

United States Senate

SPECIAL COMMITTEE ON AGING

WASHINGTON, DC 20510-6400

(202) 224-5364

October 9, 2009

Ms. Charlene Frizzera
Acting Administrator
Centers for Medicare and Medicaid Services
7500 Security Blvd
Baltimore, MD 21244

Dear Ms. Frizzera:

The Senate Special Committee on Aging, which I chair, has a responsibility to safeguard the health and financial interests of seniors and the elderly when it comes to the cost and availability of medications, especially expensive, breakthrough medical treatments. It is with those goals in mind that I write regarding the Committee's serious concern about the Centers for Medicare and Medicaid Services' (CMS) recent change in reimbursement coding rules for a widely-used, highly effective, and modestly priced treatment for age-related macular degeneration (AMD), a common cause of blindness in the elderly.

The ophthalmologic and retinal specialist communities have informed Committee staff that at least half of their members nationwide are using Genentech's biologic drug, Avastin, off-label to effectively treat their patients for wet macular degeneration and other intraocular disease conditions. The cost of these treatments is modest (approximately thirty to fifty dollars per treatment) which can be prepared and packaged in relatively tiny amounts by pharmacy compounding firms at a small additional cost.

It should be noted that another biologic, Lucentis, also manufactured by Genentech, also is a highly-effective and deservedly oft-praised treatment for macular degeneration, which has been widely used since mid-2006 when the Food and Drug Administration (FDA) approved its use. Unfortunately, Lucentis, priced at approximately twenty times as much as Avastin at \$2,000 a dose retail, is costing Medicare more than a billion dollars a year in federal reimbursements, according to information that CMS previously supplied to the Committee.

CMS also informed the Committee last year that federal reimbursements for Lucentis might eventually increase to as much as three billion dollars a year. Further, Medicare beneficiaries' copayments can reach several thousand dollars for Lucentis, and multiple treatments often are required. For many seniors, these copayments are unaffordable.

The Committee has received complaints from a variety of medical authorities and advocates that the new coding system CMS implemented on October 1 would reduce federal reimbursements to physicians for Avastin to a small fraction of the previous reimbursement rate. This will make it more difficult for physicians to recoup a fair share of the comparatively modest costs associated

with Avastin. I believe the change has the potential to cost Medicare substantial sums as physicians switch to the \$2,000 a treatment cost for Lucentis.

As Dr. Richard Bazarian, a vitreo-retinal surgeon from Portland Maine, expressed in a letter to the *New York Times* on October 7, in response to the *Times*' story on the coding change: "I offered patients a choice of Avastin or Lucentis, sometimes remarking that Avastin is the socially responsible way to treat wet age-related macular degeneration. Many would heed the call to rein in costs and choose the less expensive drug ... Today, an average day in my office, of 14 patients to be treated, 8 were scheduled for Avastin and 6 for Lucentis. When shown your article, all agreed to change to Lucentis. While they would like to be socially responsible, they don't want to see their physician lose money on their treatment."

The scientific or regulatory reasons for this policy change are not readily apparent. The FDA has not discouraged the off-label use of Avastin for intraocular purposes. To the contrary, the agency has informed the Committee that it regards Avastin as having roughly the same safety profile as Lucentis for intraocular use.

Moreover, internal FDA communications obtained by the Committee's Majority staff reveal that the FDA had encouraged Genentech to seek formal FDA approval of Avastin for intraocular uses, since there is substantial clinical data available documenting its safety and efficacy. To date, the company has declined to do so since it also manufactures the competing biologic drug, Lucentis, which is producing billions of dollars in annual revenues, much of it from federal health care program reimbursements.

I am also disturbed to learn from members of the medical eye care community that Genentech may have communicated directly with CMS officials about this proposed coding change, reportedly suggesting that CMS was over-paying for the small amounts of Avastin being used off-label for intraocular treatments. Last year, media reports related the Committee's concerns with Genentech's aggressive efforts to unilaterally discourage the use of Avastin for off-label intraocular uses. The proposed restriction of Avastin by Genentech caused considerable consternation among ophthalmologists, retinal specialists, and pharmacy compounders across the country concerned about the expense to their patients and the health care system.

The enclosed Associated Press article from August 2008 highlights Genentech's actions in refusing to cooperate with, or declining to donate free or discounted drugs to the taxpayer-funded, fifty-million dollar "CATT" clinical trial, sponsored by the National Institutes of Health, comparing the safety and efficacy of Avastin and Lucentis for intraocular uses. This was despite repeated pleading from health and research officials, and the company's earlier promises of cooperation. The Committee was recently informed that the sponsors of the clinical trials should have findings by early 2011.

