but was noted to be reversible, based on the observation that only 1% of patients had grade 3 neuropathy after 1 year of follow-up.

This is the first trial to have demonstrated a significant improvement in DFS in colorectal cancer for >10 years. In practice the use of FOLFOX4 as adjuvant treatment will likely result in thousands of lives saved each year in the United States. Importantly, the FOLFOX4 regimen, when used in the adjuvant setting was well tolerated and safe, with a toxicity profile very similar to that observed in the pivotal registration trials resulting in 2nd_line CRC approval. The incidence and severity of Eloxatin-induced neurological toxicity, a well described side effect of the use of platinum-containing chemotherapy regimens, was similar to that observed in prior Eloxatin trials. Of clinical significance was the observation that most neurological toxicity was mild to moderate in severity with only 1% of patients having functionally significant neurological toxicity 1 year after completing the FOlFOX4 treatment regimen.

The crucial benefit of EloxatinJ5-FUlLV is expressed in the statistically significant improvement in 3-yearDFS compared to the use of 5-FU/LV. Medicare currently covers the

combination of 5-FU and leucovorin. A 23% reduction of the risk of relapse in patients with stage II and III CRC will result in thousands of lives saved annually in the United States. Based on these data and the proven demonstration of the safety of the FOLFOX4 regimen in multiple clinical trials it is vital that patients are not denied access to this therapy for reimbursement reasons if their physician determines that this treatment is clinically indicated and desirable for the patient.

In summary, the sponsor believes that FOLFOX4 has been demonstrated to be substantially more beneficial than the Medicare-covered alternative (5-FU and leucovorin).

2) For the defined patient population, is there a medically beneficial alternative item or service{s) that is the same clinical modality and is currently covered by Medicare?

The answer to the first question has addressed this point. However, it is important to underline the fact that *the MOSAIC study demonstrates not only that the FOLFOX*4 regimen *is superior to the alternative, 5FU/leucovorin, but the combination of agents is necessary to derive the benefit – neither will suffice as single agents.*

3) Is there sufficient evidence that demonstrates that the item or service is medically beneficial to a defined patient population?

In the MOSAIC study, overall there was a 23% reduction in the risk of relapse for the overall study population. The benefit of treatment with FOLFOX was maintained in patients with both stage III and stage II disease. In patients with stage III disease who were treated with FOLFOX, the reduction was 24%, whereas in stage II patients the reduction was 18%. Similarly, the benefit of treatment with FOLFOX was maintained when individual prognostic factors were considered in univariate analyses.

In practice, the decision to offer adjuvant chemotherapy to an individual patient is a complex one and is dependent on a number of factors, including disease stage, the presence or absence of risk factors, patient age and patient/physician preference. In essence, the decision is always driven by an assessment of risk versus benefit for the individual patient.

Based on the above considerations, it is the position of the sponsor that FOLFOX should be accessible to all stage II and III patients with colorectal cancer, when in the opinion of the treating physician, the patient has the potential to benefit from the treatment.

4) Will the item or service result in equivalent or lower total costs for the Medicare population than the Medicare-covered alternative?

To be presented on July 11.

Sanofi-Synthelabo Inc.

90 Park Avenue, New York, NY 10016 - Tel.: (212) 551-4300 - Fax: (212) 551-4902

Commenter: Feinstein, The Honorable Dianne

Organization: United States Senate

(Comment on next page)

DIANNE FEINSTEIN
CALIFORNIA

United States Senate
WASHINGTON, DC 20510-0504
http://feinstein.senate.gov

COMMITTEE ON APPROPRIATIONS
COMMITTEE ON ENERGY AND NATURAL RESOURCES
COMMITTEE ON THE JUDICIARY
COMMITTEE ON RULES AND ADMINISTRATION
SELECT COMMITTEE ON INTELLIGENCE

March 27, 2003

Tom Scully
Administrator
Department of Health and Human Service
Center for Medicaid and Medicare Services
200 Independence Ave SW, Room 314G
Washington, DC 20201

Dear Administrator Scully:

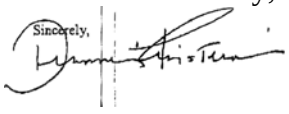
I am writing to inquire about your timeline to determine Medicare coverage for a new treatment for advanced colorectal cancer called Eloxatin. Colorectal cancer is America's second leading cause of cancer deaths, and every therapeutic advance is a critical development for patients who have been diagnosed with this disease.

It has been brought to my attention that CMS haS recently adopted a new standard requiring that a drug must be proven "clinically effective even after the FDA has determined that the new drug is "safe and effective." I am concerned that this new standard could be detrimental to patients because it could stifle access to vital new drugs and therapies, especially for diseases like advanced colorectal cancer where significant therapeutic improvements in tumor reduction and disease progression have been slow to develop.

Eloxatin received accelerated approval by the FDA last August for use as a second line colorectal cancer treatment where no other effective therapeutic option exists. My understanding is that Eloxatin is now awaiting a determination for coverage under the Medicare program.

As we all know, from many cancer battles, progress is often incremental – each advancement builds on the one that preceded it. Thank you in advance for your attention to this issue. I hope that CMS speedily completes its review of coverage of this new drug and please advise me of CMS's timeline for determination.

Sincerely,



Commenter: Filice, Joan
Organization:

(Comment on next page)

Thomas Scully, Administrator
Centers for Medicare & Medicaid Services
Department of Health & Human Services
200 Independence Avenue, S.W. – Room 314-G HHH Bldg
Washington, D.C. 20201

Dear Mr. Scully:

I am writing to express my concerns about a new policy of the Centers for Medicare & Medicaid Services (CMS) to initiate a National Coverage Analysis for new drugs that may be novel or complex, costly to Medicare, or subject to overutilization or misuse.

Medicare has historically covered new drugs when they are approved by the Food and Drug Administration (FDA), a policy that CMS has now rejected in favor of a drug-by-drug analysis of what will be covered and for what uses. This policy is troubling for procedure reasons, since it was announced without opportunity for public comment.

Aside from procedural issues, this effort by CMS appears to be in conflict with the Medicare statute. *As* a result of 1993 amendments to the Medicare statute, CMS is required to cover FDA – approved uses of cancer drugs and off-label uses of drugs in the medical compendia and to allow carriers the discretion to cover additional uses based on the medical literature. The intent of Congress to ensure cancer patients' access to FDA-approved drugs, including off-label uses of these drugs, is clearly reflected in the statute.

This issue has been brought to my attention by cancer advocates, who note that three cancer therapies are currently undergoing coverage analyses, with one of the review processes months past its projected date of completion. The initiation of the coverage analyses has had a negative impact on access to these drugs.

I urge you to abandon the policy of subjecting new cancer therapies to a Medicare coverage analysis. This practice conflicts with the Medicare statute and is not in the best interest of cancer patients.

I look forward to hearing from you on this issue.

Sincerely,

Joan M. Felice
166 Golden Ridge Rd
Alamo, Calif 94507

cc: The Honorable Tommy Thompson
Secretary, Department of Health and Human Services

Commenter: Fuchs, Charles, MD, MPH
Organization: Dana-Farber Cancer Institute

(Comment on next page)

Charles S. Fuchs, M.D., M.P.H., F.A.C.P.
Chief, Adult Ambulatory Services
Department of Adult Oncology
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School

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www.dana-farber.org

DANA-FARBER CANCER INSTITUTE

BRIGHAM AND WOMEN'S HOSPITAL

March 21, 2003

Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave SW
Room 3l4G
Washington, DC 20201

Re: Reimbursement status for oxaliplatin (Eloxatin) in the treatment of advanced colorectal cancer

Dear Mr. Scully,

I am writing to urge you to proceed forward on a National Coverage Determination for oxaliplatin in the treatment of advanced colorectal cancer. As you are aware, oxaliplatin was approved by the Food and Drug Administration in August of 2002 for patients with advanced colorectal cancer that had progressed after frontline treatment with irinotecan, 5-FU, and leucovorin. This was based on the results of a randomized trial which demonstrated a significant benefit for patients who received a combination of infusional 5-FU with oxaliplatin and leucovorin (FOLFOX4). The trial demonstrated a superior response for patients who received the FOLFOX4 regimen as well as a significant improvement in time-to-disease progression. As such, this regimen has become a standard in the treatment of patients with advanced colorectal cancer.

There is a paucity of available therapies for patients with advanced colorectal cancer. By the increasing availability of oxaliplatin through clinical trials, the survival of patients with advanced colorectal cancer has improved dramatically. Whereas the median survival for patients with metastatic colorectal cancer had historically been 9-12 months, the availability of oxaliplatin, 5-FU and irinotecan has moved this median to the range of two years. We feel that it is critical that patients have access to all drugs including oxaliplatin.

I recognize that FDA approval is necessary but not sufficient to gain reimbursement status for a drug, and that the determination of clinical effectiveness by CMS is outside the scope of the FDA's "Safe and effective" determination. Nonetheless, I believe that it is important that oxaliplatin be available for our patients with colorectal cancer, and that such a therapy is both reasonable and necessary for the Medicare/Medicaid population.

I hope that you will facilitate the ultimate approval for reimbursement for this drug.

Thank you for your consideration.

Sincerely,

Charles S. Fuchs, MD, MPH

Cc: Jeffrey Shuren, JD Director
Poppy S. Kendall, MHS

Commenter: Goldberg, Richard, MD
Organization: Mayo Clinic

(Comment on next page)

Mayo Clinic
200 First Street SW
Rochester, Minnesota 55905
507-284-2511

Richard M. Goldberg, M.D
Medical Oncology

March 11, 2003

Thomas A. Scully
Administrator Medicare/Medicaid Services
200 Independence Avenue, SW
Room 3140
Washington, DC 20201

Dear Mr. Scully:

I am writing to you to let you know of my support for coverage for oxaliplatin in patients who are being treated for advanced metastatic colorectal cancer. Mr. Shuren will know that I testified on behalf of Sanofi-Synthelabo to CMR several weeks ago regarding a study that I conducted through the North Central Cancer Treatment Group. In this study, an oxaliplatin containing regimen commonly know as FOLFOX was compared to irinotecan plus 5-FU and leucovorin containing regimen commonly known as IFL. IFL is considered the regulatory standard for patients being treated for metastatic colorectal cancer who have not had prior therapy. Our trial was a randomized study, which enrolled approximately 800 patients and compared IFL to FOLFOX to a third regimen of oxaliplatin plus irinotecan.

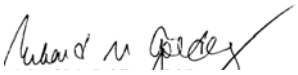
The results of this study very strongly favored FOLFOX over IFL. The improvement in median survival for this comparison was impressive at 4.5 months. By that I mean that the patients enrolled on the FOLFOX arm of the trial lived longer then 19 months, while those in the IFL regimen lived only 14 months. This increment is the largest increment in survival in a colorectal cancer advanced disease trial that has ever been noted in the United States. By comparison the increment was about 2.5 months for IFL over 5-FU and leucovorin leading the FDA to approve the IFL regimen as indicated for advanced disease and first-line therapy. In that context I believe the approval of oxaliplatin does meet an unmet medical need. The response rates and timed progression end points for FOLFOX also favored that regimen over IFL. In addition, the severe and potentially lethal toxicities favored FOLFOX over IFL. We noted that the all cause 60-day mortality for patients enrolled on the IFL regimen was about twice that of those patients enrolled in the FOLFOX arm of the regimen. This is a highly important measure of potential early chemotherapy toxicity.

The fact that the patients with the FOLFOX do so much better then those treated with IFL is a very promising development in the treatment of advanced colorectal cancer. A number of patients treated with the FOLFOX have had such a good response to therapy that then a surgeon was able to go in and remove all residual disease. This transforms the potential prognosis for these patients from lethal to possibly curable. This is a paradigm shift m the management of colorectal cancer, which can not be ignored.

I would classify the magnitude of the advances seen with oxaliplatin integration into the armamentarium of drugs used against advanced colorectal cancer as equivalent to the advances that the taxanes have provided for patients with breast and ovarian cancer. As someone who has devoted their life to the management of patients with 01 cancer it is very important to me to see that whatever can be done is done to make this drug available to patients with this disease. It is my projection that studies that are currently maturing will show that oxaliplatin improves the cure rate in the adjuvant setting after surgical resection of high risk for recurrence disease as well. However, data from this will not be available in the near future.

It would be criminal in my opinion for CMS to decide that oxaliplatin should not be available to patients of medicare age with advanced colorectal cancer. I am concerned about the fact that this particular issue was chosen for review and hope that the issue will be resolved positively for your patients and mine. Once the FDA approves treatment such as this it seems problematic for patients and researchers to contemplate the fact that approval does not mean approval for payment by federally funded insurance programs. I would be pleased to provide any additional information that you think might be helpful in support of the approval of oxaliplatin by CMS.

Sincerely,



Richard M.Goldberg, M.D.
Professor of Oncology

RMG:dmh
cc: Jeffrey Shuren, M.D.

Commenter: Gordon, David, MD
Organization: San Antonio Tumor & Blood Clinic

(Comment on next page)

SAN ANTONIO TUMOR & BLOOD CLINIC
A Division of Cancer Care Network of South Texas, P.A.

STEPHEN C. COHEN, M.D
DAVID H. GORDON, M.D.,F.A.C.P.
JOSE' A. LOPEZ, M.D., F.A.C.P.
JESSE E. MEDELLIN, M.D.
THOMAS D. FISHER, M.D.
REBECCA E. BARRINGTON, M.D.
SHARON T. WILKS, M.D., F.A.C.P.
J. DEAN McCRACKEN, M.D., F.A.C.P.
[illegible]

March 11, 2003

Thomas A. Scully, Administrator
Centers for Medicare and Medicaid Services
2000 Independence Ave. SW. Rm314G
Washington, DC 20201

Dear Mr. Scully:

It has come to my attention that a notice posted on your website on February 12, 2003 announced the fact that your agency has initiated a national coverage determination process to determine whether oxaliplatin (Eloxatin) is a reasonable and necessary drug for Medicare coverage, even though the drug is FDA approved for treatment of colon cancer. As you know, colon cancer is an extremely common entity, particularly in the older population. Unfortunately, this is a type of cancer for which we have very limited drugs that prove to be of benefit. Although oxaliplatin has a relatively low response rate, there still are patients who respond to this agent having failed other available drugs. In addition, as often proves to be the case, when the drug is in more widespread use, we may well find other malignancies for which it proves to be even more beneficial. As a Medical Oncologist I would like to have as many options as possible available for my patients, especially for diseases for which treatment options are limited.

Oxaliplatin is an FDA approved agent and should receive Medicare coverage for its approved use. I believe that to do otherwise would be inappropriate and potentially detrimental to patients' welfare.

Sincerely,

David H. Gordon, M.D., F.A.C.P.
DHG/no
Cc
Jeffrey Shuren, J.D., Director
Division of Items and Devices
Centers for Medicare and Medicaid Services
7500 Security Blvd., Mail Stop C1-09-06
Baltimore, M.D. 21244-1850

Poppy S. Kendall, MHS
Centers for Medicare and Medicaid Services
7500 Security Blvd., Mail Stop C1-09-06, RMC1-1206
Baltimore, M.D. 21244-1850

Commenter: Greenblatt, Marc, MD
Organization: University of Vermont College of Medicine

(Comment on next page)

From: "Greenblatt, Marc S." <Marc.Greenblatt@vtmednet.org>
To: <TScully@cms.hhs.gov>, <JShuren@cms.hhs.gov>, <pkendall@cms.hhs.gov>
Date: 3/14/03 5:45PM
Subject: Approval of Oxaliplatin (Eloxatin)

To: Thomas Scully, Jeffrey Shuren, Poppy S. Kendall, CMS

Ladies and Gentlemen:

I am writing to urge the CMS to approve Medicare coverage for oxaliplatin (EloxatinTM) as reasonable and necessary for the treatment of colorectal cancer. I am an oncologist who has been using Eloxatin for over five years for the treatment of colorectal cancer, both under clinical trials and as an approved agent since its approval by the FDA in August 2002.

Carefully conducted clinical trials in the US and Europe have shown that Eloxatin can improve survival and quality of life for colorectal cancer patients. This incudes both patients who have received no prior treatment and patients whose cancer has progressed on standard treatments and who have no other options. This latter group of patients clearly represents an unmet need for cancer chemotherapy for colorectal cancer. I believe that the available evidence also supports the use of Eloxatin in prolonging survival and improving quality of life when used as first line therapy. Our treatment strategies for colon cancer are expanding now that we have multiple effective agents. Studies are showing that patients with this disease are now living longer owing to the use of all of the effective drugs. CMS policy should encourage the use of all effective drugs so that our treatment regimens can continue to evolve.

Denying Medicare coverage for these indications would have numerous adverse effects on cancer treatment in older Americans. Denial would lead to earlier deaths and inferior quality of life for patients with colorectal cancer. It would also set a dangerous precedent to deny Medicare coverage for an FDA-approved drug with proven benefits. Future research and development could be affected if coverage is denied for agents that are proven effective.

Thank you very much for your consideration of this matter.

Sincerely yours,

Marc S. Greenblatt, M.D.

University of Vermont College of Medicine
1 South Prospect St, St Joseph 3210
Burlington, VT 05401
Marc.Greenblatt@vtmednet.org

Commenter: Gurtler, Jayne, MD
Organization:

(Comment on next page)

Jayne Gurtler, MD, FACP
Laura A. Brinz, MD
Janet A. Burroff, MD
(A Professional Medical Corporation)

(504) 885 -0577
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3939 Houma Boulevard Suite #6
Metairie, Louisiana 70006 -2921

Oncology - Hematology

March 10, 2003

Poppy S. Kendall, MHS
Centers for Medicare & Medicaid Services
7500 Security Blvd.
Mailstop Cl-09-06
Room Cl-12- 06
Baltimore MD 21244-1850

Dear Mr. Kendall:

As on oncologist treating colon cancer patients, I found in clinical trials and documented that CPT11, 5FU, and Eloxatin are the only available treatments. Most patients will need all options as none of these drugs will be able to cure patients. We have experienced excellent responses and tolerance with Eloxatin as well as prolonged disease control with around half the patients taking this drug. It is a shame that your reimbursement policy deny this to Medicare patients.

Your reconsideration in this matter would be appreciated.

Thank You,

Jayne Gurtler MD

Jayne Gurtler, MD, FACP

Commenter: Haller, Daniel, MD
Organization: University of Pennsylvania Health System

(Comment on next page)

UNIVERSITY OF
PENNSYLVANIA
HEALTH SYSTEM

Department of Medicine
Hematology-Oncology Division

Daniel G. Haller, M.D.
Professor of Medicine
Associate Chief for Clinical Affairs
University of Pennsylvania Cancer Cen

March 18, 2003

Mr. Thomas A. Scully
Administrator Centers for Medicare and
Medicaid Services
200 Independence Avenue S.W. Room 314
Washington, DC 20201

Dear Mr. Scully:

I am writing to you regarding the pending reimbursement determination for oxaliplatin (Eloxatin). As a Medical Oncologist specializing in colorectal cancer for the past twenty or more years, I must strenuously reject the possibility the reimbursement for this drug could be denied to the very population of patients who are most likely to develop colorectal cancer, those who are under Medicare reimbursement policy. In addition to the reimbursement issue I must enter my full support for this drug as a truly active agent in the treatment of one of our most common malignancies, having had personal experience with it over the past five years, and having treated as many patients as almost any physician of which I am aware in the United States with this the medication.

My background with this oxaliplatin began with entering patients into some of the earliest clinical trials, and this was out of my experience in speaking with the European investigators who have had the opportunity to use this agent. It quickly became apparent to me, as a clinician, that the drug clearly had activity in colorectal cancer, particularly when combined with one of the only other three available active chemotherapy drugs for this disease, 5-Fluorouracil. Because of my involvement with clinical trials, I was invited to participate in the presentation of oxaliplatin to the Oncologic Drugs Advisory Committee of the FDA in March 2000, when an application was filed for first-line therapy. The studies that were presented at the time clearly indicated that the drug was safe, but efficacy in the first-line treatment was lacking from the available data, so that it was not entirely surprising given the FDA rules that approval was not given. However, based on discussions with the FDA and on key opinion leaders, the sponsor appropriately performed a second-line study, in which we were a major participant.

The data from the preliminary data on this trial have been submitted to the FDA, leading to the accelerated approval of the drug in August 2002. Having treated many hundreds of patients with oxaliplatin, as a single agent, and in combination with 5-FU and leucovorin, there is no doubt in my mind that this is a safe and effective treatment in both second and first-line therapy, the latter supported by results of the N-9741 study, which showed the FOLFOX IV regimen to be superior to the current FDA standard of care for first-line colorectal cancer, a combination of irinotecan, 5-FU and leucovorin. Since 5-FU was first patented in 1957, and since the introduction of irinotecan in the mid-1990's, the availability of Oxaliplatin has been among the most exciting changes for oncologists specializing in colorectal cancer, and certainly this is translated to benefit for the patients that all of us have seen, who have received this drug over the past few years. To the best of my knowledge there are no new cytotoxic drugs in any stage of development that appear active in colorectal cancer, so that these three drugs will provide the only basis of treatment for this very common illness for many years to come.

As you may also be aware from some of the testing of biologic agents, none of these have been particularly active in colorectal cancer and are proving quite difficult to place in clinical trials and to establish efficacy. Indeed, bevacizumab, which appeared promising in early randomized Phase II trials, was recently dropped from a large cooperative group trial because of a survival disadvantage when compared with the FOLFOX IV regimen. Although we would all like to have some of the newer biologicals enter our routine clinical practice, this seems years away, until better intermediate end points and better markers for activity are established.

In the meantime, we are left with a very large patient population with metastatic colorectal cancer, who have only three available treatment options. With the availability of all three options, we have seen in clinical trials and clinical practice our ability to prolong overall survival in patients, with manageable toxicities and to provide choices for patients, when there were very few before. Given the fact that most patients receive combination therapy with 5-FU, leucovorin and irinotecan as first-line therapy, and many then are desirous and eligible for second line therapy, the absence of what we all conclude as active agents from our armamentarium - after many years of waiting, and after availability of the drug in most other countries - would be a disaster for the colorectal cancer population. It would be beyond reasonable to remove this option initially for the elderly population, where our own clinical experience tells us that patients tolerate the drug better than irinotecan, and where we have so few other limited options for treatment of patients.

Based on my long clinical experience, there are a huge number of patients who are eligible for both first- and second-line therapy with colorectal cancer, having had only two drugs to utilize to treat this disease, and having seen the efficacy data, both statistically and clinically, I cannot think it conceivable that I would be able to practice contemporary oncology medicine without having oxaliplatin in my pharmacy for all eligible patients.

I would be more than happy to speak with you directly on this topic if you would like, to give you now only my own further personal experience with the use of this drug, but my 20 years of experience in taking care of colorectal cancer patients to more forcibly register my concern about the possibility that a drug for which we have all worked so hard and for so long to get to our patient population may become unavailable to many of them.

