United States Senate
Committee on Finance

Sen. Chuck Grassley · Iowa
Ranking Member

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For Immediate Release
Thursday, April 3, 2008

Grassley questions increases in drug maker rebates to physicians prescribing anti-anemia drugs

WASHINGTON — Senator Chuck Grassley is asking Amgen Inc. to account for notably high rebates to some physician groups for purchasing the prescription drug Aranesp, an anti-anemia therapy given to kidney and cancer patients.

In a letter sent to the drug maker today, Grassley describes data he obtained through an earlier inquiry and requests additional information about Amgen's drug rebate and discount calculations. "The information raises questions," he said. "Some oncology practices in some states are receiving unusually high rebates for purchasing Aranesp. These trends underscore the need for greater transparency in the financial relationships between drug makers and doctors. Patients deserve to know what's going on as they make decisions about their health and safety based on the advice of their doctors."

Last year Grassley sought to increase access by the Food and Drug Administration to drug study results for anti-anemia drugs. Last month, an FDA advisory committee recommended more limited use of anti-anemia drugs due to safety concerns.

The text of the letter he sent today, along with last year's inquiry, follows here.

April 3, 2008

Mr. Kevin W. Sharer
Chairman, Chief Executive Officer and President
Amgen Inc.
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

Dear Mr. Sharer:

The United States Senate Committee on Finance (Committee) has jurisdiction over the Medicare and Medicaid programs. Accordingly, the Committee has a responsibility to the more than 80 million Americans who receive health care coverage under those programs to oversee

the proper administration of the programs and ensure that taxpayer and beneficiary dollars are appropriately spent on safe and effective drugs and devices.

Last May, I wrote to you regarding a New York Times article that doctors were profiting through rebates they received from purchasing erythropoiesis-stimulating agents (ESA) directly from Amgen, Inc. (Amgen) and then collecting payments from Medicare and private insurers, often above the price they paid for the drugs. Three weeks ago, during the Oncologic Drugs Advisory Committee discussion of the safety of ESAs, the panelists raised concerns that ESAs may be doing more harm than good in patients with certain cancer types and questioned whether or not Amgen's practice of discounting the price of its drugs for doctors who buy large quantities of ESAs may be encouraging overuse of these drugs.

As part of the Committee's inquiry into the potential impact of pricing practices on the utilization of ESAs, I sent a letter in August requesting that Amgen provide information regarding rebate payments/discounts to physicians, group practices, and others who purchased Aranesp and/or Epogen. A review of the information provided by Amgen raises some questions regarding the rebate arrangements between Amgen and physicians/group practices.

According to Amgen, almost $800 million in rebates were paid in calendar 2006 to more than 6000 facilities, including group practices, hospital inpatient and outpatient departments, home health agencies and skilled nursing facilities. About 80 percent of that total went to physicians, group practices, and physician clinics. In addition, with the exception of three states, the total amount of rebates paid to facilities in each state increased each year from calendar year 2004 through calendar year 2006, in some cases doubling in total amount.

For example, about 90 facilities in Alabama received about $7 million in total amount of rebates for Aranesp in calendar year 2004. That amount increased to more than $17 million to about 100 facilities in calendar year 2006-an increase of about $10 million. Similarly, the total amount in rebates paid to facilities in South Carolina almost doubled from more than $7.5 million to about 70 facilities in calendar year 2004 to more than $14.5 million to about 80 facilities in calendar year 2006.

When one examines the five group practices/physician clinics that received the most rebates from Amgen during calendar years 2004-2006 in a specific state, some of the payments to the same group practices also increased over time. For example, in Alabama the rebates to one cancer center more than doubled over the three-year period from $1.3 million in calendar year 2004 to almost $2 million in calendar year 2005 to more than $3 million in calendar year 2006. Based on information provided on the center's Website, there are about 10 oncologists on staff, which translates to about $300,000 in rebates per oncologist in calendar year 2006.

In Indiana, more than $15 million in rebates were paid to about 220 facilities in calendar year 2004, more than $27 million in 2005, and more than $34 million in 2006. Rebates to one 5-physician practice increased from more than $500,000 in calendar year 2004 to almost $1.3 million in calendar year 2006. Rebates to another group practice increased more than fourfold from about $1.5 million in calendar year 2004 to about $6.5 million in calendar year 2006. According to that practice's Website, there are about 10 oncologists on staff, which translates to

about_$650,000 in rebates per oncologist in calendar year 2006.