Since there is such well-established, widespread, accepted use of Avastin off-label for intraocular treatments by reputable eye care specialists—without objection by FDA—I requested in a letter dated October 18, 2007 (enclosed) that CMS consider what applicable legal and regulatory authorities it might employ to encourage more physician usage of the much cheaper Avastin, in order to possibly save Medicare billions of dollars in taxpayer funds now spent on Lucentis.

I am concerned that the recently announced coding changes will make reimbursements for intraocular Avastin even more difficult and less attractive to the many physicians and eye surgeons who wish to use it for their patients as a much more affordable treatment.

I request that the appropriate CMS personnel promptly brief Committee staff on this coding change, the reasons for its initiation, and the agency's responses to those medical professionals who have requested that this decision be reconsidered or rescinded. The agency also should be prepared to relate any involvement by or contacts with Genentech representatives relating to CMS's coding decision, or policy considerations arising from it.

Documentation, as described by the attachment to this letter, should be provided in advance of the briefing to the Committee staff, including any and all written memos, notes, e-mails, letters, and records of telephone conversations pertaining to Genentech (or its contractors) and this coding change.

Please arrange to brief the Committee staff by no later than October 23, 2009. Any questions about this request may be directed to Jack Mitchell of the Committee staff at (202) 224-0741 or Jack_Mitchell@aging.senate.gov Thank you for your attention to this matter.

Sincerely,

A handwritten signature in black ink that reads "Herb Kohl". The signature is written in a cursive, slightly slanted style.

Herb Kohl

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SPECIAL COMMITTEE ON AGING

WASHINGTON, DC 20510-6400

(202) 224-5364

October 18, 2007

Kerry Weems
Acting Administrator
Centers for Medicare and Medicaid Services
Hubert H. Humphrey Building
200 Independence Avenue, SW, Room 314G
Washington, DC 20201

Dear Acting Administrator Weems:

As Chairman of the Special Committee on Aging (Committee), I take very seriously the Committee's responsibility to protect and advocate on behalf of our nation's seniors. Part of this responsibility is ensuring that seniors are receiving appropriate and cost-effective prescription drugs.

Therefore, I read with great interest an October 12, 2007 Wall Street Journal article entitled "Genentech to Limit Avastin Availability, Use of Cancer Treatment For Eye Ailment Hurts Sales of Targeted Drug." The article detailed Genetech Inc.'s plan to stop making its cancer drug Avastin available to certain pharmacies. Most troubling about this proposed plan is the fact that it may be due in part to an effort to boost sales of a chemically similar, yet far more expensive drug- Lucentis. The article specifically states:

"Medicare, which offers health coverage for the elderly and disabled and is a big purchaser of the two drugs, has said curbing Avastin could cost taxpayers \$1 billion to \$3 billion a year. Using a cheaper drug not only would preserve Medicare funds, but would trim beneficiaries' exposure to high co-payments, program administrators say."

Any instance that could cost taxpayers potentially one to three billion dollars is of great concern to me. This past June an ophthalmologic surgeon representing Physicians for Clinical Responsibility (PCR) testified before the Committee at a hearing I chaired examining the pharmaceutical industry's influence on physicians and their prescribing behaviors. This physician related to my Committee staff troubling, detailed information regarding Genentech's refusal to allow further studies on the use of Avastin in combating many serious eye ailments- including wet macular degeneration- many of which occur primarily in the elderly.

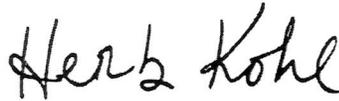
Understanding that approval of drugs for particular uses falls within the jurisdiction of the Food and Drug Administration; I am writing today to inquire what

CMS is doing to examine and address this potential cost to the taxpayers. More specifically:

- 1.) How much has Medicare spent on Lucentis and Avastin during the period 2005- present?
- 2.) What measures, if any, have CMS officials taken to explore the reduction of expenditures on expensive drugs such as Lucentis by using alternative treatments such as Avastin?

I'm sure that you agree with me that saving Medicare dollars and more importantly tax payer dollars should be of the utmost priority. I look forward to receiving your response by November 2, 2007. Should you have any questions regarding this matter, feel free to contact Jack Mitchell or Cecil Swamidoss of my staff on 202-224-5364.

Sincerely,

A handwritten signature in black ink that reads "Herb Kohl". The signature is written in a cursive, slightly slanted style.

Herb Kohl
Chairman

Study outcome won't sway company on eye drug

By KEVIN FREKING, Associated Press Writer, August 27, 2008

WASHINGTON - What does a company do when there's anecdotal evidence that two of its drugs are equally effective in treating a leading cause of blindness in the elderly, one costing patients \$60 per treatment and the other \$2,000?

In the case of Genentech Inc., nothing.

The company declined to seek federal approval for the cheaper drug, Avastin, to treat the wet form of age-related macular degeneration. Nor would it help finance — or cooperate with — a National Eye Institute study comparing the effectiveness and safety of Avastin, a cancer drug, and the more expensive eye drug, Lucentis.