Sincerely yours,

Daniel G. Haller, M.D.
Professor of Medicine
Hematology/Oncology

DGH:bb

cc: Jeffrey Shuren J.D.
Director, Division of Items and Devices
Center for Medicare and Medicaid Services
Mail Stop C1-09-06
7500 Security Blvd.
Baltimore, MD 21244-1850

Poppy S. Kendall, M.H.S.
Mail Stop C-l - 09-06
7500 Security Blvd.
Baltimore, MD 21244-1850

UNIVERSITY OF
PENNSYLVANIA
HEALTH SYSTEM

Department of Medicine
Hematology-Oncology Division

Daniel G. Haller, M.D.
Professor of Medicine
Associate Chief for Clinical Affairs
University of Pennsylvania Cancer Cen

June 28. 2003

The Honorable Thomas Scully
Administrator
Centers for Medicare and Medicaid
Department of Human Health and Services
200 Independence Avenue SW
Washington DC 20201

Dear Mr. Scully,

I am writing to continue my dialog with you concerning the status of the use of oxaliplatin in the practice of American oncology, and specifically in the use of patients with high risk of recurrence from colorectal cancer after potentially curative surgery. As the vast majority of these patients will die of their disease if they recur, preventing such recurrence is important in preventing these patients from requiring palliative, more expensive and -ultimately-futile care. I believe your prior decision, to allow the use of oxaliplatin in patients with metastatic colorectal cancer in both first- and second-line settings, was soundly based on the evidence and on the advice you received from physicians like myself, who have had extensive prior experience with this drug. We were convinced by our experience, the experience and general approval of the drug worldwide, and by the current US trials, that oxaliplatin filled an unmet need with significant clinical benefits for patients with metastases from one of the most common human malignancies. Even since that original decision, the data have been strengthened further by the presentation and publication of data supporting the use of this drug in routine practice. In my own large academic clinical practice, it has long been a mainstay, first in investigational trials, and currently for its approved routine use.

Since 1990, at the time of a paper I co-authored, it has been standard to administer 5-FU based chemotherapy to patients who are high risk for recurrence after surgery for colon cancer. Such treatments reduce recurrences after colon cancer surgery by one-third. Since most patients with recurrence ultimately die of their disease, such treatment results in saving thousands of lives each year in the US. Recently, data from the French MOSAIC trial demonstrated the first real advance in a decade. With the addition of oxaliplatin to 5-FU-based therapy, there is an additional 23% reduction in risk of recurrence, which is again likely to result in more cures, and more lives saved. The data support that this benefit is achieved with a manageable and predictable safety profile. I believe other combination chemotherapy studies will demonstrate similar benefits, and will become the standard of care over the next few years for many patients with high-risk colorectal cancer. While we await the mature 5-year survival data from the MOSAIC trials and others like it, my experience in clinical adjuvant trials of colon cancer tells me that the improved cure rates we ultimately demonstrated in my earlier studies will be reproduced and improved by the 3-year disease-free survival data to be presented to you, as they were to my colleagues recently at the 2003 Annual Meeting of the American Society of Clinical Oncology.

I believe it is now time to allow physicians and patients the option of choosing 5-FUbased adjuvant therapy with oxaliplatin based on their understanding of the data, and on the risk-benefit discussion we all must have when considering adjuvant therapy for cancer. With no other new cytotoxic chemotherapy drugs either existing or emerging that show benefit in this setting, it is now the time to expand curative treatment options for American patients suffering from a cancer that leads to the second most common cause of cancer deaths.

Sincerely yours,

Daniel G. Haller, M.D.
Professor of Medicine

cc: Gay W. Burton
Centers for Medicare and Medicaid
7500 Security Boulevard, Mailstop C1-09-06
Baltimore, MD 21244-1850

Commenter: Hambrick, Ernestine, MD
Organization: Stop Colon/Rectal Cancer Foundation

(Comment on next page)

STOP COLON / RECTAL CANCER FOUNDATION

Friday, March 07, 2003

Thomas A Scully, Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue SW
Room 314 G
Washington, DC 20201

Re: National Coverage Determination Process

Dear Mr. Scully:

I am writing to most strongly protest the new National Coverage Determination Process that you have instigated at the CMS. Though I learned of the process through its potential impact on the colorectal cancer chemotherapeutic agent oxaliplatin, my objection is directed towards the overriding principle you have set forth.

I am appalled that a non-scientific, non-medical government agency administrator would ever presume to overrun the decision of the Food and Drug Administration scientists and physicians. How dare you make null and void their collected wisdom and judgment regarding availability of any medication. Doing so with a cancer treatment drug is even more egregious.

You do not have the constitutional right, sir, to ignore the FDA's decision concerning this or any other drug. You clearly intend to use parameters other than proven efficacy and patient need. I believe it unlawful for you to set up your own, independent review process to evaluate what is reasonable and necessary in the
Medicare population based upon cost concerns.

Such unbridled use of your administration granted power is a life and death matter for Medicare and Medicaid recipients in the case of a chemotherapy agent. It also sets a dangerous precedent for blatant dictatorial abuse of any group of American citizens.

Sincerely yours,

Sincerely yours,

Ernestine Hambrick, M.D., FACS, FASCRS, FACG
Founder and Chairman

cc: Jeffery Shuren, JD
Director, Div of Items & Devices

Centers for Medicare & Medicaid Services

Poppy S. Kendall, MHS
Centers for Medicare & Medicaid Services

Elizabeth Harvey
Sanofi Synthelabo Inc.

George W. Bush, President
United States of America

Commenter: Hennessy, Daniel
Organization: County of Ocean New Jersey

(Comment on next page)

COUNTY OF OCEAN
BOARD OF CHOSEN FREEHOLDERS

DANIEL J. HENNESSY
CLERK OF THE BOARD

732-929-2005
FAX: (732) 505-1918

April 24, 2003

Ms. Gay Burton
Centers for Medicare & Medicaid Services
7500 Security Blvd., Mail Stop C1-09-06
Baltimore, MD 21244

Dear Ms. Burton:

On April 16,2003, the Ocean County Board of Chosen Freeholders adopted a resolution strongly urging a timely passage of approval of Medicare reimbursement for a specific cancer treating drug in a hospital setting.

This Resolution is sent for your use and files.

Sincerely,

Sincerely,

Daniel J. Hennessy
Clerk of the Board

DJH:cw

RESOLUTION

April 16, 2003

WHEREAS, Colorectal Cancer is the third most common cancer in men and women and is the second leading cause of cancer death; and

WHEREAS, there is a need to expedite the process to provide quick patient access to approved chemotheraputic agents for people on Medicare being treated for this cancer; and

WHEREAS, Oxaliplatin is an antineoplastic agent (a platinum analogue) approved by the Food and Drug Administration (FDA), under the trade name Eloxatin for use in patients with Colorectal Cancer whose disease has recurred or has become worse following initial therapy with a combination of irinotecan with 5-FU and leucovorin; and

WHEREAS, there exists, specifically, a need for Oxaliplatin for treatment of Colorectal Cancer, with the Center for Medicare and Medicaid Services expected completion date for review of national coverage determination being May 13, 2003; and

WHEREAS, Oxaliplatin is currently not a reimbursable service in a hospital based outpatient oncology setting under Medicare and is now awaiting a CPT code for billing Medicare Part A in an outpatient hospital setting; and

WHEREAS, providing this treatment in a hospital setting addresses

Commenter: Hochster, Howard, MD
Organization: New York University School of Medicine

(Comment on next page)

New York University
School of Medicine

Howard S. Hochster, MD; FACP
Professor of Medicine & Clinical Pharmacology
160 East 32nd Street, New York, NY 10019
telephone: 212-652-1912; fax 212-652-1901
email: howard.hochster@med.nyu.edu

March 17, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave SW
Room 314G
Washington, DC 20201

Dear Mr. Scully,

I am quite distressed at your decision to delay CMS issuing a C-code for the chemotherapy drug oxaliplatin. As a Medical Oncologist specializing in the treatment of colorectal cancer, I find this attitude perplexing, with respect to the data supporting this drug's use, and punitive in its inequity as to site of service.

Several points must be considered in your decision to delay reimbursing this drug in some settings:

1) There is a basic inequity of Medicare paying for this oxaliplatin in the practice setting (J-code billing) versus the hospital setting (C-code). This decision puts those of us in academic, essentially hospital-based treatment settings at a disadvantage in offering our patients the state of the art therapy they expect from us.

2) I am concerned that your decision derives from a small number of non-oncologists and/or non-physicians who will decide whether this drug adds to the treatment of colorectal cancer. This decision is made at the same time that prospective clinical trials involving hundreds of patients have clearly demonstrated the benefit of this agent, when major American oncologic leaders (the FDA ODAC) have recommended approval of this agent to the FDA and the FDA has considered it an important advance in the treatment of colorectal cancer (conferring a survival advantage in the treatment of this disease). The lack of process and lack of expert advice in an opaque and non-public CMS process is worrisome for physicians generally and for patients, who reasonably expect access to the latest therapies.

3) The data mentioned above constitute level I evidence that oxaliplatin added to 5FU improves survival by nearly 40% in patients with metastatic colorectal cancer compared to 5FU and leucovorin and 30% over the now-reimbursed irinotecan-based regimens. Furthermore, meta-analysis of multiple prospectively randomized trials have shown increasing survival for patients treated by all the

effective agents (oxaliplatin, irinotecan and 5FU), with median survival approaching 24 months, nearly double that of 5FU and lecovorin alone.

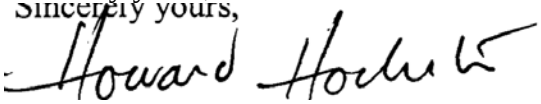
4) My personal observations in treating over one hundred patients who progressed on the other standard chemotherapy drugs have convinced me of the importance of oxaliplatin. I have seen dramatic and unprecedented responses of otherwise refractory colorectal cancer when no other treatment would be effective.

5) I can only add that as a practitioner and expert in GI oncology, oxaliplatin combination therapy is inherently reasonable and necessary. It does not constitute "novel, complex, or controversial treatment." Furthermore, its cost to Medicare is in line with other chemotherapy treatments.

I remain at your service for additional information or questions. I hope you will not opt for a path that will induce patients to seek treatment outside the major hospital-based academic centers based on reimbursement issues alone.

Sincerely yours,

Sincerely yours,



Howard Hochster, MD
Professor of Medicine and Clinical Pharmacology

Cc: Jeffrey Shuren
JD Director, Division of Items and Devices
Center for Medicare and Medicaid Services
Mailstop: C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

Poppy S. Kendall, MHS
Mailstop: Cl-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

The Honorable Hilary Clinton
476 Russell Senate Office Building
Washington, D.C. 20510-3204

The Honorable Charles Schumer
313 Hart Senate Office Building
Washington, D.C. 20510-3203

Congressman Carolyn Maloney
2331 Rayburn House Office Building
Washington, D.C. 20515-3214

Commenter: Holoye, Paul, MD
Organization: Oncology Consultants, P.A.

(Comment on next page)

ONCOLOGY CONSULTANTS, P.A.

LUIS T. CAMPOS, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

CHARLES E. MANNER, M.D.
American Board of Internal Medicine

DAVID B. SANFORD, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

MIGUEL MIRO-QUESADA, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

PAUL Y. HOLOYE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

HARRY R. PRICE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

July 7, 2003

Poppy S. Kendall, MRS
Centers for Medicare & Medicaid Services
Mailstop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244

Dear Ms. Kendall,

I would like to submitted comments in response to the notice, published on the CMS website, stating that CMS has internally generated a national coverage determination to evaluate when the newly approved anticancer drug oxaliplatin is reasonable and necessary in the Medicare population. The notice states that this review is being undertaken because of "the potential impact of this treatment on the Medicare program." our physicians at Oncology Consultants, P.A. who specialize in the treatment of cancer are very concerned about how the potential restrictions on oxaliplatin apparently contemplated by CMS may adversely affect our patients.

For most types of items and services, the Medicare statute confers broad authority on CMS to determine whether the item or service is reasonable and necessary and hence whether it is covered by Medicare. That is not the case, however, for drugs and biological used in anticancer chemotherapy regimens. Under section 1861 (t)(2) of the Social Security Act, there is mandatory coverage of drugs and biological in such regiments when used for purposes approved by the Food and Drug Administration, supported by citations in specified compendia, or determined by carriers to be medically accepted based on clinical evidence published in certain journals.

This provision was added to the statute in 1993 to stop the practice, employed by some carriers, of denying Medicare coverage for medically accepted indications on the ground that they were not included in the FDA-approved labeling. Congress amended the statute to deny any discretion to the Medicare program to deny coverage of medically accepted indications of drugs used in anticancer therapy.

Accordingly, I sees no legally permissible function of a national coverage determination on oxaliplatin. All indications approved by FDA or listed in the compendia must be covered. Other indications are covered if carriers determine that they are supported by the medical literature. In light of the special statutory rules applicable to drugs used in anticancer chemotherapy regimens, CMS lacks the authority to restrict coverage of

oxaliplatin. We therefore request that the proposed national coverage determination be withdrawn.

Sincerely,

erely,

Paul Y. Roloye, M.D.
Oncology Consultants, P.A.

Commenter: Hon, Jeremy, MD
Organization: Comprehensive Cancer Institute

(Comment on next page)

Comprehensive
Cancer
Institute
Medical Oncology/Hematology
Marshall T. Schreeder, M.D.
Jeremy K. Hon, M.D.
Richard J. Gualtieri, M.D.
Edgar F. Prasthofer, M.D.
John M. Waples, M.D.
256/551-6546
Fax 256/534-2605
Radiation Oncology
Joseph F. Schneider,Jr., M.D.
Noel C. Estopinal, M.D.
256/551-6590
Fax 256/551-6592

March 10, 2003

Mr. Thomas A. Scully
Administrative Center for Medicare and Medicaid Services
200 Independence Avenue, S.W.
Room 314G
Washington, D.C. 20201

Dear Mr. Scully:

It was quite distressing for me to find out the federal government is in the process of determining whether Eloxatin (oxaliplatin for injection) is a reasonable and necessary drug for Medicare coverage purposes.

As you know, this chemotherapeutic agent was approved by the FDA for metastatic colorectal carcinoma. I have experienced the use of this medication for more than two years. I have seen remarkable response in our patients who suffer from metastatic colorectal carcinoma. I believe the CMS new reimbursement policy is sending a negative message to cancer patients, oncologists, and the research community, that the important new treatments approved by the Food and Drug Administration may not be available to all cancer patients who need them. If this happens, this will be the first time in the U.S. that an FDA approved cytotoxic agent was not covered by the Medicare program. This is quite a dangerous precedent.

Most important of all, denying Medicare coverage will limit the chance of improved survival for elderly patients with metastatic colorectal carcinoma. In other words, this policy, if enacted, will effectively shorten the patient's survival and most important of all, it will eliminate any hope for a better quality of life, as well as any prospect of longer survival. I believe the potential impact of this decision is quite negative and may affect

more than 150,000 Americans who are diagnosed with colorectal cancer and 56,000 of them will die of this disease.

I sincerely hope that your agency will reconsider the proposal. I believe oxaliplatin is a major chemotherapeutic agent in the fight of this deadly disease of metastatic colorectal carcinoma.

Please give your helping hand to our unfortunate elderly Americans.

If you have any questions, please do not hesitate to contact me.

Sincerely,

Jeremy K. Hon, M.D.

JKH/km

cc: Jeffery Shuren, J.D. Director
Division of Items and Devices
Center for Medicare and Medicaid Services
7500 Security Blvd.
Mail Stop C1-09-06
Baltimore, Maryland 21244-1850

Commenter: Julian, Cheryl
Organization: Pfizer

(Comment on next page)

Pfizer Inc
235 East 42nd Street
New York, NY 10017-5755

May 30, 2003

Ms. Janice Flaherty
Acting Director, Division of Items and Devices
Coverage and Analysis Group
Center for Medicare and Medicaid Services
MS C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: National Coverage Analysis (NCA) - Oxaliplatin (EloxatinTM) for Colorectal Cancer (CAG-00179N)

Dear Ms. Flaherty:

Pfizer, Inc. is pleased to have the opportunity to comment on the recent NCA tracking sheet announcing CMS' intention to limit the national coverage determination review of Oxaliplatin (Eloxatin M) for colorectal cancer to consideration of off-label, adjuvant therapy of anti-cancer chemotherapy for patient in Stage III colon cancer.

While we understand that the formal public comment period for this review ends on June 2,2003, we are formally requesting that you allow us an additional six weeks to prepare a complete and thorough submission. Included in this submission will be detailed information related to 3 ongoing randomized trials investigating the role of irinotecan (Camptosar®) in the adjuvant therapy of colon cancer. We would also be happy to meet you and your staff to discuss this NCA, our submission, and issues related to the field of colon cancer therapy.

Pfizer is a global leader in discovering, developing and delivering innovative medicines and healthcare solutions essential to improving global public health and addressing unmet medical needs. We currently hold licensing rights for clinical development and commercialization in the United States, Canada, Latin Am rica, and Oceanic countries for Camptosar® (irinotican hydrochloride injection), the only anti-cancer chemotherapeutic agent currently approved for use as a first-line therapy in combination with 5-tluorouracil (5-FU) and leucovorin (LV) for patient with metastatic carcinoma of the colon or rectum. The approval for this initial indication was based on 2 well-controlled, randomized phase III clinical trials which demonstrated significant survival benefits of irinotican/5- U/LV over 5-FU/LValone. Camptosar® is also indicated for patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed following initial fluorouracil-based therapy.

Pfizer and it development partner Aventis are currently engaged in additional rigorous clinical research evaluating the effectiveness of Camptosar/5-FU/LV in the adjuvant therapy of colon cancer. These trials include:

• CALGB 89803: This ongoing U.S. study has been sponsored by multiple cooperative groups as an Intergroup trial with Cancer and Leukemia Group B (CALGB) leadership. The trial permits entry of all patients with stage III colon cancer and compares the Saltz regimen of irinotecan with bolus 5-FU/LV in the experimental treatment arm versus the standard weekly Roswell Park regimen of bolus 5-FU/LV in the control arm. The primary endpoints of this trial are overall survival and disease free survival (UFS) at three years.

• V307: This ongoing European study, sponsored by Aventis, is also focusing on enrollment of patients with stage III colon cancer. Patients receive either weekly therapy (AIO schedule) or every-2-week therapy (de Gramont schedule) with infusional 5-FU/LV and are randomized as to whether or not irinotecan is added to 5FU/ LV. The primary endpoint of this trial is DFS at 3 years.

An additional trial sponsored by a cooperative group in France, is ongoing that evaluates irinotecan/5-FU/LV therapy in patients with disease features that suggest a substantial likelihood of early relapse:

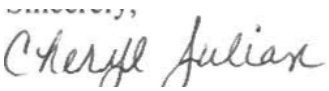
• ACCORD02: Irinotecan combined with 5-FU/LV is being compared with 5-FU/LV alone in patients with high-risk stage III colon cancer. High-risk stage III disease is defined as those patients with stage III colon cancer who have N_2 disease ($\geq$ 4 positive regional lymph nodes) or who have intestinal obstruction or localized perforation as complications associated with their primary tumor. This study is ongoing in France employing every-2-week therapy with the de Gramont schedule of *5-FU/L*V given with or without irinotecan. The primary endpoint of this trial is DFS at three years.

We have worked with the Food and Drug Administration (FDA) to assure that the protocols, data elements, and primary endpoints for these trials would be sufficient to serve as a basis for approval for this additional indication, and we intend on submitting final results to the FDA upon completion of enrollment and adequate follow-up.

Final results from CALGB 89803, which will serve as the pivotal trial for FDA approval, have not been released by the cooperative groups which independently manage this trial. However, we intend on including the protocols, any preliminary data that can be released by the data safety and management board at this time, and other pertinent information regarding the timeline of patient enrollment and data collection in our submission to CMS.

I look forward to taking with you soon, and can be reached directly at 612-839-5691 or via email at cheryl.s.julian@pfizer.com. Sumant Ramachandra.MD.PhD., Pfizer's lead clinical officer for this project and our liaison with the FDA, will also be available to work with you during your review. On behalf of Pfizer thank you for the opportunity to participate in the national coverage process.

Sincerely,



Cheryl Julian
Pfizer
Senior Director Oncology
National Accounts
952-934-4647 office
612-839-5691 cell

cc: Ms. Gay Burton, Lead Analyst

Commenter: Keech, Jr., John
Organization: American Society of Clinical Oncology

(Comment on next page)

ASCO
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

July 10, 2003

Gay Burton
Centers for Medicare & Medicaid Services
Mailstop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Ms. Burton:

These comments are submitted by the American Society of Clinical Oncology (ASCO) in response to the request for public comment on the national coverage analysis for the anticancer agents Eloxatin (oxaliplatin) and Camptosar (irinotecan) (#CAG-00179N). CMS has invited public comment regarding the adjuvant use of these agents in patients with colorectal cancer - a use that is not included in the product labeling approved by the Food and Drug Administration (FDA). ASCO is the national organization representing physicians who specialize in the treatment of cancer.

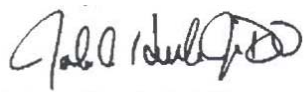
Multiple clinical studies on the adjuvant use of these agents in colorectal cancer are on-going, and some data are already available. ASCO believes that it would not be appropriate for CMS to issue a national coverage determination in situations where the evidence is under active development. Although the available study results might be preliminary at one point in time, additional information that becomes available a few months later may substantially clarify the medical value of a particular use of an anticancer a gent. The national coverage determination process should not be used in such situations, since a negative determination may take months to review and reverse in the light of new data. In the meanwhile, Medicare patients with cancer would be denied the benefit of an efficacious treatment for their serious disease.

It should also be noted that, as a legal matter, there is little or no role for national coverage determinations in the case of drugs used in anticancer therapy. Under section 1861 (t)(2) of the Social Security Act, Medicare must cover any uses of cancer chemotherapy drugs approved by FDA and any uses supported by the designated compendia. A use that is neither approved by FDA nor listed in the compendia is covered if "the carrier involved determines, based upon guidance provided by the Secretary, that such use is medically accepted based on supportive clinical literature ...." Since, in the only area of discretion, the statute assigns the deciding role to carriers and a guidance role to the Secretary, there does not appear to be any legal basis for a national coverage determination.

In summary, since a national coverage determination would be inappropriate while data are under active development, and because CMS lacks the legal authority to issue national coverage determinations for cancer drugs in any event, ASCO urges CMS to terminate this proceeding without issuing any national coverage determination.

1900 Duke Street, Suite 200 Alexandria, VA 22314 Telephone: (703) 299-0150 Fax: (703) 299-1044 E-mail: asco@asco.org

Sincerely,



John A. Keech, Jr. DO
Chair, Clinical Practice Committee

Commenter: Kleiman, Sylvia
Organization:

(Comment on next page)

Sylvia Kleiman
40 Stoner Ave.
Great Neck, NY 11021

Mr. Thomas A Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave. SW
Room314G
Washington, D. C. 20201

Dear Mr. Scully,

It has come to my attention that the Centers for Medicare and Medicaid Services are considering not to cover the life saving cancer drug Eloxatin. This drug has been approved by the FDA and is considered the last resort in the treatment of metastatic colon cancer.

This drug has prolonged the life of many colon cancer patients, one of whom was a forceful advocate for colon cancer prevention. Richard Farrell gained four years of life during his treatment for his disease, and in that time was able to reduce the colon cancer mortality of at lease 20 people by convincing them to have colonoscopies

Colon Cancer bits very hard in the over 50 year old population, a population that relies on Medicare for treatment payment. If this population is denied treatment, the incidence of colon cancer deaths will be hugely increased. Colon Cancer is second most cause of cancer deaths. This treatment will help bring down the numbers.

As a survivor, advocate, and member of the Colon Cancer Alliance, I demand the rapid approval of Eioxation so that Medicare patients are given access to this treatment as a course of standard therapy.

Sincerely,

Sylvia Kleiman

Commenter: Leichman, Lawrence, MD and Cynthia, MD
Organization: Comprehensive Cancer Centers of the Desert

(Comment on next page)

COMPREHENSIVE
CANCER CENTERS
OF THE DESERT

An Outpatient Facility of Desert Regional Medical Center

March 13, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave SW
Room 314G
Washington, DC 20201

RE: Oxaliplatin (Eloxatin®)

Dear Mr. Scully:

As experts in the filed of gastrointestinal cancers, we are writing to request Medicare and Medicaid Services expedite a billing code(s) for oxaliplatin (Eloxatin®), one of the few effective drugs against disseminated large bowel cancer. As you know, eloxatin has been approved by the Federal Drug Administration as second-line therapy for a disease state for which there is no known cure. Indeed, over 50,000 men and women in the United States will die of disseminated large bowel cancer this year. Without Medicare and Medicaid, codes, the hospitals and pharmacies cannot be reimbursed for this effective agent.

Prospective clinical trials for patients with colorectal cancer have shown that Eloxatin in combination with infusional 5-Fluourouracil gives a statistically significant increase in time to disease progression, statistically significant reduction in clinical symptoms and statistically significant response rate to therapy over 5FU alone. It was our understanding that this data brought FDA approval to Eloxatin and infusional 5FU as second-line therapy for our patients with disseminated colorectal cancer. As clinical researchers who have taken part in trials using Eloxatin, we have found the drug safe and more effective than any other we have used against colorectal cancer.

While we appreciate that the improvement in median duration of survival benefit for our patients may not seem dramatic to some observers, we have observed responses that have lasted for over a year. During that time, our patients receive the benefit of comfort, family, family events and the opportunity to live long enough so that they may benefit from new innovations in cancer therapy.

1180 N. INDIAN CANYON DRIVE, SUITE E218, PALM SPRINGS, CA 92262 (760) 416-4800 FAX (760) 416-4875

58457 TWENTY-NINE PALMS HIGHWAY, YUCCA VALLEY, CA 92284 (760) 365-7411 FAX (760) 228-0913

The etiology of polyps and the resulting colorectal cancers have not been clearly elucidated. Patients do not bring this disease upon themselves. Thus, we urge you to use your position to make the lives of cancer patients more hopeful, more comfortable and more fulfilling. Certainly, in our society that prides itself in scientific progress, our citizens should be allowed the fruits of that progress.

We have enclosed our Curriculum Vitae for your perusal.

Sincerely,

Lawrence Leichman, MD FACP

Cynthia Gail Leichman, MD

CC

Jeffrey Shuren
JD Director, Division of Items and Devices
Center for Medicare and Medicaid Services
Mailstop: C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

Poppy s. Kendall, MHS
Mailstop: C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-185

The Honorable Mary Bono

The Honorable Barbara Boxer
United States Senator

The Honorable Diane Feinstein
United States Senator

Commenter: Levine, Richard, MD
Organization: Space Coast Medical Associates, L.L.P.

(Comment on next page)

SPACE COAST MEDICAL ASSOCIATES, L.L.P.
BREVARD HEMATOLOGY and ONCOLOGY CONSULTANTS

Richard M. Levine, M.D. Solomon Zimm, M.D., F.A.C.P. R. Duff Sprawls, M.D.
Juan L. Castro, M.D. Ashish V. Dalal, M.D.

March 11, 2003

Mr. Thomas Scully, Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave., S.W.
Room 3140
Washington DC 20201

Dear Mr. Scully:

I am a medical oncologist in private practice in Florida. I strongly recommend coverage for the chemotherapeutic agent Eloxatin (oxaliplatin for injection) for colorectal cancer. My practice participated in the clinical trial that demonstrated benefit to patients and provided the data upon which the FDA approved the drug. We continue to use it in our patients with recurrent or advanced colorectal cancer. It is an effective anti-cancer therapy which helps patients extend their life and maintain quality. Our treatments for metastatic colorectal cancer are limited, and in my opinion it would be harmful not to provide Medicare coverage for Eloxatin.

Thank you very much for your time and consideration. If you have any questions, please do not hesitate to contact me.

Sincerely,

Richard M. Levine, MD

RML/amn
cc: Jeffery Shuren, JD Director
Division of Items and Devices
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Baltimore Maryland 21244-1850

Poppy Kendall, MHS
Centers for Medicare and Medicaid Services
7500 Security Blvd.
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Baltimore, Maryland 21244-1850

850 CENTURY MEDICAL DRIVE
TITUSVILLE, FL 32796
Telephone (321) 268-4200
FAX (321) 268-1386
Correspondence to Titusville Office

225 CONE ROAD
MERRITT ISLAND, FL 32952
Telephone (321) 453-1361
FAX (321) 452-4939

699 W. COCOA BEACH CSWY #606
COCOA BEACH, FL 32931
Telephone (321) 783-9544
FAX (321) 783-0212

7057 U.S. HWY 1 #600
COCOA, FL 32927
Telephone (321) 639-2598
FAX: (321) 639-2590

Commenter: Lewis, Kevin
Organization: Colon Cancer Alliance

(Comment on next page)

COLON CANCER ALLIANCE

To: Mr. Thomas A. Scully, Administrator, Centers for Medicare & Medicaid Services
CC: Jeffery Shuren. Poppy S. Kendall, Tommy G. Thompson
From: Kevin Lewis, Chairman, Colon Cancer Alliance
Date: March 8, 2003
Subject: Support for Eloxatin Medicare Coverage Approval

Dear Mr. Scully,

As you know colon cancer is the second leading cancer killer in the United States and a troubling public health issue. Each year some 57,000 Americans die from colorectal cancer and close to 150,000 are diagnosed with the disease. Colon cancer is highly survivable if detected local to the colon, but it is highly lethal for the roughly 60% of colon cancer patients whose cancer is detected after breaking through the colon wall. Until recently these metastatic colon cancer patients found no good options for treating their disease and little hope for long term survival. In fact very little progress was being made in colon cancer treatment. The chemotherapy treatment my father received for localized colon cancer in 1980 remained the only metastatic treatment until combinational therapies became the standard of care around 2000.

In 1998 the Colon Cancer Alliance (CCA) was founded to represent the voice of colorectal cancer survivors. At the time our voices demanded options to prevent deaths of our many friends who were fighting but mostly losing the battle against the disease. The fortunate patients were able to enroll in a clinical trial for Irinotecan or Xeloda, but not everyone responded. At the same time Oxaliplatin became available in France and later across Europe. Patients in the United States could not understand why they didn't have access to this promising new option, and every patient that could flew to Europe to get the treatment. Clearly, access to this treatment was denied to most patients.

Some time later Oxaliplatin became available in the United States through clinical trial. On one of these studies, the late Richard Farrell, one of the CCA's founders, showed remarkable response to the metastatic colon cancer in his liver. Richard survived four rich, long years with metastatic colon cancer in large part to his Oxaliplatin treatments, and during that time Richard became an outspoken advocate for colon cancer screening. He alone reduced colon cancer mortality by 1020 people by convincing everyone he met to get a cotonoscopy. The extended time that Richard received in this world was well worth the cost of the Oxaliplatin treatment he received. Similar toRichard, through clinical trials and expanded access programs, combinational Oxaliplatin treatment is the standard of care for second line treatment of metastatic colon cancer for most patients.

However, clinical trial and expanded access programs do not provide access to everyone that needs treatment, and patients continue to be frustrated with the lack of availability of Oxaliplatin. In May 2002, everything seemed to change. At the American Society Clinical Oncologists (ASCO), the biggest news, the release of Oxaliplatin clinical trial data, showed the best ever clinical trial improvements for metastatic colon cancer. As patients advocates we have never seen as much excitement and activity at the NCI and the FDA to rapidly translate these dramatic results into therapeutic access for all.

On August 12, 2003 Secretary Thompson personally heralded the FDA's fast track approval of Eloxatin (Oxaliplatin) for second line treatment in metastatic colon cancer treatment, a treatment that US patients have been waiting far too long for access. He stated “Patients diagnosed with colorectal cancer will now have access to another treatment option for this disease. I want to commend the FDA for reviewing the drug's safety and effectiveness so quickly."

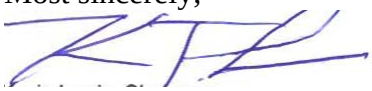
Unfortunately, Medicare patients with metastatic colon cancer do not yet have access to the treatment and face almost certain disease progression and death. In what seems to patients an unprecedented move, CMS is delaying the implementation of the NCl's and the FDA's recommendations for cancer treatments and held up approval of Eloxatin for Medicare patients.

As patients and advocates, we do not understand why Eloxatin was singled out for National Coverage Analysis (NCA). Not one of the other newly FDA-approved cancer treatments: Mesna Tablets (MesneX®), Fulvestrant (FaslodeX®), Anastrozole (ArimideX®), Docetaxel (Taxotere@), Imatinib Mesylate (Gleevec™) for CMl, and Polifeprosan 20 Carmustine Implant (GlIADEl Wafer) required NCA, and few of these treatments demonstrated the response rates that Eloxatin is demonstrating.

You must understand that metastatic colon cancer patients die too quickly and too frequently without second line treatment Eloxatin combinational therapy is the only approved second line treatment; these patient's only option other than rapid deterioration and death. These Medicare patients need this treatment, and they need it now. Please give them the chance for survival, and the chance to live long enough to utilize the results of the rapid technique and treatment improvements we are now experiencing in the fight against metastatic colon cancer.

The Colon Cancer Alliance and its survivor members demand the rapid approval of Eloxatin so that Medicare patients are given access to this treatment as a course of standard therapy.

Most sincerely,



Kevin Lewis, Chairman
Colon Cancer Alliance

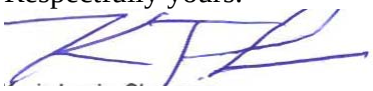
COLON CANCER ALLIANCE

The Honorable Thomas Scully
Administrator
Centers for Medicare and Medicaid
Department of Human Health and Services
200 Independence Avenue SW
Washington DC 20201

RE: CMS Review of Adjuvant Use of Oxaliplalin

Dear Mr. Scully:
We understand that CMS is in the process of reviewing Oxaliplalin for use in the adjuvant treatment of high risk Colon Cancer patients. At the Colon Cancer Alliance we believe patients should have the right to use all the treatments that improve their chances of survival or their quality of life. We also believe that the data available demonstrates that Oxaliplatin in the adjuvant selling demonstrates a survival benefit. On behave of the thousands of patients with high risk colon cancer we request that you allow the use of this treatment in the adjuvant setting.

Respectfully yours.



Chairman of The Board
Colon Cancer Alliance

cc: Gay W. Burton
Centers for Medicare and Medicaid
7500 Security Blvd, Mailstop C1-09-06
Baltimore, MD 21244-1850

From: "Kevin Lewis" <kevintlewis@msn.com>
To: <hhsmail@os.dhhs gov>
Date: 3/6/03 3:46PM
Subject: Delay in Access to Eloxatin for Medicare Patients

Date: March 6, 2003

Secretary Tommy Thompson
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Secretary Thompson,

On August 12, 2003 you personally heralded the FDA's fast track approval of Eloxatin for second line treatment in metastatic colon cancer treatment, a treatment that US patients have been waiting far too long for access. You stated "Patients diagnosed with colorectal cancer will now have access to
another treatment option for this disease. I want to commend the FDA for reviewing the drug's safely and effectiveness so quickly-"

Unfortunately, medicare patients with metastatic colon cancer do not yet have access to the treatment which and face almost certain disease progression and death In an unprecedented move CMS has broken with the tradition of following the NCl ‘s and the FDA's recommendations for cancer treatments and help up approval of Elaxtin for medicare patients.

You must understand that colon cancer patients need this treatment now, and you must get CMS in line with the recommendations of the governments experts in cancer treatment, the NCI and the FDA. Here is the link to the CMS action delaying access http://www.cms.hhs.gov/mcd/viewtrackingsheet.asp?id=90. Please help us to resolve this Issue. Colon cancer patients are counting on your efforts.

I will be in Washington DC on March 19th, 23rd, and 24th and April 4th. Who can I meet with to express the concerns of patients about l this access to treatment issue?

Sincerely

Kevin T. Lewis
Chairman. Colon Cancer Alliance
175 Ninth Avenue
New York, NY 10011
cell 617 – 899 - 0773

From: "Kevin Lewis" <kevintlewis@msn.com>
To: <pkendall@cms.hhs.gov>
Date: 3/11/03 9:54PM
Subject: Eloxatin NCA

Poppy,
My name is Kevin Lewis, and I am the Chairman of the Colon Cancer Alliance. As patient survivors, caregivers and advocates we are concerned about patients losing Eloxatin as a treatment option. I have mailed a letter, and I want to make sure it is received. Can you let me know if you have not received it yet.

In addtion I am in Washington frequently over the next few weeks and would like to discuss this issue with CMS if that is possible.

Thank you,
Kevin

Commenter: Malik, Imtiaz, MD
Organization: Loma Linda University

(Comment on next page)

LOMA LINDA UNIVERSITY

School of Medicine
Department of Medicine
Division of Hematology and
Medical Oncology

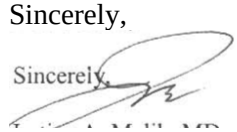
MC 1531
Loma Linda, California 92350
(909) 558-4910
FAX: (909) 558-0219

Hematology/Oncology Clinic
(909) 796-4884
FAX: (909) 558-2415

Poppy S. Kendall MHS
Centers for Medicare and Medicaid Services
Mailstop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244

Dear MS Kendall:
This is in response to the notice, published on your website, stating that CMS has internally generated a national coverage determination to evaluate when the newly approved anticancer drug oxaliplatin is reasonable for the Medicare population and use of irinotecan in adjuvant setting in the same population. I am extremely concerned about potential restrictions such an attempt will create on delivery of cancer care.
I take care of GI cancer and hence use these drugs extensively. This is an area of enormous research and many treatments are offered on the basis of phase II trials which are promising but do not meet FDA requirements for changing the off-label use. As you know confirmatory phase III trials take long time to accrue and mature. Withholding promising therapies to cancer patients with relatively short life span is inappropriate and inhumane. I want to voice my deepest concern and hope that such a regressive move will be abandoned.

Best wishes,
Sincerely,



Imtiaz A. Malik, MD
Professor of medicine
Lorna Linda University medical center
Lorna Linda, CA 92354

Commenter: Maloney, The Honorable Carolyn
Organization: House of Representatives

(Comment on next page)

CAROLYN B. MALONEY
14TH DISTRICT, NEW YORK

2430 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-3214
(202) 225-7944

COMMITTEES
FINANCIAL SERVICES

GOVERNMENT REFORM

JOINT ECONOMIC COMMITTEE

Congress of the United States

House of Representatives

Washington, DC 20515–3214

DISTRICT OFFICES:

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SUITE 311
NEW YORK, NY 10128
(212) 860-0606

28-11 ASTORIA BOULEVARD
ASTORIA, NY 11102
(718) 932-1804

March 14, 2003

Mr. Thomas Scully
Administrator
Department of Health and Human Services
Centers for Medicare and Medicaid Services (CMS)
200 Independence Ave SW, Room 314G
Washington, DC 20201

Dear Administrator Scully:

I was recently contacted by Sanofi-Synthelabo, a global pharmaceutical company, with U.S. headquarters located in my Congressional District. The company recently received FDA approval of Eloxatin, a new chemotherapy drug for treatment of advanced colorectal cancer.

I am writing to encourage your speedy and positive approval of Eloxatin for Medicare coverage. As you are aware, colorectal cancer is America's second leading cause of cancer deaths, and every therapeutic advance is a critical development for patients.

Eloxatin received accelerated approval by the Food and Drug Administration last August for use as a second line colorectal cancer treatment where no other effective therapeutic option exists. Indeed, I am advised that this approval and the demonstration of a highly significant survival advantage over standard treatment in first line colorectal cancer treatment prompted the National Comprehensive Cancer Network to rapidly modify its treatment guidelines for advanced colorectal cancer to recognize the advent of oxaliplatin.

I find CMS' recent decision to initiate a National Coverage Review, which puts into question the coverage of Eloxatin (oxaliplatin) by Medicare, to be troubling.

As we all know, from many cancer battles, progress is often incremental – each advancement builds on the one that preceded it. I hope that CMS speedily completes its review of, and approves coverage of, this new drug for this most vulnerable of patient population.

Sincerely,

Carolyn B. Maloney
Member of Congress

Commenter: Manner, Charles, MD
Organization: Oncology Consultants, P.A.

(Comment on next page)

ONCOLOGY CONSULTANTS, P.A.

LUIS T. CAMPOS, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

CHARLES E. MANNER, M.D.
American Board of Internal Medicine

DAVID B. SANFORD, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

MIGUEL MIRO-QUESADA, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

PAUL Y. HOLOYE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

HARRY R. PRICE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

July 7, 2003

Poppy S, Kendall, MRS
Centers for Medicare & Medicaid Services
Mailstop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244

Dear Ms. Kendall,

I would like to submitted comments in response to the notice, published on the CMS website, stating that CMS has internally generated a national coverage determination to evaluate when the newly approved anticancer drug oxaliplatin is reasonable and necessary in the Medicare population. The notice states that this review is being undertaken because of "the potential impact of this treatment on the Medicare program." Our physicians at Oncology Consultants, P.A. who specialize in the treatment of cancer are very concerned about how the potential restrictions on oxaliplatin apparently contemplated by CMS may adversely affect our patients.

For most types of items and services, the Medicare statute confers broad authority on CMS to determine whether the item or service is reasonable and necessary and hence whether it is covered by Medicare. That is not the case, however, for drugs and biological used in anticancer chemotherapy regimens. Under section 1861 (t)(2) of the Social Security Act, there is mandatory coverage of drugs and biological in such regiments when used for purposes approved by the Food and Drug Administration, supported by citations in specified compendia, or determined by carriers to be medically accepted based on clinical evidence published in certain journals.

This provision was added to the statute in 1993 to stop the practice, employed by some carriers, of denying Medicare coverage for medically accepted indications on the ground that they were not included in the FDA-approved labeling. Congress amended the statute to deny any discretion to the Medicare program to deny coverage of medically accepted indications of drugs used in anticancer therapy.

Accordingly, I see no legally permissible function of a national coverage determination on oxaliplatin. All indications approved by FDA or listed in the compendia must be covered. Other indications are covered if carriers determine that they are supported by the medical literature. In light of the special statutory rules applicable to drugs used in anticancer chemotherapy regimens, CMS lacks the authority to restrict coverage of oxaliplatin. We therefore request that the proposed national coverage determination be withdrawn.

Sincerely,

Charles E. Manner, M.D.
Oncology Consultants, P.A.

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Houston, Texas 77024
(713) 827-9525
Fax (713) 468-3561

ST. CATHERINE
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Katy, Texas 77450
(281) 578-0201
Fax (281) 578-0217

PARK PLAZA
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Houston, Texas 77004
(713) 529-3619
Fax (713) 529-4964

ST. LUKES
6624 Fannin, Ste. 1610
Houston, Texas 77030
(713) 797-6323
Fax (713) 797-6325

ST. JOSEPH
1315 St. Joseph Pkwy., Ste. 1103
Houston, Texas 77002
(713) 6500709
Fax (713) 650-6904

SUGAR LAND
15200 Soutwest Frwy., Ste. 292
Sugar Land, Texas 77478
(281) 491-5511
Fax (281) 491-5513

Commenter: Marsh, Robert de W., MD
Organization: University of Florida

(Comment on next page)

UNIVERSITY OF FLORIDA

College of Medicine
Health Science Center
Department of Medicine
Division of Hematology/Oncology

1600 S.W. Archer Road
PO Box 100277
Gainesville, FL 32610-0277
(352) 392-3000
Fax (352) 392-8530

March 19, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare and Me3dicaid Services
200 Independence Avenue, SW
Room 314G
Washington, DC 20201

Dear Mr. Scully:

As a senior member of the University of Florida Shands Cancer Center, I am writing to express my concern regarding the possibility of denial of Medicare coverage for Eloxatin for the therapy of colorectal cancer. If this were to occur my strong belief is that this would send a very negative message to the community of cancer patients and oncologist that new treatments approved by the FDA will not be available to those who most urgently need them. Such a denial of coverage for an FDA approved cytotoxic agent would be a very dangerous precedent in my opinion and could open the door for future such denials of critically needed treatments. This will no doubt have a profound impact on all Americans, but most particularly, older Americans with a diagnosis of colorectal cancer. My experience with this particular drug has been very positive. We typically see a very large number of patients with this condition each month and the addition of a new drug to our armamentarium has significantly alleviated the burden of suffering experienced by many of these patients. This drug has impressed all of us at the University of Florida Shands Cancer Center with its ease of administration and relative lack of toxicity while maintaining outstanding efficacy in heavily pretreated patients. The addition of a new drug to our current armamentarium has meant that we have been able to design multiple new regimens to treat this condition, and as a result, our choices for patients are now significantly increased. This has given us the ability to tailor our therapy to an individual patient to a much larger extent than previously possible, such that we are able to significantly limit toxicity and also extend the hope of effective treatment to many more people.

Future research into exciting new drugs like this would be severely discouraged if ultimately coverage and reimbursement for these drugs are denied. To place this into perspective, over 150,000 Americans are diagnosed with colorectal cancer each year and in excess of 56,000 die of this disease. Twenty-seven percent or more of these patients are treated in a hospital setting and would be severely affected by this proposed denial of coverage by CMS. I strongly urge you to reconsider and give your full support to its approval. It is an urgently needed addition to our current armamentarium and would be sorely missed if unavailable.

I thank you very much, indeed, for your consideration.

Respectively yours,

Robert de W. Marsh, M.D.
Associate Professor

cc to:

Jeffery Shuren
JD Director
Division of Items and Devices
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Baltimore, MD 21244-1850

Poppy S. Kendall, MHS
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Room CI-12-06
Baltimore, MD 21244-1850

RdeWM/js

Commenter: Marshall, John, MD
Organization: Georgetown University Hospital

(Comment on next page)

Georgetown
University
Hospital
Lombardi Cancer
Center

NCI CCC
A Designated
Comprehensive
Cancer Center

March 13, 2003

Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independent Avenue, SW, Rm 314-G
Washington, D.C. 20201

Re: Medicare C-Code for Eloxatin in Colorectal Cancer

Dear Mr. Scully,

I am writing to you as one of the leading colon cancer clinical researchers in the United States and as a representative of the colon cancer patients from the Washington, DC community. It came to my attention that Eloxatin may not be covered for Medicare patients with metastatic colon cancer. I believe this would be a mistake.