The financial stakes stemming from the study are huge. Medicare officials estimate there could be 50,000 or more additional cases of macular degeneration a year. Treating just one year's worth of new patients with Lucentis would cost \$1.2 billion a year, compared with \$60 million if they're treated with Avastin, Medicare officials said.

Genentech is making no promises that it will act upon the trial's final results, which are expected in two to three years.

The company has raised concerns that safety issues were not properly addressed. In particular, the trial doesn't have enough patients to show some of the rare but serious side effects that could occur with use of the cheaper drug, the company contends.

"No matter the outcome, we continue to believe Lucentis is the most appropriate treatment for wet AMD," said Krysta Pellegrino, a company spokeswoman.

Wet AMD occurs when abnormal blood vessels leak blood and fluid affecting the part of the eye that allows you to see fine detail.

Many eye doctors believe Avastin works just as well in treating macular degeneration even though it hasn't been approved for that purpose. It's not unusual for drugs to be used off-label — treating diseases other than ones the drug was approved for.

Both drugs target a protein that causes blood vessels in the back of the eye to grow, but Lucentis is a much smaller molecule. It was specifically designed — at great expense — to penetrate the retina.

Companies routinely help finance clinical trials, but such trials almost never pit two products from the same company against each other.

"It's a very unusual situation where a company would be trying to compare its own drugs," said Dr. Frederick Ferris, director of clinical research at the National Eye Institute. "I'm not sure usual situations are all that relevant in this particular case."

Still, health officials pleaded with Genentech to participate in the clinical trial comparing the two drugs. At one point the company considered doing so by providing the medicines in masked, identical vials, according to e-mail exchanges obtained by the Senate Aging Committee.

"Good news is that the Board supports the proposed studies," said one e-mail sent in June 2007 from Charlie Johnson, a company vice president, to Dr. Daniel Martin, the chairman of the study who works at the Emory University School of Medicine.

In the end, the board did not support the study. Martin made a final plea.

"The fact that we are comparing your drugs and you are not involved is very awkward and can easily give way to anti-Genentech sentiments," Martin said. "The leaders of this study are only interested in answering the many scientific and patient management questions that we face with our patients every day, but some investigators and the press want this study to be more than that. Your involvement would be very helpful to both of our causes."

Genentech routinely provides financial support for clinical trials, Pellegrino said in an interview. But in this case, she said, "Our resources would be better spent looking at other diseases where there are no treatments.

Dr. Philip Rosenfeld, who has treated hundreds of his eye patients in South Florida with Avastin, said Genentech had little economic incentive to help finance the trial — unless it was confident Lucentis was truly superior.

"By fact that they didn't support the clinical study leads me to conclude that in reality there is no difference between the two drugs," Rosenfeld said. "The result is clearly not in Genentech's best interest."

Avastin was approved to treat colon cancer in February 2004. It's a genetically engineered product that inhibits the growth of blood vessels, thus denying tumors blood, oxygen and other nutrients needed for growth. It's expensive, costing \$2,200 for a typical treatment for colon cancer. However, for treating eye disease, pharmacy compounding firms split the drug into many tiny doses suitable for injection into the eye. That's what brings the price down to about \$60 per injection.

Rosenfeld said the study could put doctors at ease about potential litigation if they prescribe Avastin instead of the FDA-approved drug.

"I see this as a public health study, not only for us, but for the whole world. It gives everyone the license to use both drugs interchangeably," Rosenfeld said. "Clearly, for Medicare it would make economic sense to put preference on the use of Avastin.

As lawmakers await the results of the trial, they are already considering what steps, if any, could be taken to steer the Medicare program to the less costly drug — if it's indeed comparable.

An internal memorandum from congressional aides to the Senate Aging Committee's chairman, Herb Kohl, D-Wis., recommends that lawmakers consider urging Medicare officials to pay no more for one drug than the other when it comes to treating the eye disease.

Medicare's contractors already have authority to pay the same amount for items that achieve much the same result — such as hormones used to treat prostate cancer.

If the drugs are shown to work comparably, "it would surprise me if the contractors did not quickly use that concept," said Dr. Steve Phurrough, director of coverage and analysis at the Centers for Medicare and Medicaid Services.

Pellegrino said it's too early in the comparison trial to comment about the staff's recommendation.

Pellegrino said Genentech's pricing for Lucentis reflects the cost of developing the drug, which the FDA approved in June 2006. The development program included a clinical trial involving more than 6,000 patients at a cost of more than \$45,000 a patient.

"It took decades and hundreds of millions of dollars to develop the drug," she said.

On the Net:

Senate Aging Committee: <http://www.senate.aging.gov>

Genentech: <http://http://www.genentech.com>

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