I have over the past three years administered Eloxatin to over 350 patients, almost all of them from the Washington, DC area. I participated in the clinical trials that were the foundation of the FDA's approval of this drug and. I am very familiar with its benefits to patients. Many of the patients who have benefited from this treatment are prominent members of the Washington community and would be supportive of discussing this issue with you or anyone you thought might be appropriate.

The supporting data speaks for itself. Eloxatin adds significantly to the survival of patients with metastatic colon cancer. Just four years ago, the median survival of stage four colon cancer patients was 12 months. Since the development of irinotecan (14 - 15 months) and now Eloxatin, the median survival for these patients has been extended to over 20 months. *This* represents a significant improvement in outcome for these patients who before had very few treatment options. It is also important to note that in those patients who respond well to Eloxatin, there is a significant improvement in not only their survival but also their quality of life. It has taken us a great deal of effort and time to discover new medicines which have an impact on *this* dreadful disease, and it would be wrong to limit access to Eloxatin for Medicare patients.

MedStar Health
3800 Reservoir Road, NW, Washington, DC 20007
phone: 202 687 2198 • *website:* lombardi.georgetown.edu

We hope that you will see the benefits of this medicine and choose to support the decision for giving it a C-Code. As a faculty member of the Lombardi Cancer Center and Georgetown University, our Medicare patients who we take care of either do not have access to this drug or we choose to administer the drug at a loss to our institution. We hope that you would see that this medicine plays a key role in the management of these patients and therefore will support it.

I would likewise invite you to meet with me or members of our community to discuss this in more detail.

Sincerely yours,

John L. Marshall, M.D.
Associate Professor of Medicine
Division of Hematology/Oncology

Georgetown
University
Hospital
Lombardi Cancer
Center

NCI CCC
A Designated
Comprehensive
Cancer Center

July 16, 2003

The Honorable Thomas Scully
Administrator
Centers for Medicare and Medicaid
Department of Human Health and Services
200 Independence Avenue SW
Washington DC 20201

Dear Mr. Scully:

I am writing to support your decision to not restrict the chemotherapy choices for patients with stage II and stage III colon cancer. It is becoming increasingly clear that the new medicines Oxaliplatin (Eloxatin) and CPT-II (Camptosar) will increase the number of patients who are cured of their colon cancer. It is also likely that the next wave of agents (Xeloda. Avastin. Erbilux, and others) will not only add to the number of patients, but will also reduce the side effects these patients experience during their treatments.

As a leader in colorectal cancer in the Washington DC area, I care for approximately 250 new patients each year with this diagnosis. Many of these have undergone surgery to remove the primary cancer, and this surgery alone will have cured many of these patients. However, most patients will not have been cured as colon cancer cells have spread and will kill the patients (in under five years) if effective chemotherapy is not delivered.

For twenty years, we have been limited by having only one agent which helps in this setting, 5-FU. However, both CPT-I I and Oxaliplatin have been shown to more than double the benefits for patients when combined with 5-FU. In the immediate postoperative setting, this translates into a significantly higher number of patients cured of their disease. It is certainly less expensive to cure more patients with 6 months of effective therapy than to under treat them, only to have to give them an average of two years of therapy once their disease comes back, only to have them die of the recurrent cancer.

MedStar Health
3800 Reservoir Road, NW, Washington, DC 20007
phone: 202 687 2198 • *website:* lombardi.georgetown.edu

Oxaliplatin and CPT-J I (and those that will certainly follow) represent the first true progress we have in colon cancer since President Nixon declared war on cancer many years ago. After decades of research paid for by the taxes of the American public, how can we now restrict the access to the fruits of our labors. Please do not restrict access to these medicines. It would be short sighted and only result in more patients dying of colon cancer in the years to come.

Sincerely,

John L. Marshall, MD
Associate Professor of Medicine
Director Developmental Theraputics
and GI Oncology
Lombardi Cancer Center
Georgetown University Medical Center

cc:
Gay W. Burton
Centers for Medicare and Medicaid
7500 Security Bldg, Mailstop C1-09-06
Baltimore, MD 21244-1850

Commenter: Mayer, Robert, MD
Organization: Dana-Farber Cancer Institute

(Comment on next page)

DANA-FARBER CANCER INSTITUTE | BRIGHAM AND WOMEN'S HOSPITAL

Robert J. Mayer, M.D.
Vice Chair for Academic Affairs
Department of Medical Oncology
Director, Center for Gastrointestinal Oncology
Dana-Farber Cancer Institute

Professor of Medicine
Harvard Medical School

Dana-Farber Cancer Institute
44 Binney Street
Boston, Massachusetts 02115
617.632.3474 tel, 617.632.2260 fax
robert_mayer@dfci.harvard.edu
www.dana-farber.org

March 10, 2003

March 10, 2003

Thomas A. Scully
Administrator
Medicare and Medicaid Services
200 Independence Avenue, S.W.
Room 314G
Washington, DC 20201

Dear Mr. Scully:

I am writing to urge the Center for Medicare and Medicaid Services to support the decision of the Food and Drug Administration and to make oxaliplatin (Eloxatin) available to all appropriate cancer patients.

I am a medical oncologist at the Dana-Farber Cancer Institute in Boston where I direct the Center for Gastrointestinal Oncology. Additionally, I am a Professor of Medicine at the Harvard Medical School. I chair the Gastrointestinal Cancer Committee for the Cancer and Leukemia Group B - a national cooperative group organized and supported by the National Cancer Institute - and I am a Past President of the American Society of Clinical Oncology.

Colorectal cancer is the second most common cause of cancer-related deaths in the United States. For many years, only one form of systemic treatment (5-fluorouracil) had been shown to be effective in the treatment of this condition. Several years ago, a second drug - irinotecan (Camptosar) was also found to be beneficial. Based on recent clinical studies, the' Food and Drug Administration approved the availability of oxaliplatin (Eloxatin) last autumn, representing a third independently effective form of systemic treatment for colorectal cancer. At present, oxaliplatin (Eloxatin) has been approved for non-investigational use only for patients who had previously been treated with such other therapies as 5-fluorouracil and irinotecan (Camptosar). Quite likely, the indication for oxaliplatin (Eloxatin) will be expanded in the near future to include newly diagnosed patients. The median age for patients with colorectal cancer is between 60 to 65 years, indicating that almost half of colorectal cancer patients are at an age where they are candidates for Medicare coverage.

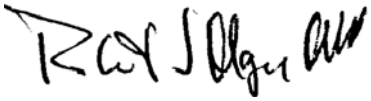
DANA-FARBER/PARTNERS
CANCERCARE

Teaching Affiliates
of Harvard Medical School

I finished my oncology training in 1974. At that time, the probability of a patient with colorectal cancer surviving five years (which in this disease setting is tantamount to cure) was 50 percent. Based on data from the American Cancer Society, that probability has increased to 62 percent (a 24 percent improvement) by the mid-1990's. The use of newer, more innovative systemic, surgical, and radiation approaches has contributed greatly to this step forward. Making oxaliplatin (Eloxatin) available to appropriate patients will ndoubtedly further this encouraging trend.

I urge you and your office to support coverage for oxaliplatin (Eloxatin) for Medicare and Medicaid patients. For your information, I have no formal or fiscal relationship with the pharmaceutical company that manufactures oxaliplatin (Eloxatin).

Sincerely yours,



Robert J. Mayer, M.D.

RJM/kb
cc: Jeffrey Shuren, J.D.

DANA-FARBER CANCER INSTITUTE | BRIGHAM AND WOMEN'S HOSPITAL

Robert J. Mayer, M.D.
Vice Chair for Academic Affairs
Department of Medical Oncology
Director, Center for Gastrointestinal Oncology
Dana-Farber Cancer Institute

Professor of Medicine
Harvard Medical School

Dana-Farber Cancer Institute
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Boston, Massachusetts 02115
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robert_mayer@dfci.harvard.edu
www.dana-farber.org

June 26, 2003

June 26, 2003

The Honorable Thomas Scully
Administrator
Centers for Medicare and Medicaid
Department of Human Health and Services
200 Independence Avenue, S.W.
Washington, DC 20201

Dear Mr. Scully:

I am writing in support of the request of Sanofi-Synthelabo to extend coverage for the use of oxaliplatin (as part of the oxaliplatin/5-FU/leucovorin [FOLFOX] chemotherapy regimen) to the management of patients receiving prophylactic "adjuvant" therapy following the resection of a stage III colon cancer.

The use of 5-FU and leucovorin alone has constituted the "standard" of care for patients with stage III colon cancer for the past 10 years. Recent data from a randomized trial conducted in Europe involving more than 800 patients has indicated that the addition of oxaliplatin (Eloxatin) to the 5-FU/leucovorin, as part of the FOLFOX regimen, improved the likelihood of remaining free of relapse after three years of time by five percent. This difference was particularly evident in patients with stage III tumors (i.e. tumor spread from the bowel to adjacent lymph nodes), While the results of this important study remain preliminary and the effect of the addition of oxaliplatin on overall survival is yet to be determined, it would appear that FOLFOX should represent an appropriate and logical treatment option for patients with stage III colon cancer - particularly in those in whom clinical, biological, or molecular characteristics would make them at higher than usual risk for recurrence.

I would ask that you and your colleagues grant patient access to oxaliplatin as part of adjuvant treatment for stage III colon cancer if so requested by a treating physician. Such therapy has the potential of saving several additional thousand lives in the United States each year.

Thank you for your consideration.

Sincerely yours,

Robert J. Mayer, M.D.

RJM/kb
cc: Gay W. Burton

Commenter: McAllister, Pamela, Ph.D.
Organization: Colorectal Cancer Network

(Comment on next page)

Board of Directors
Colorectal Cancer Network
P.O. Box 182
Kensington, MD 20895

March 10, 2003

Mr. Thomas A Scully Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW
Room 314G
Washington, DC 20201

Those of us in the colorectal cancer advocacy community have become very concerned that Eloxatin oxaliplatin) has not been approved for reimbursement by Medicare despite the fact that it has been approved by the FDA since it meets an important unmet need. This drug is an important new development that offers an additional option to patients who have otherwise exhausted all treatment opportunities.

Denying reimbursement for Eloxatin to Medicare patients significantly reduces the treatment options available to them and erodes their level of cancer treatment. This sets a dangerous precedent since at this time the best chance for improved survival that a cancer patient has is in having a wide range of treatment options. Each patient is unique and that which is helpful to one may be of no value to another. Further, those who are able to respond to more than one treatment option have the chance of much longer survival and in some cases the opportunity for shrinkage of their cancer to a point that potentially curative resection becomes a possibility. Limiting the options open to senior citizens decreases the chances of longer survival and effectively denies any chance for many patients of qualifying for a potentially curative resection. More treatment options to patients with advanced disease can result in the conversion of a disease from one that is universally fatal to one that is a treatable chronic condition allowing many patients additional years with a high quality of life.

Of even greater concern is the dampening effect on new cancer therapy development that such a decision could have. Denial of reimbursement to new treatments that have been approved by the FDA may result in a reduction in research that leads to new treatments.

Eloxatin is an effective treatment that offers those with advanced colon and rectal cancers an additional option for treatment. It is through expansion of treatment option", to colorectal cancer patients, that we may achieve an improvement in survival such as has already been seen in breast and ovarian cancer patients by virtue of their access to expanded treatment options. CMS policy should support advances in cancer treatment so that all citizens, including those who receive their care under the Medicare program, are afforded the best chance currently available to fight their cancer.

Colorectal cancer is one of the most prevalent cancers in this country and is second only to lung cancer in cancer deaths each year. More than 150,000 cases of colorectal cancer are diagnosed each year and 56,000 patients die of this disease. This reimbursement policy sends a dangerous clear signal to the oncology community, namely that important new treatments that have been approved by the FDA may not be available to all of those who need them.

Sincerely,

Pamela McAllister

Pamela McAllister Ph.D. Chair
Priscilla Savary, Executive Director
Board members:
J. Laurette Savary
Eddie Leigh
Ken AShman
James C. McMichael
Merrylue Charmaine
Liza B Frampton

cc:
Jeffery Shuren
Poppy S. Kendall, MHS

Commenter: McGovern, The Honorable James
Organization: House of Representatives

(Comment on next page)

JAMES P. McGOVERN
3RD DISTRICT, MASSACHUSETTS

COMMITTEE ON RULES

Congress of the United States
House of Representatives
Washington, DC 20515–2103

June 18, 2003

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http://www.house.gov/mcgovern/

June 18, 2003

Thomas Scully, Administrator
Canters for Medicare and Medicaid Services
Department of Health & Human Services
100 Independence Avenue, S.W. - Room 314-G HHH Bldg.
Washington D.C. 20201

Dear Mr. Scully:

I am writing to express my concerns about a new policy of the Centers for Medicare & Medicaid Services (CMS) to initiate a National Coverage Analysis for new drugs that may be novel or complex, costly to Medicare, or subject to overutilization or misuse.

Medicare has historically covered new drugs when they are approved by the Food and Drug Administration (FDA), a policy that CMS has now rejected in favor of a drug-by-drug analysis of what will be covered and for what uses. This policy is troubling for procedural reasons, since it was announced without opportunity for public comment.

Aside from procedural issues, this effort by CMS appears to be in conflict with the Medicare statute. As a result of 1993 amendments to the Medicare statute, CMS is required to cover FDA-approved uses of cancer drugs and off-label uses of drugs in the medical compendia and to allow carriers the discretion to cover additional uses based on the medical literature. The intent of Congress to ensure cancer patients' access to FDA-approved drugs, including off-label uses of these drugs, is clearly reflected in the statute.

This issue has been brought to my attention by cancer advocates, who note that three cancer therapies are currently undergoing coverage analyses, with one of the review processes months past its projected date of completion. The initiation of the to coverage analyses has had a negative impact on access to these drugs.

I urge you to abandon the policy of subjecting new cancer therapies to a Medicare coverage analysis. This practice conflicts with the Medicare statute and is not in the best interest of cancer patients.

I look forward to hearing from you on this issue.

Sincerely,

James McGovern
Member of Congress

cc: The Honorable Tommy Thompson
Secretary, Department of Health and Human Services

Commenter: Means, Kathy
Organization: Patton Boggs, L.L.P.

PATTON BOGGS LLP
ATTORNEYS AT LAW

20037

2550 M Street NW
Washington DC

(202) 457-6000

Facsimile (202)

457-6315

April 28, 2003

Mr. Thomas A Scully
Administrator
Centers for Medicare and Medicaid Services
U.S. Department of Health and Human Resources
200 Independence Avenue, SW
Room 314G
Washington, DC 20201

Dear Administrator Scully:

The purpose of this letter is to thank you, on behalf of Sanofi-Synthelabo Inc. (Sanofi), for the recent opportunity to meet with you and members of your staff to present information in support of Medicare coverage of EloxatinTM, a major new drug for the treatment of colorectal cancer. I would like to recap the key points provided in the presentation materials. These supplement initial presentation materials provided to the coverage review team in Baltimore in February, supplemented by highly detailed supporting materials in a letter to Poppy Kendall dated March 14, 2003.

Overview

First, Sanofi is the manufacturer of Eloxatin™ (oxaliplatin by injection), a chemotherapeutic agent that received accelerated approval by the Food and Drug Administration (FDA) last year, as a significant new addition to the treatment of patients with advanced colorectal cancer (CRC). Eloxatin™, in combination with 5-fluorouracil (5-FU) and leucovorin (LV), was approved as a 2nd line therapy for an unmet medical need in patients whose advanced colorectal cancer has recurred or progressed following 1st line therapy. At the time of the approval, noted health leaders, including Secretary Tommy Thompson, voiced strong approval of this significant addition to CRC care.

Since then, oxaliplatin, in the regimen approved by FDA, was rapidly incorporated in the major cancer treatment guidelines promulgated by the National Comprehensive Cancer Network (NCCN), a leading professional health care organization in the U.S. There should be no question of the value of this therapy from the perspective of professionals engaged in oncology care, nor in the improvement in cancer care that this therapy will bring to the Medicare population relative to currently covered therapies.

Centers for Medicare and Medicaid Services (CMS) Coverage Review

Eloxatin™ is undergoing a national coverage determination (NCD) by the Centers for Medicare and Medicaid Services (CMS) to determine whether the drug is suitable for Medicare coverage in the treatment of Medicare beneficiaries suffering from CRG. Sanofi applied last Fall for recognition of Eloxatin™ as a pass-through drug in the Medicare hospital outpatient prospective payment system, with expected approval to have been effective with hospital payment updates on January 1, 2003. There was surprise and dismay throughout the oncology care community at the Agency's decision to delay consideration of that application and instead divert this drug for a national coverage determination. Not only does this action delay access for Medicare beneficiaries with CRC to the clearly and demonstrably superior 2nd line therapy for advanced CRC it places a financial burden on hospitals and major cancer centers that wish to incorporate oxaliplatin into their therapeutic regimens.

3) First-line treatment: In addition, highly promising, but at this stage proprietary and confidential, data were presented on the value of EloxatinTM in combination with other drugs for first-line treatment of CRC. These data are based on a National Cancer Institute funded trial and will be made public in an oral presentation to be delivered at the June 1 ASCD conference. Many clinical investigators in the u.s. are already aware of the clinical value and consequently, are beginning to use the drug for first-line therapy.

4) Functional Equivalence: Last Fall, CMS announced a new regulatory concept of functional equivalence in the context of the final rule governing calendar year 2003 rates for Medicare hospital outpatient services. There is great uncertainty and confusion in the affected drug and medical device industries as to the meaning, requirements and implications of this new concept in the Medicare program, and specific questions about whether it applies to coverage determinations. For the record, information was provided to demonstrate that the mechanisms of action are different for the three major drugs under discussion, 5-FU (thymidylate synthase inhibitor), irinotecan (topisomerase I inhibitor) and oxaliplatin (induction of DNA damage). Oinically, Eloxatin™ is not" functionally equivalent" to Camptosar™. When Eloxatin™ is provided as 2nd line therapy relative to Camptosar™, it is because the previous irinotecan- based therapy failed. In the 1st line setting, EloxatinTM, combined with 5-FULV (FOLFOX 4 regimen), demonstrated significant superiority for both safety and efficacy parameters when compared to Camptosar™, also combined with 5-FULV (IFL regimen).

5) Medicare program costs: Finally, Sanofi presented proprietary information, including modeling of the potential impact of Eloxatin™ on Medicare's hospital outpatient pass-through budget, that should make it clear that Eloxatin™ has been fairly priced at levels comparable to that of competitor products, and in second-line therapy, lower than the major competitor products. All of the competitor products are currently covered and reimbursed by Medicare. It was agreed that the important addition of EloxatinTM to the array of treatment options for CRC, m*a*y increase Medicare costs due to a possible increase in the total number of chemotherapy regimens offered in the U.S. for treatment of CRC. This is because Eloxatin™ provides a rare and genuine advancement in the

treatment of CRC, one that will affect the standard of care. This will be of great benefit to patients suffering from this terrible disease.

Conclusion

In closing, thank you again for the opportunity to provide CMS the latest information on EloxatinTM. In our view, the clinical advancements provided by Eloxatin™ in regimens for the treatment of CRC are unquestionable. We trust that CMS will come forward with a coverage determination that in no way acts to restrict Medicare CRC patients' access to this major advance in therapy, and provides full recognition as a new drug therapy in the hospital outpatient payment system, as intended by Congress. Please contact me directly if further information is needed. I can be reached on 202-457-6328. My best personal wishes.

Commenter: Meropol, Neal, MD
Organization: Fox Chase Cancer Center

(Comment on next page)

FOX CHASE CANCER CENTER

Department of Medical Oncology
Neal J. Meropol, M.D.
Director, Gastrointestinal Cancer Program

7701 Burholme Avenue
Philadelphia, Pennsylvania 19111

215 728 2450
FAX 215 728 3639

March 10, 2003

Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave SW
Room 3140
Washington, DC 20201

Dear Mr. Scully:

I write this letter on behalf of my patients with colorectal cancer. I am a medical oncologist and clinical researcher with a focus on colorectal cancer. I encourage the Centers for Medicare and Medicaid Services to approve reimbursement for Oxaliplatin far patients with metastatic colorectal cancer. I have a great deal of personal experience with Oxaliplatin, having participated in several clinical trials with this agent before it *was* FDA-approved, and in treating many patients with Oxaliplatin since it has become commercially available. I have witnessed the benefits of Oxaliplahn in shrinking colorectal cancer, improving symptoms, and prolonging patient survival. These personal observations have been validated by large, well-conducted, prospective, multicenter, randomized trials. There is not an equivalent substitute for Oxaliplatin; this drug has conclusively shown benefit for patients who fail the other standard treatments for metastatic colorectal cancer (5-FluofOUfaciI and Irinotecan) Finally, Oxaliplatin is a well-tolerated drug for the treatment of colorectal cancer. This has also been borne out by large studies in both the United States and Europe.

In summary, O'laliplatin provides us with a new effective weapon in the fight against colorectal cancer. Please consider these comments in rendering your decision regarding reimbursement for this agent.

Sincerely.

Neal J. Meropol. M.D.
Director, Gastrointestinal Cancer Program

CC: Jeffrey Shuren
JD Director. Division of Items and Devices
Center for Medicare and Medicaid Services
Mailstop: C1-09-06
7500 Security Boulevard
Baltimore. MD 21244-1850

Poppy S. Kendall. MHS
Mailstop: C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

Commenter: Miro-Quesada, Miguel, MD
Organization: Oncology Consultants, P.A.

(Comment on next page)

ONCOLOGY CONSULTANTS, P.A.

LUIS T. CAMPOS, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

CHARLES E. MANNER, M.D.
American Board of Internal Medicine

DAVID B. SANFORD, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

MIGUEL MIRO-QUESADA, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

PAUL Y. HOLOYE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

HARRY R. PRICE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

July 7, 2003

Gay Burton
Centers for Medicare & Medicaid Services
Mailstop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244

Dear Mr. Burton,

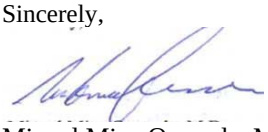
I would like to submitted comments in response to the notice, published on the CMS website, stating that CMS has internally generated a I national coverage determination to evaluate when the newly approved anticancer drug oxaliplatin is reasonable and necessary in the Medicare population. The notice states that this review is being undertaken because of “tbe potential impact of this treatment on the Medicare program." our physicians at Oncology Consultants, P.A. who specialize in the treatment of cancer are very concerned about how the potential restrictions on oxaliplatin apparently contemplated by CMS may adversely affect our patients.

For most types of items and services, the Medicare statute confers broad authority on CMS to determine whether the item or service is reasonable and necessary and hence whether it is covered by Medicare. That is not the case, however, for drugs and biological used in anticancer chemotherapy regimens. Under section 1861 (t)(2) of the Social Security Act, there is mandatory coverage of drugs and biological in such regiments when used for purposes approved by the Food and Drug Administration, supported by citations in specified compendia, or determined by carriers to be medically accepted based on clinical evidence published in certain journals.

This provision was added to the statute in 1993 to stop the practice, employed by some carriers, of denying Medicare coverage for medically accepted indications on the ground that they were not included in the FDA-approved labeling. Congress amended the statute to deny any discretion to the Medicare program to deny coverage of medically accepted indications of drugs used in anticancer therapy.

Accordingly, I sees no legally permissible function of a national coverage determination on oxaliplatin. All indications approved by FDA or listed in the compendia must be covered. Other indications are covered if carriers determine that they are supported by the medical literature. In light of the special statutory rules applicable to drugs used in anticancer chemotherapy regimens, CMS lacks the authority to restrict coverage of oxaliplatin. We therefore request that the proposed national coverage determination be withdrawn.

Sincerely,



Miguel Miro-Quesada, M.D.
Oncology Consultants, P.A.

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(281) 491-5511
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Commenter: O’Connell, Michael, MD
Organization: NSABP Foundation, Inc.

(Comment on next page)

March 18, 2003

Thomas A. Scully
Administrator
Center for Medicare and Medicaid Services
200 Independence Ave SW
Room 3140
Washington, DC 20201

Dear Mr. Scully:

We are corresponding with you because we are extremely concerned that CMS may choose not to provide coverage for advanced colorectal cancer patients treated with oxaliplatin (Eloxatin).

There is conclusive recent data that demonstrates the value of oxaliplatin for the treatment of patients with advanced colorectal cancer. A large, prospectively randomized clinical trial coordinated by the North Central Cancer Treatment Group was presented at the annual meeting of the American Society of Clinical Oncology (ASCO) in 2002 by Goldberg, et al. This study directly compared a regimen combining oxaliplatin with 5FU and leucovorin with a regimen currently approved by the Food and Drug Administration (FDA) for the first line treatment of advanced colorectal cancer (IFL: irinotecan. 5FU and leucovorin). Clinically and statistically significant benefits in terms of tumor response rates, duration of disease control, and survival with a decrease in 60-day mortality rate were associated with the oxaliplatin-containing regimen. The National Comprehensive Cancer Network (NCCN), a national consortium of NCI-funded Cancer Centers, now recommends oxaliplatin combined with 5FU and leucovorin as an option for the treatment of metastatic or unresectable colorectal cancer.

In addition, the oxaliplatin, 5FU, leucovorin regimen addresses an unmet need for patients with advanced colorectal cancer who have failed first line treatment with irinotecan combined with 5FU and leucovorin (IFL). This was demonstrated in a randomized, controlled trial in which treatment with oxaliplatin in combination with infusional 5-FU (FOLFOX4) was compared to infusional 5-FU alone. The results were as follows: 9.9% of the patients on the FOLFOX4 arm had objective responses and 60% of the FOLFOX4 patients experienced disease stabilization (for a total of 70% of FOLFOX4 patients with tumor control) compared to 0% responses and 46% disease stabilization on the infusional 5-FU arm (or 46% of patients wth tumor control, $p<0.0001$). To further highlight this difference in tumor control, there was a significant difference in time to disease progression(4.6 months on FOLFOX4) versus 2.7 months on infusional5-FU.$p<0.0001$). Moreover, a difference in reduction of tumor-related symptoms was observed (35.4% on the FOLFOX4 ann versus 14.3% on the infusional5-FU arm, $p<0.0001$), which correlated with tumor control. The FDA approved the FOLFOX regimen for this indication in 2002.

We understand that the mechanism by which CMS may deny coverage for new chemotherapeutic agents is a notice filed in the Federal Register November 1, 2002. In that notice, the steps are spelled that which could, ultimately, preclude reimbursement for any therapeutic agent. CMS describes several such circumstances "including but not limited to the following: the drug or biological…represents a novel, complex. or controversial treatment. ..would be too costly to Medicare...or received marketing approval based on surrogate outcomes."

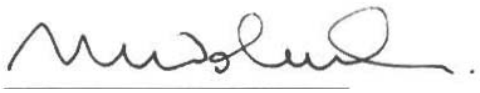
We also understand that CMS has stated that FDA approval is necessary but insufficient to gain reimbursement status for a drug, and that the determination of "clinical effectiveness" by CMS is outside the scope of the FDA"s "safe and effective" determination. (FDA approval would no longer provide the 'default' status for Medicaid/Medicare patients.) In addition, CMS would assess whether or not a compound or therapeutic modality is "reasonable and necessary"(or "inherently reasonable") for the Medicare/Medicaid population.

Thus, the new CMS guidance may have far-reaching deleterious effects on quality care. At present, it will impact only on select populations: the elderly and the poor with progressive colorectal cancer after failure of the IFL regimen. But, given the potential for carry-over to private insurers, CMS denial of coverage for any agent may lead to universal denial of c coverage by all insurers, which could broadly limit access to many new drugs, with catastrophic effects on pharmaceutical innovation and improvements in patient care.

On behalf of the thousands of patients afflicted with metastatic colorectal cancer each year in the United States, we strongly recommend that CMS provide coverage for the FDA-approved drug oxaliplatin.

Sincerely,

Michael J. O'Connell, M.D.
Physician Coordinator,
NCI-Sponsored Gastrointestinal Cancer
Intergroup Clinical Trials
Director, Allegheny Cancer Center



Norman Wolmark, MD
Chairman,
National Surgical Adjuvant
Breast And Bowel Project
Chairman, Department of
Human Oncology,
Allegheny General Hospital

cc: Jeffrey Shuren
JD Director, Division of Items and Devices
Center for Medicare and Medicaid Services
Mailstop: C 1 -0-06
7500 Security Boulevard
Baltimore. MD 21244-1850

Poppy S. Kendall. MHS
Mailstop: C1 -09-06
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Commenter: O’Dwyer, Peter, MD
Organization: University of Pennsylvania Abramson Cancer Center

(Comment on next page)

UNIVERSITY OF PENNSYLVANIA
Abramson Cancer Center

Peter J. O'Dwyer, MD
Professor of Medicine

Department of Medicine
Hematology-Oncology Division

Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave SW
Room 3l4G
Washington, DC 20201 *3/12/03*

Dear Sir:

I write to protest in the strongest terms the threat from CMS to withhold approval of reimbursement of oxaliplatin for patients with colon cancer.

This agent has established itself over the past ten years as the most active drug ever tested in this cancer. While the data presented to the FDA (and approved by them) show the benefit that patients obtain from oxaliplatin-containing chemotherapy, these data represent but the tip of an iceberg of supportive trial results that all show the same thing: that patients treated with oxaliplatin live longer and have a better quality of life. As a specialist in treating colorectal cancer, I can assure you that I have not observed activity in this disease with any drug until the arrival of oxaliplatin. I have no doubt that patients will respond to the CMS plan with their own stories, and I'd like you to know that these are not successes that come along frequently in can or treatment. Colon cancer is a relentless and resistant disease, but oxaliplatin has provided an opportunity for patients to benefit from chemotherapy that is just about twice as effective as what was available just five years ago.

It is also a little shocking to observe CMS taking a dictatorial position in deciding what cancer patients may or may not receive if they are unfortunate enough to have to rely on your beneficence. The circumstance is the more unreal in the present political environment considering that the only precedent for such an administrative action in cancer treatment was in the National Health Service of the U.K., which determined that taxol should not be made available to women in Britain with breast or ovarian cancer. That position was reversed of course, but only after the loss of benefit to thousands of women who had no private insurance. I am bemused that your administration should copy some of the worst characteristics of socialized medicine.

But politically opaque or no, the decision does a great disservice to colon cancer sufferers. To take such a position when experts both within and without the Government have endorsed the value of oxaliplatin in colon cancer is indefensible, and in the absence of expert evidence to the contrary, morally wrong. I ask that this issue be rethought, and that for the sake of cancer patients, approval for oxaliplatin coverage be given forthwith.

University of Pennsylvania Health System
MAB – Suite 103 • 39th and Market Streets • Philadelphia, PA 19104 • 215-662-8947 • Fax: 215-243-3269

Yours faithfully,

Peter J. O'Dwyer, M.D.
Professor of Medicine

cc:
Jeffery Shuren
JD Director, Division of Items and Devices
Center for Medicare and Medicaid Services
Mailstop: C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

Poppy S. Kendall, MHS
Mailstop: C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

Commenter: O’Rourke, Mark, MD
Organization: Cancer Centers of the Carolinas

(Comment on next page)

CancerCenters of the Carolinas

March 10, 2003

Mr. Thomas A. Scully
Administrator
Centers For Medicare and Medicaid Services
200 Independence Avenue, SW
Room 314-G
Washington, DC 20201

Dear Mr. Scully:

I am a physician specializing in cancer care, and practice in Greenville, South Carolina. I have followed Medicare policy for coverage of cancer chemotherapy drugs closely over the past five years. I have served as the oncology representative to the South Carolina Medicare Pan-B Carrier Advisory Committee. I have had the occasion to deal with the South Carolina Carrier and with CMS on issues of regional and national importance. I am writing now to address the national coverage determination CD) process to determine whether Eloxatin (oxaliplatin for injection) is a reasonable and necessary drug for Medicare coverage purposes.

I know that you have the data that has been presented to the FDA and the data from the National Cancer Institute clinical trials that have demonstrated the efficacy of this drug. I am writing as a practicing medical oncologist to tell you that this has become an important drug for the chemotherapy management of colorectal cancer. Indeed, a large number of medical oncologists in the United States and in Europe, myself included, consider it to be the best drug to be included in the initial chemotherapy for metastatic colon cancer. I practice with fourteen medical oncologists and six radiation oncologists, and we take pride in providing state of the art cancer care to our patients across the Upstate of South Carolina.

If there were an NCD that excluded coverage for oxaliplatin, it would create a large dichotomy in my practice. Patients who are not covered by Medicare would have access and would be treated with the drug. Patients who are covered by Medicare Part-B would face an insurmountable financial barrier to treatment with the drug. I appreciate your time and effort on behalf of this issue, and I urge you not to deny coverage for this important drug.

Sincerely,

M O'Rourke

Mark A. O'Rourke, M.D.
Cancer Centers of the Carolinas

MAO/ss/mds
cc: Jeffery Shuren
J. D. Director
Division ofltems and Devices
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Mail Stop C1-09-06
Baltimore, MD 21244-1850

Poppy S. Kendall, MRS
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Mail Stop C1-09-06
Room C1-12-06
Baltimore, MD 21244-1850

The Honorable Jim DeMint
The United States House of Representatives
432 Cannon House Office Building
Washington, DC 20515

The Honorable Ernest F. Hollings
The United States Senate
125 Russell Building
Washington, DC 20510

The Honorable Lindsey Graham
The United States Senate
Russell Building
Washington, DC 20510

Ms. Laurie Lamar
Assistant Director of Reimbursement
Public Policy and Practice Department
American Society of Clinical Oncology
225 Reinekers Lane, Suite 650
Alexandria, VA 22314

Mr. Christian Downs
Association of Community Cancer Centers
11600 Nebel Street, Suite 201
Rockville, MD 20852-2557

Commenter: Osborn, Dustan, MD
Organization: Western Washington Oncology, Inc.

(Comment on next page)

Western Washington Oncology, Inc. P.S.

Olympia - Westside
3920 Capital Mall Drive SW
Suite 100
Olympia, WA 98502
Phone: 360-754-3934
Fax: 360-943-8023

March 12, 2003

CMS
7500 Security Blvd
Mail Stop C1-09-06, Room C1-12-06
Baltimore, Maryland 21244·1850
Attn: Poppy Kendall, CMS Lead Analyst

RE: Oxaliplatin

To Whom It May Concern:

Oxaliplatin has been approved by the FDA for the treatment of metastatic colorectal cancer in second line therapy. Clinical trials that led to the approval by the FDA demonstrated efficacy in this setting. Therefore, the use of this agent for the treatment of metastatic colorectal cancer is clearly indicated and the use of this drug is following FDA approved standards. The denial of the use of this drug in that setting would therefore be inappropriate.

Respectfully yours,

Dustan C. Osborn, MD

dco:smw

Commenter: Patton, Allen, MD
Organization: Hematology-Oncology Associates, P.A.

(Comment on next page)

Hematology-Oncology Associates, P.A.

Allen J. Patton, M.D. • Elmer P. Brestan, M.D. • Thomas D. Sunnenberg, M.D. • Alejandro Inclan, M.D.
German Herrera, M.D. • Thomas B. Tan, M.D. • D. Frank Andrews, III, M.D., F.A.C.P.
Shailesh J. Patel, M.D. • Thomas J. Fitzgerald, M.D.

March 10, 2003

Mr. Thomas A. Scully, Administrator
Center for Medicare & Medicaid Services
200 Independence Ave SW, Rm 314G
Washington, D.C. 20201

Dear Mr. Scully:

As medical oncologists, my associates and myself care for thousands of individuals with cancer in the panhandle of Florida and southern Alabama region. Individuals with colon cancer comprise a large portion of those patients. The CMS website has announced a "national coverage determination" process to determine whether Oxaliplatin will be covered by Medicare. We are writing in support of the coverage of Oxaliplatin and to discourage the non-coverage of any FDA-approved cancer agent.

We have firsthand seen the benefits of Oxaliplatin in treating colorectal cancer. We have seen cancer responses and lives prolonged by its use. It is used in a situation where patients with advanced colorectal cancer would have no other treatment options. The availability of this drug has given new hope to our colorectal cancer patients and Medicare coverage is essential to help these individuals fight their cancer. Denying Medicare coverage for Oxaliplatin would be a dangerous precedent, restricting patient access to effective FDA-approved medications. This denial would also discourage research and further advances in the field if promising and effective drugs are ultimately denied reimbursement.

Your consideration for these cancer patients is requested before a national coverage determination is made.

Sincerely,

Allen J Patton

ALLEN J. PATTON, M.D.

AJP/sdd

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5153 N. 9th Ave. • Suite 404 • Pensacola, Florida 32504 • (850) 478-5700
1703 Bunner Street • Foley, Alabama 36535 • (251) 970-3952

Commenter: Paulson, R. Steven, MD
Organization: Texas Oncology, P.A.

(Comment on next page)

Texas Oncology, P.A.

March 10. 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare/Medicaid Services
200 Independence Avenue, SW, Rm 314G
Washington, DC 20201

Dear Mr. Scully:

I am both amazed and concerned at the recent discussions about considerations regarding the new drug Oxaliplatin. It appears that CMS is considering not covering Oxaliplatin for use in metastatic colorectal cancer. I think this is an extremely dangerous precedent to set since this drug has been approved by the FDA. While it may be an expensive agent, it is also shown to be effective in metastatic colorectal cancer. I think failure to cover this drug would lead to a significant number of Medicare patients who would be unable to receive this agent. Since this is an extremely common diagnosis, especially in the Medicare age population, the backlash from this could be significant.

I personally participated in the trials with Oxaliplatin to document its effectiveness and have seen numerous responses. White it is not curative, clearly patients get another 6-12 months of reasonable quality of life out of treatments such as this. I certainly would not personally want to have to tell patients that they are unable to receive this drug since it is well documented in medical literature as well as in the lay press that it is an effective agent.

I hope that you will consider all of the ramifications of the decision such as this and move to approve this drug in medicare patients as well as in the general population. Thank you for your attention to this matter.

Best regards,

R. Steven Paulson, MD

cc: Jeffrey Shuren
JD Director, Nuline Div of Items and Devices
NuLine Centers for Medicare/Medicaid Services
7500 Security Blvd, Mail Stop C1-09-06
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tv

3535 Worth Street Dallas, TX 75246 214-370-1000 Fax 214-370-1055

Commenter: Perry, Daniel
Organization: Alliance for Aging Research

(Comment on next page)

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March 13, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare & Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Room C1-12-06
Baltimore, MD 21244-1850

Attn: Poppy Kendall

Dear Administrator Scully:

I am writing to provide my comments on CMS's national coverage determination review for Eloxatin™ (oxaliplatin for injection) to treat advanced colorectal cancer (#CAG-00179N).

The Alliance for Aging Research is a nonprofit, independent organization dedicated to supporting and accelerating the pace of biomedical, behavioral and social science research to improve the human experience of aging. The efforts of the Alliance have helped make aging-related research a fast growing priority in this country. This goal is vital in ultimately helping millions of older Americans have access to medical interventions that can improve their quality of life and in some cases extend it.

Colorectal cancer is the second leading cause of cancer death in the United States. Each year approximately 57.000 Americans die from colorectal cancer and close to 150,000 are diagnosed with the disease. Colorectal cancer largely affects the senior population. According to the American Cancer Society, 90% of all cases diagnosed are in people over 50 years of age. Further, the incidence of colorectal cancer is six times higher among people age 65 and older than among people age 50-64. Therefore, you can see why Medicare coverage for colorectal treatments is critical for this population. A decision not to reimburse Medicare beneficiaries will significantly limit their access to Eloxatin and other approved therapies that may prolong their lives.

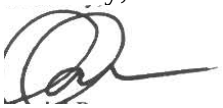
Eloxatin is an example of a new cancer therapy that meets and unmet medical need. When Eloxatin was approved by the FDA in August 2002, Secretary Thompson personally heralded the fast track approval of Eloxatin for second-line treatment in metastatic colon cancer treatment. He stated "Patients diagnosed with colorectal cancer will now have access to another treatment option for this disease. I want to commend the FDA for reviewing the drug's safety and effectiveness so quickly." Moreover, in an immediate move to respond to FDA approval, The National Comprehensive Cancer Network (NCCN) now includes Eloxatin in its 2003 NCCN Clinical Practice Guidelines in Oncology, the Colon and Rectal

Cancer Treatment Guidelines. Given this level of support from both the FDA and the NCCN, is of particular concern that the reimbursement status of Eloxatin is in question.

It makes little sense to "fast track" the FDA approval of a drug, then deny coverage of this potentially life saving drug for the people who need it most-Medicare beneficiaries who are most likely to have a diagnosis of colorectal cancer. This is not the intent of the Medicare statute, which is supposed to ensure that older Americans have the same access to new therapies as the rest of the U.S. population.

We strongly urge you approve Eloxatin for reimbursement without delay. Everyday that a decision is delayed impacts the lives of seniors who have no other options to fight this deadly disease.

Sincerely,



Daniel Perry,
Executive Director

Commenter: Popeo, Daniel/ Price, David
Organization: Washington Legal Foundation, Abigail Alliance for Better Access to Developmental Drugs, and Lorenzen Cancer Foundation

(Comment on next page)

CAG-00163N and 00179N

COMMENTS

of the

WASHINGTON LEGAL FOUNDATION, ABIGAIL ALLIANCE FOR BETTER ACCESS TO DEVELOPMENTAL DRUGS, AND LORENZEN CANCER FOUNDATION

to the

CENTERS FOR MEDICARE & MEDICAID SERVICES, U.S. DEPT. OF HEALTH AND HUMAN SERVICES

Concerning

NATIONAL COVERAGE REVIEWS OF CANCER DRUGS

Daniel J. Popeo
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February 10, 2004

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February 10, 2004

Dennis G. Smith
Acting Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
Hubert H. Humphrey Bldg.
200 Independence Ave., S.W.
Washington, D.C. 20201

Re: National Coverage Reviews of Reimbursement Policy for Cancer Drugs (Ref. Nos. CAG-00163N and 00179N)

Dear Mr. Smith:

The Washington Legal Foundation (WLF), the Abigail Alliance for Better Access to Investigational Drugs, and the Lorenzen Cancer Foundation are submitting these comments to express our concerns regarding the two CMS national coverage reviews that are underway for important anti-cancer therapies: namely, "off-label" use of the colorectal cancer drugs Eloxatin and Camptosar and the non·Hodgkin's lymphoma drugs Zevalin and Bexxar. As detailed below, we believe these reviews have created prolonged and unnecessary uncertainty about the status of these medicines, and that CMS lacks the authority to deny reimbursement for these medicines to Medicare patients who are fighting cancer.

I. Interests of Commenters

Commenter WLF is a nonprofit public interest law and policy center based in Washington, D.C., with supporters nationwide. Since its founding in 1977, WLF has engaged in Comments on National Coverage Reviews of Cancer Drugs litigation and advocacy to defend and promote individual rights and a limited and accountable government including in the area of patients' rights. For example, WLF successfully challenged the constitutionality of Food and Drug Administration restrictions on the ability of doctors and patients to receive truthful information about off-label uses of FDA-approved medicines. *SeeWashington Legal Found. v. Friedman,* 13 F. Supp. 2d 5 J (D. D.C. 1998), *appeal dism 'd, 202* F.3d 331 (D.C. Cir. 2000).

Commenter Abigail Alliance is a nonprofit organization based in Arlington, Virginia, dedicated to helping terminally ill patients obtain access to the medicines they need. Abigail

Alliance was founded in 200 1 by Frank Burroughs, who is now its president. The group is named for Burroughs's daughter, Abigail, an honors student at the University of Virginia. Abigail died of cancer on June 9, 2001, after she was stymied in her efforts to obtain new cancer drugs that her oncologist believed could save her life, but which were still in clinical trials. Abigail Alliance has numerous members and supporters who are suffering from terminal illness or who have lost family members to terminal illness.

Commenter Lorenzen Cancer Foundation is a nonprofit organization based in Monterrey, California, providing assistance to patients fighting pancreatic cancer. The Foundation maintains a large database of clinical trials of pancreatic cancer therapies, as well as current medical news, to aid these patients and their physicians in keeping up to date on the range of available treatment options for pancreatic cancer. The chairman of the Foundation is Lee Lorenzen, who founded it in response to the diagnosis and subsequent passing of his brother Gary Lorenzen due to metastatic adenocarcinoma of the pancreas.

II. Background

After the Food and Drug Administration approves a new drug for marketing, physicians may prescribe the drug for indications other than the specific ones for which the FDA has given marketing approval. Such' off-label" prescribing allows physicians to take advantage of the most current research and experience concerning a drug's properties for the benefit of their patients. "OfT-label prescribing is common in the areas of obstetrics, oncology, pediatrics, and infectious disease (particularly with AIDS patients)." V. Henry, *Off-Label Prescribing: Legal Implications.* 20 1. Legal Med. 365, 365 (Sept. 1999).

In the late 1980's and early 1990's, Members of Congress learned of reports that the Medicare program, through the exercise ofcontractor discretion, was denying reimbursement in some instances for off-label uses of cancer medicines. A General Accounting Office survey and analysis released in 1991 confirmed that off-label prescribing is integral to oncology practice: One-third of all drug administrations to cancer patients were found to be off-label, and over half of all cancer patients were found to receive at least one off-label drug. The study also revealed that federal and private denials of reimbursement were directly affecting the quality of care. Some 62 percent of oncologists in the survey reported that they had admitted patients to hospitals within the past three months to avoid anticipated problems with reimbursement for cancer medicines. Eight to ten percent of oncologists reported altering therapies on account of expected reimbursement problems. Thus, on a broad scale, cancer patients were either being subjected to unnecessary hospital stays or being deprived of the therapy of choice for their Comments on National Coverage Reviews of Cancer Drugs cancer. **Oncologists named the reimbursement policies of Medicare contractors as the number one cause of these unwanted practices**. *See* General Accounting Office, *Off-Label Drugs: Reimbursement Policies Constrain Physicians in Their Choice o/Cancer Therapies* 3, 5 (Sept. 1991) (GAOIPEMD-91-14); General Accounting Office, *Off-Label Drugs: Initial Results of a National Survey* 21, 23-24 (Feb. 1991) (GAO/PEMD-91-12BR).

Congress properly decided to put an end to this situation in Title XIII of the Omnibus Budget Reconcilialion Act of 1993. In a subsection entil1ed "Uniform Coverage of 'Off-Label' Anticancer Drugs," Congress amended 42 U.S.c. § 1395x to require the Medicare program to reimburse for off-label uses of oncologic drugs if the use appears in any of a number of recognized medical compendia. *See* 103 Pub. L. 66, 107 Stat. 312 (1993), § 13553(b). (We detail the applicability of this requirement to CMS's current coverage reviews in section III below.)

CMS appears to have largely heeded this congressional directive in the ensuing years until the release on November I, 2002, of its final rule on the Hospital Outpatient Prospective Payment System (HOPPS). In the preamble to the rule, CMS announced that it "may choose to perform a reasonable and necessary determination {with respect to FDA-approved medicines] in several circumstances, including, but not limited 10 the following: the drug or biological in question represents a novel, complex or controversial treatment, may be costly to the Medicare program, may be subject to overutilization or misuse, or received marketing approval based on the use of surrogate outcomes." *Medicare Program; Changes to the Hospital Outpatient Prospective Payment System and Calendar Year 2003 Payment Rates; and Changes to Payment Suspension for Unfiled Cost Reports,* 67 Fed. Reg. 66718, 66756 (Nov. 1, 2002). CMS asserted that it could undertake such reviews even with regard to indications approved by the FDA for marketing. CMS cited no legal authority for this view - with regard to either off-label *or* on-label uses - except for one of its own proposed rules that predated the 1993 legislation. Id.

CMS made good on its threat to cancer patients when, on July 26, 2002, it initiated a national coverage review of the non-Hodgkin's lymphoma drug ibritumomab tiuxetan (Zevalin). In the course of its review, CMS focused the review on reimbursement for off-label uses and also broadened its scope to include the non-Hodgkin's lymphoma drug tositumomab (Bexxar). *See NCA Tracking Sheet jor Radioimmunotherapyjor Non-Hodgkin's Lymphoma* (CAG-00163N).

CMS initiated a second national coverage review on February 12, 2003, for the cancer drug oxaliplatin (Eloxatin), which has been in use in treatment regimens for colorectal cancer and pancreatic cancer. As with the ZevaLin/Bexxar review, CMS later focused on off-label uses and added a second drug, irinotecan (Camptosar). *See NCA Tracking Sheet for Oxaliplatin (Eloxatin) and Irinotecan (Camptosar) for Colorectal Cancer* (CAG-00179N).

Both reviews have continued far past their original due dates. The due date of the Zevalin/Bexxar review was initially extended to November 4, 2003, then December 31, and now is entirely open-ended. The Eloxatin/Camptosar review, likewise, was initially extended to August 14, 2003, then November 17, then December 31, then January 31, 2004. It, too, now has no announced completion date. In the meantime, Medicare contractors are apparently free in CMS's eyes to exercise discretion to deny reimbursement for off-label uses of these medicines.

III. CMS's Lack of Authority to Deny Reimbursement for the Uses At Issue

Contrary to CMS's assertion, CMS has no authority to deny reimbursement on the basis of the extra-statutory factors identified in the HOPPS announcement - namely, that a cancer drug "represents a novel, complex or controversial treatment, may be costly to the Medicare program, may be subject to overutilization or misuse, or received marketing approval based on the use of surrogate outcomes." Any such policy would violate the direction of Congress, specifically the 1993 amendments codified at 42 U.S.C. § 1395x(t).

The statute provides as follows in pertinent part;

> (1) The term "drugs" and the term "biologicals", except for purposes of subsection (01)(5) of this section and paragraph (2), include only such drugs (including contrast agents) and biologicals, respectively, as are included (or approved for inclusion) in the United States Pharmacopoeia, the National

> Formulary, or the United States Homeopathic Pharmacopoeia, or in New Drugs or Accepted Dental Remedies (except for any drugs and biologicals unfavorably evaluated therein), or as are approved by the pharmacy and drug therapeutics committee (or equivalent committee) of the medical staff of the hospital furnishing such drugs and biologicals for use in such hospital.
>
> (2)(A) For purposes of paragraph (1), the term "drugs" also includes any drugs or biologicals used in an anticancer chemotherapeutic regimen for a medically accepted indication (as described in subparagraph (B)).
>
> (B) In subparagraph (A), the term "medically accepted indication", with respect to the use of a drug, includes any use which has been approved by the Food and Drug Administration for the drug, and includes another use of the drug if –
> (i) the drug has been approved by the Food and Drug Administration; and
> (ii)(I) such use is supported by one or more citations which are included (or approved for inclusion) in one or more of the following compendia: the American Hospital Formulary Service-Drug Information, the American Medical Association Drug Evaluations, the United States Pharmacopoeia-Drug Information, and other authoritative compendia as identified by the Secretary, unless the Secretary has determined that the use is not medically appropriate or the use is identified as not indicated in one or more such compendia, or
> (II) the carrier involved determines, based upon guidance provided by the Secretary to carriers for determining accepted uses of drugs, that such use is medically accepted based on supportive clinical evidence in peer reviewed medical literature appearing in publications which have been identified for purposes of this subclause by the Secretary.

42 U.S.C. § 1395x(t) (emphasis added).

Congress has provided that CMS is to reimburse for off-label uses of FDA-approved cancer drugs. If the drug has received FDA approval, and if the use is listed in one of the references named in the statute, that is the end of the inquiry - unless the Secretary of the Department of Health and Human Services determines that the use is "not medically appropriate," Simply put, the fact that the treatment may be "novel, complex or controversial" is neither here nor there. Costliness is also not an issue: Congress has explicitly limited CMS's inquiry to whether the treatment is *medically* appropriate. Whether the FDA granted marketing approval "based on the use of surrogate outcomes" is also immaterial under the statute.

CMS's pursuit of its announced policy in the face of clear statutory language seems to be based on an essentially lawless - and ghoulish - calculation that that it can simply evade legal review of that policy by virtue of the legal prerequisites to filing suit: By the time agency processes have run their course, it can be expected that an individual victim of an aggressive cancer who has appealed for reimbursement will be dead. We believe that judicial review of denials of reimbursement is more available than this calculation would imply, given the well-established exceptions to the rules of mootness in federal courts, but the more important point is that federal agencies should not be flouting federal statutes in the first place.

IV. The Profound Effect of a Denial of Reimbursement Upon Patients and Oncologic Drug Research

CMS's policy, as announced in the HOPPS rule and as carried out in the national coverage reviews of these anti-cancer drugs, substitutes bureaucratic judgment for the judgment of experienced physicians who are familiar with the needs of an individual patient. While the national coverage decisions at issue here do not extend to FDA-approved indications, CMS has asserted the authority to second-guess even the FDA's own approvals of drugs with respect to specific indications. As the advocacy group Patients Against Lymphoma has noted, the policy "forces these patients to first use toxic therapies proven not to cure and which often compromise the cancer patient's ability to benefit from emerging therapies." Letter of Karl Schwartz, President. Patients Against Lymphoma, to Thomas Scully, Administrator. CMS, Dec. 17, 2002.

Moreover, the message to medical innovators, including sponsors of new cancer medicines, could not be more clear: Even after clearing the significant and costly hurdles associated with clinical trials and FDA approval, even after producing a medicine that is proven to extend or save the lives of cancer patients, investments of hundreds of millions of dollars may be undercut by CMS based on amorphous standards like "novel, complex or controversial." This can only deter the drug innovation that cancer patients need today and will need in the future.

CONCLUSION

The Washington Legal Foundation respectfully requests that CMS terminate the national coverage reviews at issue and clarify that the Medicare program will reimburse for off-label uses of these cancer medicines.

Respectfully submitted,

Daniel J. Popeo

David Price

WASHINGTON LEGAL FOUNDATION
2009 Massachusetts Ave., N.W.
Washington, D.C. 20036
(202) 588-0302

Counsel for Commenters

Commenter: Price, Harry, MD
Organization: Oncology Consultants, P.A.

(Comment on next page)

ONCOLOGY CONSULTANTS, P.A.

LUIS T. CAMPOS, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

CHARLES E. MANNER, M.D.
American Board of Internal Medicine

DAVID B. SANFORD, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

MIGUEL MIRO-QUESADA, M.D.
American Board of Internal Medicine
American Board of Medical Oncology
American Board of Hematology

PAUL Y. HOLOYE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

HARRY R. PRICE, M.D.
American Board of Internal Medicine
American Board of Medical Oncology

July 7, 2003

Poppy S. Kendall, MHS
Centers for Medicare & Medicaid Services
Mailstop C1·09·06
7500 Security Boulevard
Baltimore, MD 21244

Dear Ms. Kendall,

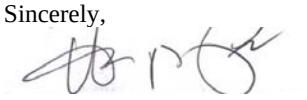
I would like to submtted comments in response to the notice, published on the CMS website, stating that CMS has internally generated a national coverage determination to evaluate when the newly approved anticancer drug oxaliplatin is reasonable and necessary in the Medicare population. The notice stales that this review is being undertaken because of "the potential impact of this treatment on the Medicare program." our physicians at Oncology Consultants, P.A. who specialize in the treatment of cancer are very concerned about how the potential restrictions on oxaliplatin apparently contemplated by CMS may adversely affect our patients.

For most types of items and services, the Medicare statute confers broad authority on CMS to determine whether the item or service is reasonable and necessary and hence whether it is covered by Medicare. That is not the case, however, for drugs and biological used in anticancer chemotherapy regimens. Under section 1861 (t)(2) of the Social Security Act, there is mandatory coverage of drugs and biological in such regiments when used for purposes approved by the Food and Drug Administration, supported by citations in specified compendia, or determined by carriers to be medically accepted based on clinical evidence published in certain journals.

This provision was added to the statute in 1993 to stop the practice, employed by some carriers, of denying Medicare coverage for medically accepted indications on the ground that they were not included in the FDA-approved labeling. Congress amended the statute to deny any discretion to the Medicare program to deny coverage of medically accepted indications of drugs used in anticancer therapy.

Accordingly, I sees no legally permissible function of a national coverage determination on oxaliplatin. All indications approved by FDA must be covered. Other indications are covered if carriers determine that they are supported by the medical literature. In light of the special statutory rules applicable to drugs used in anticancer chemotherapy regimens, CMS lacks the authority to restrict coverage of oxaliplatin. We therefore request that the proposed national coverage determination be withdrawn.

Sincerely,



Harry R. Price, M.D.
Oncology Consultants, P.A.

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Commenter: Raju, Robert, MD
Organization: Dayton Oncology & Hemotology, P.A.

(Comment on next page)

DAYTON ONCOLOGY & HEMATOLOGY, PA

March 7, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Avenue, SW, Room 314G
Washington, DC 20201

RE: CD for oxaliplatin coverage for colon cancer

Dear Mr. Scully:

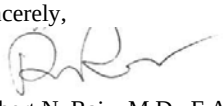
I am a practicing oncologist heading a group, which treats about 10,000 cancer patients in the Dayton area. I was recently made aware of the CMS posting on its website to determine if oxaliplatin is a reasonable and necessary drug for Medicare coverage for patients with colon cancer. As you know colorectal cancer afflicts 150,000 American and 56 000 die each year from this disease. Unless detected early most of these patients will develop metastasis and eventually succumb to the disease.

Patients with colon cancer have very limited choice of drugs which are active and oxaliplatin, clearly is one of the highly effective drugs and this has been approved by the FDA. Most of the colon cancer patients are elderly and are on Medicare and it i extremely important that these patients have access to
this drug to improve their quality of life in addition to lengthening their survival. It is extremely important that you consider this particular drug as a necessity for these patients as I personally have many patients treated with this drug and some of them have attained a complete remission and are
leading an active productive life contributing to the community and their families.

I am somewhat puzzled and greatly concerned that CMS is questioning the need for coverage of this particular drug on the website when it has already been approved by the FDA and has been established as an effective agent for patients with colon cancer. Hopefully, this is not a precedent that is being set for cancer care in general. I am certain that if the Medicare payment for this drug is rejected the response from the cancer community in general, and specifically from the patients and their families will be very intense and this could be avoided by considering this as an "extremely necessary drug" for these patients.

Again, I do appreciate your attention in this regard.

Sincerely,



Robert N. Raju, M.D., F.A.C.P.

RNR/Pradot//pre/pk

cc: Jeffery Shuren J.D.. Director
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Commenter: Ramanathan, Ramesh, MD
Organization: University of Pittsburgh Cancer Institute

(Comment on next page)

University of Pittsburgh

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March 4, 2003

Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave SW
Room 314G
Washington, DC 20201

Dear Mr. Scully,

I was surprised and dismayed by the action taken by The Centers for Medicare and Medicaid Services to deny coverage of oxaliplatin (Eloxatin) for the treatment of colorectal cancer patients.

I am an oncologist who specializes in the treatment of gastrointestinal cancers and have a tremendous amount of experience treating colorectal cancers. There are very few drugs which have activity for the treatment of these cancers and till recently only 5-flurouracil (5-FU) and irinotecan (CPT-II) had reproducible activity.

Randomized clinical trials have shown the activity of oxaliplatin in combination with 5FU in both treated and untreated patients with colorectal cancer and as you aware, oxaliplatin received FDA approval in August 2002.

I have been involved with a number of oxaliplatin clinical trials since 1996. In my opinion oxaliplatin is easy to administer, is well tolerated and has significant activity as shown in randomized clinical trials, and is one of the best regimens for colorectal cancers. Colorectal cancer patients have very few treatment options. Denial of oxaliplatin, an FDA approved drug, for these patients would be a huge disservice to patients and physicians.

If I can be of assistance or if you have questions, please do not hesitate to contact me.

Sincerely,

R. Ramanathan

Ramesh K. Ramanathan, MD
Associate Professor of Medicine
Director, GI Oncology Program
Phone: 412-648-6507
FAX: 412-648-6579

cc: Jeffrey Shuren
JD Director, Division of Items and Devices

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July 1, 2003

The Honorable Thomas Scully
Administrator
Centers for Medicare and Medicaid
Department of Human Health and Services
200 Independence Avenue SW
Washington, DC 20201

Dear Mr. Scully:

I am a physician at the University of Pittsburgh Cancer Institute and Medical Center and have been involved with a number of oxaliplatin clinical trials as an investigator. I would like to comment on the results of the study presented by Dr. DeGramont at the American Society of Clinical Oncology Meeting held in Chicago recently. (Results of the International Randomized MOSAIC Trial, Proc Am. Soc Clin Oncol. A1015: 22, 2003). This is a large randomized trial in which patients were treated with FUILV or the addition of oxaliplatin to FUILV (FOLFOX4) after surgical resection. As you are aware the study showed a highly statistical significant three-year disease free survival for patients treated with the FOLFOX4 regimen. In my opinion this is an extremely important trial. As you are aware, in other randomized studies, a three-year disease free survival has corresponded to an improvement in overall survival as well. I feel that this is an important advance for patients with stage II-III colorectal cancer after surgery, and this should be an option offered to patients and physicians. I hope that CMS will approve FOLFOX4 as a regimen to be considered as an adjuvant therapy for colorectal cancer patients.

Thank you for your consideration. Please do not hesitate to contact to me if you need further information.

Sincerely,

R. Ramanathan

Ramesh K. Ramanathan, MD
Associate Professor of Medicine
Director, GI Oncology Group
Phone: 412-648-6507
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RKR/cad

Commenter: Ratkin, Gary, MD
Organization: Midwest Hematology-Oncology Consultants, Inc.

(Comment on next page)

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Gary A. Ratkin, M.D.
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Paul K. Schultz, M.D.
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Deborah A. Wienski, M.D.
314-996-5512

March 10, 2003

Mr. Thomas A. Scully, Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW
Room 314G
Washington, DC 20201

Re: Eloxatin (oxaliplatin for injection) Reimbursement Coverage

Dear Mr. Scully:

I am a medical oncologist in practice at the Missouri Baptist Cancer Center in St. Louis County, Missouri. I care for a large number of patients with colorectal cancer many of whom have metastatic disease. Over 50% of my practice are Medicare and Medicaid patients.

The recent approval of Eloxatin (oxaliplatin for injection) by the Food and Drug Administration for the treatment of metastatic colon and rectal cancer is a significant advance in my practice. Eloxatin gives medical oncologist an important new tool in the treatment of widespread and advanced colorectal cancers. Our patients are experiencing important palliative benefits and extending their meaningful survival.

Eloxatin is a reasonable and necessary drug for the treatment of cancer patients covered by Medicare and Medicaid. If CMS denies coverage for Eloxatin, the agency will be making decisions that should be made only by the FDA or the physicians who prescribe the drug. An adverse decision about Eloxatin is a harmful precedent and will stifle research and the progress being made in the war against cancer.

Sincerely,

G. A. Ratkin

Gary A. Ratkin, MD FACP
Clinical Associate Professor of Medicine
Washington University School of Medicine

CC: Jeffery Shuren, JD Director Division of Items & Devices
Poppy S. Kendall, MHS

Commenter: Roach, Nancy
Organization: Marti Nelson Cancer Foundation

(Comment on next page)

Marti Nelson Cancer Foundation
607 Elmira Road PN8 331
Vacaville, CA 95687
707421 5886

March 11, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare &Medicaid Services
200 Independence Avenue, SW
Room 314G
Washington, DC 20201

Dear Mr. Scully,

We are writing to urge that Medicare coverage of Eloxatin for second-line therapy against advanced colorectal cancer be approved.

People with advanced cancer can often gain years of productive life as they go through multiple treatments against their cancer. For example, breast cancer patients have multiple opportunities to achieve a remission through treatments such as hormone therapy, many combinations of chemotherapy and finally Herceptin. This combination of treatment options has given countless breast cancer patients longer lives with a better quality of life than was possible even a decade ago.

Patients with advanced colorectal cancer currently have two Food and Drug Administration (FDA)-approved treatments: Camptosar and Eloxatin (both are given in combination with other chemotherapies). Each year, more than 150,000 Americans are diagnosed with colorectal cancer and 56,000 die of the disease. Of these individuals, 27 percent are treated in a hospital setting and would be affected by this CMS policy.

We are alarmed that CMS may not accept the FDA's expert opinion when determining whether to cover Eloxatin for its labeled indications. FDA approval is the gold standard of safety, effectiveness and clinical benefit. We believe that Congress supports this standard, as shown by 42 U.S.C. §1395x (t)(2)(A and B), where "drugs" are defined to include "any drugs or biologicals used in an anticancer chemotherapeutic regimen for a medically accepted indication," including **"any use which has been approved by the Food and Drug Administration."**

Similarly, the fact that Eloxatin may be costly to the Medicare program is not a reason for non-coverage under the Medicare statute. Cancer care generally is more costly that many other diseases because it involves patients who are very ill and require aggressive treatment for their condition. Congress has never authorized CMS to deny coverage based on the cost of therapy, and it has not been the practice of the Medicare program to do so.

Our country has made a huge investment in cancer research and application of the research. The National Cancer Institute 2004 budget request alone is $5.9 billion. If promising drugs are ultimately denied coverage and reimbursement, incentives for research - both public and private - will disappear and our nation's war against cancer will be lost.

Again, we urge that CMS approve reimbursement for Eloxatin.

Sincerely,

Nancy Roach, Director
Marti Nelson Cancer Foundation
607 Elmira Road PNB 331
Vacaville, CA 95687
425.822.3602

cc: Jeffery Shuren via email and mail
JD Director
Division of Items and Devices
Centers for Medicare & Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Baltimore, MD 21244-1850

Poppy S. Kendall, MHS via email and mail
Centers for Medicare & Medicaid Services
7500 Security Blvd.
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Room C1-12-06
Baltimore, MD 21244-1850

Commenter: Rosenbloom, Barry, MD
Organization: Tower Hematology Oncology

(Comment on next page)

TOWER HEMATOLOGY ONCOLOGY

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Philomena E. McAndrew, M.D.
David L. Rosenbaum, M.D.
Barry E. Rosenbloom, M.D.
Fred P. Rosenfelt, M.D.

Irwin M. Weinstein, M.D.
(Emeritus)

Steven Elconin, M.B.A.
Executive Director

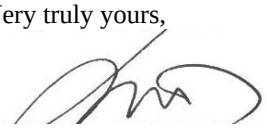
March 11, 2003

Thomas A. Scully, Administrator
Centers for Medicare and Medicaid Services
200 Independence Avenue, SW
Room 314-G
Washington, DC 20201

Dear Mr. Scully:
I am writing with respect to the drug Eloxatin, as one of the investigators involved with its development. This drug has had proven benefit in patients with metastatic colon cancer as a second-line agent, and is totally reasonable and a necessary drug for Medicare coverage purposes. In addition, the drug is very well tolerated, and is especially good for older patients with metastatic disease.

Hopefully, you will see fit to approve this agent so that our patients can be treated with it when appropriate.

Very truly yours,



BARRY E. ROSENBLOOM, M.D.

BER:el

cc: Jeffrey Shuren, J.T.
Poppy S. Kendall, M.H.S.
Mr. Mike Presson

Commenter: Ros-Lehtinen, The Honorable Ileana
Organization: House of Representatives

(Comment on next page)

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SUBCOMMITTEE ON WELLNESS AND HUMAN RIGHTS

Congress of the United States
House of Representatives
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18TH DISTRICT, FLORIDA

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June 26, 2003

Thomas Scully, Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
200 Independence Avenue, S.W.
Room 314-G HH Building
Washington, D.C. 20201

Dear Mr. Scully:

I am writing to express concern over a new policy of the Centers for Medicare & Medicaid Services (CMS) to initiate a National Coverage Analysis for new drugs that may be novel or complex, costly to Medicare, or subject to over utilization or misuse.

Medicare has 'historically covered new drugs when they are approved by the Food and Drug Administration (FDA), a policy that CMS has now rejected in favor of a drug-by drug analysis of what will be covered and fur what uses. According to cancer advocates, this effort by CMS appears to be in conflict with the Medicare statute.

This issue has been brought to my attention by cancer advocates, who note that three cancer therapies are currently undergoing coverage analyses, with one of the review processes months past its projected date of completion. The initiation of the coverage analyses has had a negative impact on access to these drugs.

Thank you for your time and attention.

Sincerely,

Ileana

Ileana Ros-Lehtinen
Member of Congress

IRL:ml

cc. Vicki Anderson
Federal Reserve Financial Services
Retail Payments Office
5811 S.W, 56th Street
Miami, Florida 33155

Commenter: Rothenberg, Mace, MD
Organization: Vanderbilt University Medical Center

(Comment on next page)

Vanderbilt University Medical Center

Division of Hematology/Oncology
Department of Medicine
777 Preston Research Building
Nashville, TN 37232-6307

(615) 322-4967
FAX: (615) 343-7602

March 14, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue SW
Room 3l4G
Washington, DC 20201

Dear Mr. Scully.

Jam writing to you to voice my support for the coverage of oxaliplatin by Medicare and Medicaid in the treatment of patients with advanced colorectal cancer. In my roles as both a researcher and a clinician who specializes in the care of patients with cancer, I have been extremely impressed with the beneficial effects of oxaIiplatin in patients with colorectal cancer. With the median age for diagnosis of colorectal cancer being 70, this issue is especially relevant for seniors for whom Medicare may provide the only means of medical coverage.

As Principal Investigator on the randomized trial that provided the basis for FDA approval of oxaliplatin in August, 2002, I can attest to the tangible benefit conferred by oxaliplatin in patients with progressive, metastatic colorectal cancer following 1st-line chemotherapy. The combination of oxaliplatin, 5fluorouracil (5-FU) and leucovorin produced tumor shrinkage and a delay in the time-to-tumor progression that could not be achieved by any other therapy. This combination regimen known as FOLFOX4 fills an unmet medical need and truly represents a breakthrough therapy for this group of patients. In clinical practice, FOLFOX4 has rapidly emerged as the new standard of care for patients with progressive colorectal cancer.

Based on data from several clinical trials, the availability of all known effective drugs in the treatment of colorectal cancer - 5-FU, leucovorin, irinotecan, and oxaliplatin - is associated with the longest survival (> 20 months). Limiting treatment options to only 5-FUlleucovorin or 5-FUILV and irinotecan also limits survival to II months (for 5-FUILValone) or 14-16 months (with 5-FU/LV and irinotecan). I would hate to see the clock turned back by limiting the availability of oxaliplatin for seniors in the United States.

Thank you for this opportunjty to share my perspectives on oxaliplatin with you.

Sincerely

Mace L. Rothenberg, MD, FACP
Professor of Medicine
Vanderbilt University Medical Center,
Ingram Professor of Cancer Research
Vanderbilt-Ingram Cancer Center

Commenter: Ruppersberger, The Honorable Dutch
Organization: House of Representatives

(Comment on next page)

C.A. DUTCH RUPPERSBERGER
2ND DISTRICT, MARYLAND

PERMANENT SELECT COMMITTEE ON INTELLIGENCE
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Congress of the United States
House of Representatives
Washington, DC 20515–2002

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www.house.gov/ruppersberger

June 24, 2003

145808

2003 JUN 25 P 1:15

Mr. Thomas Scully
200 Independence Ave. SW
Rm 314-G
Washington, D.C. 20201

Dear Mr. Scully:

I am writing to express my concerns about a new policy of the Centers for Medicare & Medicaid Services (CMS) to initiate a National Coverage Analysis for new drugs that may be novel or complex, costly to Medicare, or subject to over utilization or misuse.

Medicare has historically covered new drugs when they are approved by the Food and Drug Administration (FDA), a policy that CMS has now rejected in favor of a drug-by-drug analysis of what will be covered and for what uses. This policy is troubling for procedure reasons, since it was announced without opportunity for public comment.

Aside from procedural issues, this effort by CMS appears to be in conflict with the Medicare statute. As a result of 1993 amendments to the statute, CMS is required to cover FDA approved uses of cancer drugs and off-label uses of drugs in the media compendia and to allow carriers the discretion to cover additional uses based on the medical literature. The intent of Congress to ensure cancer patients' access to FDA-approved drugs including off-label uses of these drugs is clearly reflected in the statute.

This issue has been brought to my attention by cancer advocates, who note that three cancer therapies are currently undergoing coverage analyses, with one of the review processes months past its projected date of completion. The initiation of the coverage analyses has had a negative impact on access to these drugs.

I urge you to abandon the policy of subjecting new cancer therapies to a Medicare coverage analysis. This practice conflicts with the Medicare statute and is not in the best interest of cancer patients.

I look forward to hearing from you on this issue.

Sincerely,

C.A. Dutch Ruppersberger

C.A. Dutch Ruppersberger
Member of Congress

CADR:wg

Commenter: Saltz, Leonard, MD
Organization: Memorial Sloan-Kettering Cancer Center

(Comment on next page)

March 13, 2003

Poppy S. Kendall, MHS
Office of Clinical Standards and Quality
Coverage and Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Baltimore, MD 21244-1850

Re: Oxaliplatin (Eloxatin) for Colorectal Cancer (#CAG-00179N)

Dear Ms. Kendall:

This letter represents the consensus of the senior clinicians in our Colorectal Disease Management Team at Memorial Sloan Kettering Cancer Center in New York.

We believe that the use of oxaliplatin is both reasonable and necessary for optimal care of Medicare patients with colorectal cancer. Studies have demonstrated that oxaliplatin-based treatments can provide improved response rates and can delay tumor progression in patients who have progressed through first line treatment with irinotecan-based chemotherapy (Rothenberg et al: Ann Oncol 2oo2;13(Suppl 5):2). In addition, the most recent national intergroup trial, N9741, conducted in patients with previously untreated colorectal cancer (i.e., first-line use) demonstrated that response rate, time to tumor progression, and overall survival were superior for the patients who received the oxaliplalin based "FOLFOX" regimen compared to the irinotecan-based IFL regimen (Goldberg RM: Proc ASCO 2002, abst #511, Goldberg RM: Clin Colorectal Cancer 2002 Aug 2(2):81).

While all chemotherapy for colorectal cancer, including oxaliplalin, has significant limitations, both in efficacy and in its potential for toxicity, in the overall therapeutic context, oxaliplatin provides meaningful palliation to a significant number of patients with colorectal cancer. Oxaliplatin is not a "me too" drug. Its anti-tumor activity is complementary to that of other available agents. Specifically. tumors that are resistant to irinotecan may respond to oxaliplatin and vice versa.

Based on available clinical data, use of oxaliplatin as a first-line or second-line treatment depends on a patient's specific clinical situation. Some patients have clinical characteristics that are relative contraindications to first-line use of an irinotecan-containing regimen, such as biliary obstruction, Gilbert's Disease, or problems with gastrointestinal hypermotility and/or absorption. Oxaliplatin affords an important alternative first-line option for these individuals.

In summary, our clinicians agree that use of oxaliplatin figures into the treatment plans of a large number of colorectal cancer patients, and that oxaliplatin needs to be available as a treatment option, if we are to provide our patients with the most effective treatment.

We hope these comments will be useful to you in your evaluation of this drug.

Sincerely,

Leonard Saltz, MD
Associated Attending Physician,
Co-Leader, Colorectal Disease Management Team

Memorial Sloan-Kettering Cancer Center
Laurance S. Rockefeller Outpatient Pavilion
160 East 53rd Street, New York, New York 10022
NCI-designated Comprehensive Cancer Center

July 2, 2003

The Honorable Thomas Scully
Administrator
Center for Medicare and Medicaid Services
Department of Human Health and Services
200 Independence Avenue SW
Washington DC 20201

Dear Mr. Scully,

I understand that the Center for Medicare and Medicaid Services is reviewing the appropriateness of reimbursement of either irinotecan or oxaliplatin for the adjuvant treatment of surgically resectable colorectal cancer. As medical leader of the Colorectal Disease Management Team at Memorial Sloan Kettering Cancer Center in New York, as well as Gastrointestinal Track Leader for the Education Committee of the American Society of Clinical Oncology, I have considerable familiarity with both of these drugs, and considerable experience with their use in both the metastatic and adjuvant settings for treatment of colorectal cancer. I would like to take this opportunity to share some thoughts with you on this subject.

The world of colorectal cancer management has substantially improved over the past decade, with more active agents and more treatment options becoming available to doctors and their patients. Both irinotecan and oxaliplatin represent important steps forward in our attempts to improve outcomes for our patients. Neither drug is a cure, nor is either correct for all patients. However, each has important attributes which make it appropriate for use in selected stage II, III, and IV colorectal cancer patients.

It is the responsibility of medical oncologists to make an appropriate assessment of the potential risks and benefits of treating patients with oxaliplatin or irinotecan. These decisions must be based on an understanding of available literature. as well as careful interviews and discussions with the patient. We are long past the "one size fits all" approach in colorectal cancer, and treatment regimens must be individually tailored. There will be patients for whom expectant observation alone may be the most appropriate therapy. Other patients will be best managed with fluoropyrimidine-based therapy. Yet there are clearly patients for whom the risks of adding either irinotecan or oxaliplatin to their treatment regimen will be outweighed by the potential benefits.

It is worth noting that although the evidence indicates that irinotecan and oxaliplatin have similar degrees of antitumor activity, their side effect profiles are dramatically different. These differences may favor one drug over the other, or vice versa, for any given patient. Hence, access to both drugs is necessary if oncologists are to be able to provide each patient with the best available option.

My concern is that in order for oncologists to practice state of the art medicine, our patients must have full access to all active and approved drugs. including both irinotecan and oxaliplatin. To deny Medicare and Medicaid patients full access to these agents runs the risk of giving many of these patients suboptimal management of their potentially curable cancers.

I thank you for the opportunity to share these thoughts with you.

Respectfully,

Leonard Saltz, MD

cc: Gay W. Burton
Centers for Medicare and Medicaid
7500 Security Bldg, Mailstop C1-09-06
Baltimore. MD 21244-1850

Memorial Sloan-Kettering Cancer Center
Laurance S. Rockefeller Outpatient Pavilion
160 East 53rd Street, New York, New York 10022

NCI-designated Comprehensive Cancer Center

Commenter: Schilsky, Richard, MD
Organization: The University of Chicago

(Comment on next page)

Richard L. Schilsky, M.D.
Professor of Medicine
Associate Dean for Clinical Research
Division of the Biological Sciences
and the Pritzker School of Medicine

The University of Chicago

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e-mail: rschilsk@medicine.bsd.uchicago.edu

March 10, 2003

Thomas A. Scully
Administrator
Medicare and Medicaid Services
200 Independence Ave S.W.
Room 314
Washington, DC 20201

Dear Mr. Scully,

I am writing in my capacity as a medical oncologist at the University of Chicago who treats patients with colorectal cancer and as chaimlan of the Cancer and Leukemia Group B, a national clinical trials group sponsored by the National Cancer Institute. As a physician and clinical investigator, I am concerned that The Centers for Medicare and Medicaid Services has taken several actions that could have broad-ranging implications with respect to patient access to oncology drugs and the ability of publicly-sponsored research organizations to successfully complete cancer clinical trials.

The key elements from the CMS guidance published in the Federal Register on November 1, 2002 are:

> • FDA approval is necessary but insufficient to gain reimbursement status for a drug, and that the determination of "clinical effectiveness" by CMS is outside the scope of the FDA's' safe and effective" determination. Moreover CMS will assess whether or not a compound or therapeutic modality is "reasonable and necessary" (or' inherently reasonable") for the Medicare population.
>
> • Reimbursement may be denied when the drug or biological represents a novel, complex, or controversial treatment; would be to costly to Medicare, or received marketing approval based on surrogate outcomes.

This policy could, in effect, prevent access to many novel agents currently in development or recently approved for use in cancer by FDA.

A case in point is oxaliplatin (Eloxatin), one of only two chemotherapeutic drugs approved in the last 50 years by FDA for treatment of advanced colorectal cancer. Eloxatin fills an **unmet medical** need: as an efficacious therapy for patients with advanced colorectal carcinoma that has progressed after front-line treatment with irinotecan/5-FU/leucovorin (IFL). This was demonstrated in a randomized, controlled trial in which treatment with Eloxatin in combination with infusional5-FU (FOLFOX4) was compared to infusional5-FU alone. The results were as follows: 9.9% of the patients on the FOLFOX4 arm had objective responses

and 60% of the FOLFOX4 patients experienced disease stabilization (for a total of 70% of FOLFOX4 patients with tumor control) compared to 0% responses and 46% disease stabilization on the infusional 5-FU arm (or 46% of patients with tumor control, p<0.0001). To further highlight this difference in tumor control, there was a significant difference in time to disease progression (4.6 months on FOLFOX4 versus 2.7 months on infusionaI5-FU, p<0.0001). Moreover, a difference in reduction of tumor-related symptoms was observed (35.4% on the FOLFOX4 arm versus 14.3% on the infusional 5-FU arm, p<O.OOI), which correlated with tumor control.

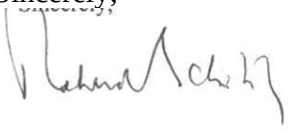
In addition, as demonstrated in an important cooperative group trial (N9741, interim results presented at ASCO and ESMO in 2002), Eloxatin in combination with infusional 5-FU/leucovorin (FOLFOX4) had significantly higher response rates times to disease progression and **survival,** and significantly less toxicity than IFL in the first-line setting.

At present, there is no effective treatment for patients with metastatic colorectal cancer that has progressed after first-line chemotherapy and, although the benefits of Eloxatin are modest, they are real and important to patients. A decision by CMS to deny reimbursement for this drug will make it inaccessible to thousands of patients who could potentialiy benefit from its use.

Furthermore, a negative coverage decision will negatively impact the ability of national research groups, such as the Cancer and Leukemia Group B (CALGB), to complete accrual to other trials that will refine the role and extend the utility of this important new drug for colorectal cancer.

On behalf of the 3000 members of CALGB and the thousands of patients we serve, I urge CMS to approve reimbursement for Eloxatin and to revise the proposed policies so as to insure that promising new cancer therapies are quickly deployed in the community setting.

Sincerely,



Richard L. Schilsky, M.D.
Professor of Medicine
Associate Dean for Clinical Research
Chairman, Cancer and Leukemia Group B

Cc: Jeffrey Shuren, JD
Director, Division of Items and Devices
Center for Medicare and Medicaid Services Mailstop: C1-09-06
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Baltimore, MD 21244-1850

Cancer and Leukemia Group B
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Richard L. Schilsky, M.D.
Chairman

July 1, 2003

The Honorable Thomas Scully
Administrator
Centers for Medicare and Medicaid
Department of Human Health and Services
200 Independence Avenue SW
Washington, DC 20201

Dear Mr. Scully,

Randomized clinical trials have clearly shown that adjuvant chemotherapy for node positive and high risk node negative colon cancer reduces recurrence and saves lives. The definitive trials began more than two decades ago and oncologists have been using the same 5-FU/leucovorin regimen in the adjuvant setting for more than 10 years. At the 2003 meeting of the American Society of Clinical Oncology, results of the MOSAIC trial were presented for the first time and clearly t.howed that an oxaliplatin-based regimen (FOLFOX 4) is superior to 5-FU /leucovorin as adjuvant treatment. A 5% absolute improvement in 3 year disease-free survival was observed for patients treated with FOLFOX 4. These results represent the first advance in adjuvant chemotherapy for colon cancer in many years and are likely to result in improved survival for patients over time. I am aware that Sanofi-Synthelabo will continue to follow patients on this trial for survival and the results should be forthcoming in the next few years.

Although the absolute difference in disease-free survival for FOLFOX is small, it is on the order of that commonly seen for other successful and widely used adjuvant therapies for breast and colon cancer. Given the high incidence of colon cancer in the United States, even a small incremental benefit has the potential to translate into many thousands of lives saved. For this reason, I believe that patients should have access to oxaliplatin-based chemotherapy in the adjuvant therapy setting and urge that CMS extend coverage for this purpose.

Thank you for carefully considering this opportunity to make an important impact on the lives of patients with colon cancer.

Sincerely,

Richard L. Schilsky, M.D.
Professor of Medicine
Associate Dean for Clinical Research
University of Chicago
Chairman, Cancer and Leukemia Group B

cc: .Gay W. Burton
Elizabeth Harvey, Ph.D.

Commenter: Schlabach, Larry, MD
Organization: University Oncology & Hematology Associates

(Comment on next page)

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LARRY SCHLABACH, M.D.
959 EAST THIRD STREET
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FAX: 423-778-8182

March 11, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW
Room 314G
Washington, DC 20201

Re: Denial of FDA-approved Eloxatin

I am a practicing medical oncologist in Chattanooga, Tennessee. It has come to my attention that the Centers for Medicare and Medicaid Services (CMS) is considering denial of access to an important chemotherapeutic agent for patients with metastatic colorectal cancer. This drug is Eloxatin and recently was approved by the Food and Drug Administration for treatment of patients with metastatic colon cancer. I have used this drug now on numerous occasions for patients with metastatic colon cancer and have seen some incredible results as to remission of their malignancies.

This group of patients (metastatic colorectal cancer) often had very few treatment options available for fighting their advanced malignancy. It is administered along with 5-fluorouracil and leucovorin. By denying Medicare coverage of Eloxatin, you would be removing an important treatment option for these patients.

Colorectal cancer frequently, adversely effects older Americans, and by restricting these patient's access to such treatment would come at a time when the best chances of survival have come available to these people. More importantly, such an action by CMS would discourage research if promising drugs are ultimately denied coverage and reimbursement when they become FDA approved. My understanding is that this is unprecedented for CMS to deny FDA-approved cytotoxic chemotherapy in this group of patients, and I would most certainly trust that you would make a decision here in favor of providing coverage for this group of individuals.

Your attention to this matter would be greatly appreciated.

Sincerely,

Larry L. Schlabach, M.D.
University Oncology & Hematology Associates

Lls/ahf

Commenter: Stansfield, Lynn
Organization: Roche Laboratories, Inc.

(Comment on next page)

Roche

Pharmaceuticals

March 19, 2003

Poppy S. Kendall, MHS
Lead Analyst
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Baltimore, MD 21244-1850

Dear Ms. Kendall:

RE: Comments on National Coverage Analysis (NCA)
Oxaliplatin (Eloxatin) for Colorectal Cancer (#CAG-00179N)

On behalf of Roche Laboratories Inc., a research based pharmaceutical company, I offer the following comments to CAG-OOI79N, regarding the National Coverage decision for oxaliplatin (Eloxatin) for Colorectal Cancer. We are aware that CMS is analyzing the use of Eloxatin in the Medicare population. I am submitting the following information to assist those efforts.

Oncology and the use of chemotherapeutic and biotechnology compounds to treat cancer is highly complex and dynamic. Treatment guidelines have been created to provide oncologists with the wisdom of collective thought and experience, however, these serve only as guides and not as definitive answers to treatment questions. No single agent, dosage or treatment regimen can be looked upon as the sole method to treat a particular cancer or patient. Therefore, oncologists must be given latitude to adjust treatment guidelines or protocols based on new and existing peer reviewed data. Currently, CMS and the majority of insurers recognize the complex dynamics of cancer treatment and the importance of physicians being able to exercise their best professional judgement in tailoring drug administration when use can be justified based on sound, peer-reviewed clinical data. The use of oxaliplatin under question by CMS falls into this realm.

Singling out an FDA approved drug that meets the Medicare definition of a covered drug for national coverage review is highly unusual. Reviewing an oncology drug for potential coverage restrictions as to its use is unprecedented. In addition, a policy that restricts when and how an oncology drug is used or that eliminates coverage entirely is contrary to guidance set forth under the Medicare Memorandum No.AB-94-2, entitled 'COVERAGE OF ORAL ANTI-CANCER DRUGS AND UNIFORM COVERAGE OF OFF-LABEL USES OF ANTI-CANCER DRUGS PROVIDED FOR BY THE OMNIBUS BUDGET RECONCILIATION ACT OF 1993 (OBRA 1993). To date, by reviewing the use of oncology drugs under this provision, CMS has not actively hindered or encouraged the use of any specific oncology treatment and the creation of a "formulary" or a "best practice" rule has, therefore, been avoided. Initiating the review of a new drug by a different process is an ominous indication of potential coverage restrictions that may apply to new products and to expanded indications for currently approved oncology therapies. This could lead to onerous administrative processes and result in decisions that conflict with treatment dynamics and patient needs.

Roche Laboratories Inc. 340 Kingsland Street
Nutley, New Jersey 07110-1199

The drug in question, oxaliplatin, was shown to be highly active in advanced colorectal cancer when combined with 5FU-based therapy. Several large clinical trials evaluating oxaliplatin with either infusionaJ 5FU or with the Medicare covered oral chemotherapy drug Xeloda™ (capecitabine) documented substantial benefits to patients with metastatic disease: tumor response rates, time to disease progression and overall survival observed were among the best achieved thus far with any approved or experimental treatment for metastatic colorectal cancer.

The combination of oxaliplatin with the oral Xeloda (rather than with infusional 5FU), offers patients an effective and safe treatment with unique attributes; i.e., a simplified and more cost effective pharmacoeconomic combination. This combination is commonly referred to in literature as the XELOX regimen. The XELOX regimen can be contrasted with the FDA approved regimen for oxaliplatin (oxaliplatin + infusional 5FULV), sometimes referred to in literature as the FOLFOX4 regimen. Employing a clinically equivalent regimen that incorporates oral Xeloda in place of intravenous 5-fluorouracil with oxaliplatin (XELOX) can save approximately $5,000.00.

The pharmacoeconomic benefits realized with the XELOX combination are also supported by data published at the International Society of Pharmacoeconomic and Outcomes Research. An abstract that demonstrates these results is attached for your reference.

In summary, the data noted above indicate that oxaliplatin is a valuable addition to treatment for colorectal cancer and that overall costs for the Medicare program can be reduced when it is used in combination with another product, such as Xeloda. I respectfully request that the enclosed information be included in the analysis for this coverage decision. If you have questions or require further information or documentation, please do not hesitate to call me.

Sincerely,

Lynn Stansfield
Director
Reimbursement and Patient Assistance
Roche Laboratories Inc.

cc: Secretary Tommy G. Thompson
The U.S. Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

Mr. Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Avenue, S.W.
Room 314G
Washington, DC 20201

Jeffrey Shurren, JD
Director
Division of Items and Devices
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mailstop C1-09-06
Baltimore, MD 21244-1850

Commenter: Steele, Ellen
Organization:

(Comment on next page)

March 16, 2003

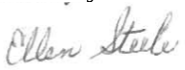
Mr. Thomas Scully
Administrator, Centers for
Medicare & Medicaid Services
200 Independence Ave. S.W.
Hubert Humphrey Bldg. Rm. 422G
Washington DC 20201

Dear Mr. Scully;

Have any of your family or friends been touched by cancer? Would you deny them a drug that would keep them alive?

Oxaliplatin is a necessary drug for a significant portion of the cancer patient population. This drug has been approved by the FDA. Please do not deny medicare patients from treatment with oxaljplatin. Our lives are at stake.

Sincerely



Ellen Steele
colon cancer patient, stage IV

Commenter: Stovall, Ellen
Organization: National Coalition for Cancer Survivorship

(Comment on next page)

July 11, 2003

The Honorable Thomas Scully
Administrator
Centers for Medicare & Medicaid
Department of Health & Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Mr. Scully:

Patient advocacy groups representing people with colorectal cancer have recently informed us that the Center for Medicare and Medicaid Services (CMS) has posted a notice indicating its intention to review data on coverage for the combination chemotherapy regimen, FOLFOX4, in the adjuvant setting.

The National Coalition for Cancer Survivorship (NCCS) is the oldest survivor-led cancer organization advocating on behalf of this nation's more than 9 million cancer survivors. Our organization advocates for quality cancer care for all Americans, and as such, we expect reasonable and expedient reimbursement for evidence-based medicine and practice. The level of evidence we have reviewed comes from several sources, including the Food & Drug Administration (FDA), data presented in a recent meeting of the American Society of Clinical Oncology (ASCO) and from the sponsors of the clinical trial using the FOLFOX4 regimen as adjuvant treatment for Stage 3 colorectal cancer. We also understand that the sponsor, Sanofi-Synthelabo, will conduct long-term follow up studies of the patient involved in these trials as p<U1 of its overall drug development plan. This is an important factor in our consideration in support of a coverage decision regarding use of this and any other drugs that meet these criteria in the adjuvant setting.

We are writing to express our support for all reimbursement practices that will facilitate access to any drug regimen supported by good clinical data that may result in patients with stage 3 colorectal cancer being treated with a potentially curable intervention. The data indicating the three-year disease-free survival seen with FOLFOX4 should be a sufficient endpoint for making a coverage determination in this case. We understand you will be examining this shortly and we ask for your timely review to expedite reimbursement.

Very truly yours.

Ellen L. Stovall

Ellen L. Stovall
President & CEO National Coalition for Cancer Survivorship

cc: Katie Couric, National Colorectal Cancer Research Alliance
Kevin Lewis, Colon Cancer Alliance
Priscilla Savary. Colorectal Cancer Network
Gay W. Burton, Centers for Medicare and Medicaid

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info@canceradvocacy.org • www.canceradvocacy.org

Commenter: Takimoto, Chris, MD, Ph.D.
Organization: University of Texas Health Science Center at San Antonio

(Comment on next page)

The University of Texas
Health Science Center at San Antonio
Mail Code 7884
7703 Floyd Curl Drive
San Antonio, Texas 78229-3900

Department of Medicine
Division of Medical Oncology

(210) 567-4777
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4 March 2003

Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave, S.W.
Room 314G
Washington, DC 20201

Dear Mr. Scully:

I am writing to express my deep concern about the status of the ongoing review of the new anticancer agent, oxaliplatin, which is currently undergoing a National Coverage Analysis by the Centers for Medicare and Medicare Services. I am an academic medical oncologist who specializes in the treatment of patients with gastrointestinal tumors and colorectal cancer. I am currently on the faculty of the University of Texas Health Science Center in San Antonio; however, before I moved to Texas just over two years ago, I worked for 10 years at the National Cancer Institute in Bethesda, Maryland in the Gastrointestinal Tumor group. I have been active in clinical trials and developmental therapeutics for gastrointestinal tumors for over 12 years. Currently, 80% of patients in my clinical practice are medically indigent and do not have any type of medical insurance, let alone Medicare.

Based on scientifically sound clinical trials, oxaliplatin was shown to be an active and effective agent in the treatment of colorectal cancer. As Dr Richard Goldberg of the Mayo Clinic has demonstrated in the N974 I Intergroup Trial, this agent has the ability to prolong survival in patients with advanced colorectal cancer. As a physician who has treated many patients with oxaliplatin, I have been impressed by its efficacy and low toxicity profile. I have seen first hand how this agent can significantly and substantially benefit patients with this terrible disease.

For over 35 years, we have only had one clearly active agent, 5-f1uorouracil, for the treatment of advanced colorectal cancer. In 1996, the US Food and Drug Administration (FDA) approved the first new drug for colorectal cancer in 4 decades, irinotecan. In 2002, the second new agent, oxaliplatin, was FDA-approved. Oxaliplatin is chemically distinct, and completely different from any other type of chemotherapeutic agent used for advanced colorectal cancer. The sequential use of combinations of 5-fluorouracil, irinotecan and oxaliplatin in patients with advanced disease can alleviate symptoms and prolong survival. Because of the use of all three of these active agents, the median survival in large randomized studies of patients with advanced colorectal cancer has doubled from 10 to about 20 months.

In a sense, the greater issue is how will the Centers for Medical and Medicaid Services view any new therapy with activity in the treatment of advanced cancer. According to the CMS guidance published in the Federal Register on November 1, 2002, reimbursement may be denied when the drug or biologic represent a novel, complex or controversial treatment; would be too costly to

Medicare, or received marketing approval based on surrogate outcomes. However, these criteria could apply to virtually any anticancer agent. I have serious concerns about how the unthoughtful application of these vague criteria could adversely impact patient access to novel new therapies that can prolong survival and reduce the pain and suffering caused by cancer.

Finally, it is important to realize that a negative action in the case of oxaliplatin could dramatically affect many patients beyond just those who critically depend upon Medicare. *As* a physician who primarily cares for patients lacking any type of medical insurance, I can personally attest that our treatment guidelines are heavily influenced by Medicare coverage decisions. On behalf of the over fifty-thousand Americans who will develop advanced colorectal cancer in 2003, I strongly urge you to consider granting Medicare coverage for oxaliplatin and for other new agents that meet the rigorous standards of safety and efficacy established by the FDA. Thank you for your considerable efforts to bring quality hea1thcare to all Americans.

Sincerely,

Chris H. Takimoto, MD, PhD, FACP
Associate Professor
Division of Medical Oncology, Department of Medicine
University of Texas Health Science Center at San Antonio

Cc:
Jeffrey Shuren, JD
Director, Division of Items and Devices
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Poppy S. Kendall, MHS
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Baltimore, MD 21244-1850

June 25, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave, S.W.
Room 314G
Washington, DC 20201

Dear Mr. Scully:

I am writing to express opinion about the anticancer agent oxaliplatin, which is currently undergoing review by the Center for Medicare and Medicare Services for the potential use of this agent in patients with resectable, and therefore potentially curable, colon cancer. I am an academic medical oncologist who specializes in the treatment of patients with gastrointestinal tumors and colorectal cancer. I am currently on the faculty of the University of Texas Health Science Center in San Antonio; however, before I moved to Texas just over two years ago, I worked for 10 years at the National Cancer Institute in Bethesda, Maryland in the Gastrointestinal Tumor group. I have been active in clinical trials and developmental therapeutics for gastrointestinal tumors for over 12 years. My practice is predominantly limited to gastrointestinal oncology and the majority of my patients are medically indigent, with a much smaller percentage covered by Medicare or Medicaid.

At our most recent international meeting of the American Society of Clinical Oncology in Chicago in June 2003, Dr. Avery de Gramont presented data from the MOSAIC trial showing that oxaliplatin and 5-fluorouracil administered to patients with resected stage ITI colon cancer generated an absolute 5% improvement in 3-year disease free survival. The reason why this is an important advance is that a statistically significant improvement using generated by adjuvant chemotherapy in this setting can translate in to a higher overall long term cure rate. Thus, the magnitude of benefit even if it only occurs in a percentage of patients, is great. This represents an important advance that provides a benefit to our cancer patients.

At the very same meeting where these results were presented the expert discussant Dr. Robert Mayer of the Harvard Medical School and the Dana-Farber Cancer Institute recommended that the oxaliplatin/5-fluorouracil regimen be considered in the adjuvant treatment of selected patients with resected colon cancer, especially those at high risk for potential recurrence. The decisions of the Centers for Medical and Medicaid Services greatly impact upon the accessibility of a new therapy even for those patients not covered by Federally-funded healthcare programs. Therefore, I am motivated to write you out of genuine concern for those patients of mine with colon cancer, who, I am convinced, will derive benefit from this therapy. I would like to urge you in making your important decision to do all that you can to allow fair access to oxaliplatin based adjuvant chemotherapy for those patients who may

substantially benefit from and even be cured by this treatment. I realize these are difficult decisions; nonetheless, I would like to thank you for your considerable efforts to bring quality healthcare to all Americans.

Sincerely,

Chris H. Takimoto, MD, PhD FACP
Associate Professor
Division of Medical Oncology, Department of Medicine
University of Texas Health Science Center at San Antonio
Institute for Drug Development
Cancer Therapy and Research Center

Cc:
Gay W. Burton
Centers for Medicare and Medicaid
7500 Security Boulevard, Mailstop CI-09-06
Baltimore, MD 21244-1850

Commenter: Turpin, Alan
Organization:

(Comment on next page)

From: <Saturpin10@aol.com>
To: <pkendall@cms.hhs.gov>
Date: 3/12/03 10:44AM
Subject: Oxaliplatin

Having recently learned of CMS plan to potentially deny coverage for some cancer treatments based upon criteria which includes "treatments which were FDA-approved based upon surrogate outcomes and treatments which are costly to the Medicare program", I find it necessary to write in strong opposition to this policy.

In my opinion, it is unconscionable that CMS would deny a Medicare beneficiary access to an FDA-approved cancer treatment, just because clinical studies evaluating survival have not yet matured. By the nature of FDA-approval, it has been deemed by the government agency that is charged and authorized to make such determinations, that there is credible evidence that the treatment provides a clinical benefit to the patient and that its use in the labeled indication is reasonable and appropriate.

Should CMS choose to ignore the FDA guidance and deny coverage for labeled indications provided by the agency, the following scenario is going to occur:

A 64 y.o. patient with metastatic colorectal cancer and commercial insurance will be able to get access to the latest FDA-approved treatment, in this instance oxaliplatin.

In contrast, a 65 y.o. Medicare beneficiary with the exact same disease will be denied access to the FDA-approved treatment. In this instance, the physician will then have to attempt to treat the patient with agents that are non-FDA approved or labeled for this indication, have no data to support their use in this specific setting, and are likely to produce no clinical benefit to the patient.

How can CMS discriminate this way against the very people it is supposed to assist and protect? Which is a better use of taxpayer funds, the use of an FDA-approved treatment or a treatment with no evidence whatsoever to support its reasonable and appropriateness?

I urge CMS not to usurp the authority of the medical experts at the FDA in determining which treatments are medically appropriate, especially in the case of patients that are afflicted with a terminal disease and have very limited treatment options to begin with.

Sincerely,
Alan Turpin
638 Silverman Drive
Collierville. TN 38017

901-854-0187

cc: The Honorable Bill Frist, M.D.
Senate Majority Leader
United States Senator from the great state of Tennessee

Commenter: Venook, Alan, MD
Organization: University of California, San Francisco

(Comment on next page)

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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ALAN P. VENOOK, M.D.
PROFESSOR OF CLINICAL MEDICINE
CHIEF, GASTROINTESTINAL ONCOLOGY
DIVISION OF HEMATOLOGY & ONCOLOGY

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VENOOK@CC.UCSF.EDU

March 10, 2003

Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave SW
Room 3l4G
Washington, DC 20201

Re: Medicare assessment of Oxaliplatin

Dear Mr. Scully:

I am writing to offer public comment on the Center for Medicare and Medicaid Services (CMS) review of the coverage of oxaliplatin. I hope that *this* letter will help inform the decision-making on this issue.

As an academic medical oncologist who has focused on the development of new and effective treatments for patients with colorectaI cancer, I am surprised by the decision to hold a National Coverage Determination (NCD) for oxaliplatin. This is not a matter of a me-too drug. While it is not dramatically effective in a great percentage of patients who have been previously treated with irinotecan, it is certain that there is some meaningful benefit in some patients in that setting. What's more, oxaliplatin appears to be very effective as initial therapy for colon cancer patients. The data strongly supports the utility of offering patients BOTH irinotecan and oxaliplatin, not one or the other.

This NCD is strikingly ironic considering the fact that the National Cancer Institute has put its weight behind a national study I am chairing. In CALGB #80203, two of the treatment arms will include oxaliplatin - a failure to cover this drug would substantially compromise the clinical and scientific integrity of this trial, which is designed to assess the additive value of a growth factor inhibitor.

While I fully support the CMS decision to carefully review the coverage of new drugs, some of which are of dubious value and merely represent scams to prolong industry profits, oxaliplatin is a bad test case. Patients will suffer the consequences!!

I assume that my letter is one of many suggesting that this determination is a mistake. While I appreciate the need for process, please also realize that the decision to hold a NCD has also inhibited Medicare patients from having insurance coverage for oxaliplatin, a gruesome and terrifying state of affairs for patients who stand to benefit from the drug.

I am happy to speak with you further if I can answer any questions.

Sincerely,

Alan P. Venook, M.D.
Professor of Clinical Medicine
University of California, San Francisco

Cc:

Jeffrey Shuren
JD Director, Division of Items and Devices
Center for Medicare and Medicaid Services
Mailstop: C1-09-06
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June 25, 2003

The Honorable Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Ave SW
Room 3140
Washington, DC 20201

Re: Medicare assessment of Oxaliplatin

Dear Mr. Scully:

I am writing to offer public comment on the Center for Medicare and Medicaid Services (CMS) review of oxaliplatin for the adjuvant treatment of patients with colon cancer. I hope that this letter will help inform the decision-making on this issue.

As an academic medical oncologist who has focused on the development of new and effective treatments for patients with colorectal cancer, it is a great pleasure to advocate for the implementation of new coverage policies because of newly effective therapies. Such is the case for oxaliplatin in patients with node-positive colon cancer.

For many years, the standard of care for node-positive (Stage III) colon cancer has been 5-Fluorouracil-based. By using such chemotherapy, the 5-year survival rate for Stage III patients approached 65%. Data just analyzed from the MOSAIC trial suggests that the use of oxaliplatin in combination with 5-fluorouracil (FOLFOX) Improves those outcomes.

The results from this European trial, although preliminary, are quite promising. The study was conducted as planned and the study arms were well-balanced. The control arm patients fared as would have been expected from prior studies. There was a 5% absolute improvement in 3-year Disease Free Survival with FOLFOX. While 3-years may not be an absolute indicator, it is an accepted clinical endpoint in prior and on-going adjuvant trials in numerous cancers. Patients will be followed through at least a 5-year end-point to confirm these findings. Importantly, this therapy was delivered with minimal acute toxicity and with a chronic neurotoxicity that persisted in only about 5% of patients.

Clearly, mature and complete data that has been peer-reviewed should remain the gold standard for decision-making and FOLFOX may not be the appropriate choice for many patients. However, this data is persuasive and change is important, since the application of FOLFOX in Stage III colon cancer patients could result in the cure of more than 2000 patients a year who would not have been cured with the current standard therapy.

I appreciate your consideration of my comments and am happy to speak with you further if I can answer any questions.

Sincerely,

Alan P. Venook, M.D.
Professor of Clinical Medicine
University of California, San Francisco

Cc: Gay W. Burton
Center for Medicare and Medicaid Services
Mailstop: C1-09-06
7500 Security Boulevard
Baltimore, MD 21244-1850

Commenter: Walsh, The Honorable James
Organization: House of Representatives

(Comment on next page)

JAMES T. WALSH
MEMBER OF CONGRESS
25TH DISTRICT, NEW YORK

ASSISTANT MAJORITY WHIP

CHAIRMAN
FRIENDS OF IRELAND

Congress of the United States
House of Representatives
Washington, DC 20515–3225

COMMITTEE ON APPROPRIATIONS
SUBCOMMITTEES:
VA, HUD,
AND INDEPENDENT AGENCIES
CHAIRMAN
AGRICULTURE,
RURAL DEVELOPMENT,
FOOD AND DRUG ADMINISTRATION,
AND RELATED AGENCIES
MILITARY CONSTRUCTION

April 14, 2003

Mr. Thomas Scully, Administrator
Centers for Medicare and Medicaid Services (CMS)
U.S. Department of Health and Hunan Services
200 Independence Avenue, SW
Washington, D. C. 20201

Dear Administrator Scully,

I am writing to express my concern over CMS's revised policy for approval of drug coverage after the FDA has already approved the same drug.

The case recently brought to my attention is for a new colorectal center product which as already been determined by the FDA to be "safe and effective" and now mid-process has been confronted with an additional set of criteria by CMS dictating that it must also be determined to be "clinically effective."

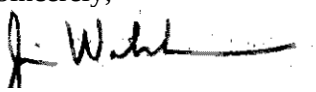
This change in procedure makes the playing field seemingly uneven with researchers not knowing when this additional application will be applied and then it won't. This in my view will also slow patient access to newer drugs.

CMS' recent decision to initiate a national coverage review of Eloxatin (oxaliplarin), a new drug for advanced colorectal cancer, is particularly troubling. Eloxatin received accelerated approval by the FDA last August for use as a second line colorectal cancer treatment where no other effective therapeutic option exists. Indeed, this approval and the demonstration of a highly significant survival advantage over standard treatment in first line colorectal cancer treatment prompted the National Comprehensive Cancer Network to rapidly modify its treatment guidelines for advanced colorectal cancer to recognize the advent of oxaliplaun.

As we all know, from many cancer battles, progress is often incremental – each advancement builds on the one that preceded it. I (we) hope that CMS speedily completes its review of and approves coverage of this new drug for this most vulnerable of patient population.

I would appreciate hearing from you on the rationale for this change in policy.

Sincerely,



James T. Walsh
Member of Congress

Commenter: Williamson, Stephen, MD
Organization: The University of Kansas Medical Center

(Comment on next page)

The University of Kansas Medical Center

Department of Internal Medicine
Division of Hematology/Oncology and
Bone Marrow Transplantation

March 12, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue, SW
Room 314G
Washington, DC 20201

Dear Mr. Scully:

I am writing to you in regards to Center for Medicare and Medicaid Services' (CMS) upcoming decision to determine whether Eloxatin TM (oxaliplatin for injection) is a reasonable and necessary drug for Medicare coverage purposes. This drug is definitely a reasonable and necessary drug for Medicare patients. In fact, I consider it the drug to use first line for metastatic colon and rectal cancer based on overall tolerability, response rate and improved survival. I am also concerned about the new reimbursement policy by CMS for the following reasons.

This new reimbursement policy by CMS is sending a negative message to cancer patients, oncologists and the research community that important new treatments approved by the Food and Drug Administration may not be available to all cancer patients who need them.

An adverse decision by CMS could result in the denial of Medicare coverage for Eloxatin and would be the first time in the U.S. that an FDA-approved cytotoxic agent was not covered by the Medicare program - indeed, a dangerous precedent.

Denying Medicare coverage for Eloxatin would adversely affect older Americans who are most likely to have a diagnosis of colorectal cancer. Restricting patient access would come at a time when the best chances for survival depend upon having a range of treatment options available. In this case, Eloxatin is an effective regimen for patients who have very few treatment options. These patients need a range of therapies to improve their chances of survival.

Hematology: 3901 Rainbow Blvd, Kansas City, KS 66160-7233 • (913) 588-6077 • FAX (913) 588-3996
Oncology: 3901 Rainbow Blvd, Kansas City, KS 66160-7353 • (913) 588-6029 • FAX (913) 588-4085

Eloxatin is an example of a new cancer therapy that addresses an unmet need. Used in combination with two other oncology drugs (5-fluorouracil and leucovorin), Eloxatin is used to treat patients with advanced colorectal cancer who otherwise would have no treatment options.

The availability of more than one effective regimen for advanced colorectal cancer may be the start of a sea change in the treatment of the disease, similar to the changes in how breast and ovarian cancers are now treated. CMS policy should support these advances to ensure that all cancer patients under Medicare have the best chance of fighting their cancer.

CMS's action could discourage research if promising drugs are ultimately denied coverage and reimbursement.

Because of the prevalence of colorectal cancer in this country, the potential impact of a CMS decision denying or restricting coverage of Eloxatin would be significant. Each year, more than 150,000 Americans are diagnosed with colorectal cancer and 56,000 die of the disease. Of these individuals, 27 percent are treated in a hospital setting and would be affected by this CMS policy.

I have treated over 25 patients with this new drug. I have found that the drug is much better tolerated than the alternative therapy employing irinotecan. The irinotecan containing regimen results in severe diarrhea in over 30% of patients of which at least 50% are hospitalized for this complication. I have not had any of my patients who have received the oxaliplatinum regimen have to be hospitalized due to a complication of the drug regimen. In addition, more patients respond favorably to the drug with a longer duration of survival. I just cannot imagine not being able to offer this drug to my Medicare patients.

I have no stock in Sanofi-Synthelabol or other potential financial conflicts of interest. I have participated in clinical trials with this agent.

I trust that you will make the right decision for our patients.

Thank you,

Stephen K. Williamson, MD
Professor of Medicine
Director, Division of Hematology/Oncology

CC:

Jeffery Shuren
JD Director
Division of Items and Devices
Centers for Medicare & Medicaid Services
7500 Security Blvd.
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Poppy S. Kendall, MHS
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Commenter: Yee, Sharon, MD
Organization: Hematology/Medical Oncology

(Comment on next page)

Sharon J. Yee, M.D., F.A.C.P.
Richard A. Shapiro, M.D. and Benjamin T. Stafford, M.D.

Board Certified In:
Internal Medicine Hematology
& Medical Oncology

March 11, 2003

Mr. Thomas A. Scully
Administrator
Centers for Medicare and Medicaid Services
200 Independence Avenue, S
Room 3140
Washington, DC 20201

Dear Mr. Scully:

As a physician treating patient~ with advanced metastatic colon carcinoma over the past fifteen years, I am urging you to allow the coverage of Eloxatin for therapy in patients with metastatic colon carcinoma.

I have had extensive experience with Eloxatin in the treatment of patients with metastic colon carcinoma. It is an extremely safe and effective drug in this devastating disease. It is well tolerated and allows patients with far advanced colon cancer a longer survival. These patients are fighting for their lives and the additional months of survival means a great deal to them and their loved ones.

The CMS new reimbursement policy is conveying a negative message to cancer patients and the oncology community that new drugs approved by the FDA may not be available to the patients who need them. I have had patients attempt to get the drug in South America and Mexico where it had been approved years before it was approved by the FDA in August 2002.

An adverse decision by CMS could result in the Medicare denial for Eloxatin and would be the first time in the US that an FDA approved cytotoxic agent was not covered by the Medicare program, setting a dangerous precedent.

There are very few treatment options for patients with advanced metastatic colon carcinoma and Eloxatin fills an unmet need in this group of older Americans. Prior to the approval of Eloxatin, we only had 3 oncology drugs available for use.

Colon carcinoma is one of the most prevalent cancers in this country. The potential impact of a CMS decision in either denying or restricting coverage of Eloxatin would be significant. Each year, more than 150,000 Americans are diagnosed with colorectal cancers and 56,000 die from this disease. Of these, 27 percent are treated in a hospital setting and would be affected by tbis CMS policy.

Mr. Scully, I urge you to evaluate Eloxatin as a new therapeutic options for use in patients with metastatic colorectal cancers.

Thank you for your time and attention.

Sincerely yours,

Sharon J. Yee, MD., FACP
Hematology/Medical Oncology

Cc: Jeffrey Shuren
JD Directory
Division of Items and Devices
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