I have cited only a few examples in this letter, but based on the information submitted by Amgen, it seems that group practices/physician clinics in some states are receiving significant amounts of rebates for purchasing Aranesp. To understand what accounts for these rebate totals, I would appreciate a discussion of the factors that are considered in determining the rebates/discounts Amgen pays to physicians, group practices, and physician clinics. For example, do the rebates/discounts take into account the purchase of another drug and/or other product(s) from Amgen or are rebates related to amounts purchased in certain time frames? Please also describe any factors specific to individual states that may impact Amgen's rebate/discount calculations.

Thank you in advance for your continued cooperation and assistance.

Sincerely,
Charles E. Grassley
United States Senator
Ranking Member of the Committee on Finance

For Immediate Release
Wednesday, May 16, 2007

Grassley seeks to empower FDA to access drug-risk information from drug makers

WASHINGTON — Sen. Chuck Grassley wants to make sure drug makers fully disclose data from their drug studies to the Food and Drug Administration, and he's asking the drug-safety agency if it needs new power to collect such information and a major drug maker to account for how it handled requests from the FDA for information about anti-anemia drugs given to kidney and cancer patients.

In letters sent this week, Grassley has asked the FDA to identify any new tools it might need to gain access to necessary information from drug makers. He also has asked Amgen to respond to allegations that it limited FDA access to the results of company studies and did not provide complete responses to the agency's requests for data.

"The Senate has already passed its FDA revitalization legislation, but the House of Representatives hasn't acted yet, so there's still time for congressional leaders to consider new and important measures to strengthen the hand of the FDA in looking out for American consumers," Grassley said. "There could be important lessons to learn from this particular case, and since Congress doesn't act very often on FDA legislation, so we ought to focus on what happened in a very time-sensitive way."

Amgen is the maker of erythropoisesis-stimulating agents, which are used for the treatment of anemia in patients with chronic kidney failure as well as chemotherapy-induced

anemia. Last week an FDA advisory panel recommended that more information should be provided about the risks of these drugs and new studies should be conducted to assess the drugs' safety. In addition, news organizations reported assertions that Amgen had not provided study data to the FDA upon request and had not been up front about safety risks.

Last month, Grassley asked the Centers for Medicare and Medicaid Services to address reimbursement and drug safety concerns related to the use of these anti-anemia drugs. Grassley said he has received a preliminary response to this inquiry and will continue to pursue a payment policy that guards both tax dollars and patient safety.

The text of Grassley's letters to the FDA, Amgen and CMS follows here.

May 16, 2007

The Honorable Andrew C. von Eschenbach, M.D.
Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Commissioner von Eschenbach:

The United States Senate Committee on Finance (Committee) has jurisdiction over the Medicare and Medicaid programs and, accordingly, a responsibility to the more than 80 million Americans who receive health care coverage under those programs to oversee the proper administration of the programs, including the payment for prescription drugs regulated by the Food and Drug Administration (FDA).

Last Thursday, FDA's Oncologic Drugs Advisory Committee (Advisory Committee) met to discuss the use of erythropoiesis-stimulating agents (ESAs) in cancer patients. As you know, the Advisory Committee recommended new restrictions on prescribing information for ESAs and additional clinical trials to assess the drugs' safety in light of reports of increased risk of cardiovascular disease, tumor growth, and even death associated with higher than recommended doses of the drugs.

I read with great concern the Los Angeles Times article, dated May 11, 2007, which noted that some members of the Advisory Committee suggested that Amgen Inc. (Amgen), manufacturer of the ESAs, Aranesp, Epogen and Procrit, the latter of which is marketed by Ortho Biotech Products, L.P., a subsidiary of Johnson & Johnson, "was not being upfront about all the drug's risks." What further troubled me was a Bloomberg article, also dated May 11, 2007, which reported that that the FDA was given limited access to results from company studies and Amgen did not provide complete responses to the FDA's requests for data. This troubles me because the FDA cannot do its job well if it lacks complete and accurate information.

According to Bloomberg, Amgen responded that academic researchers often do not make

full results available to the FDA. Through my investigations, I also have learned that there are certain types of information that manufacturers are not required to provide to the FDA, although they may submit such information voluntarily. However, FDA should have access to any data or information that is relevant to its assessment of the safety and efficacy of a drug.

In other letters to you, I have emphasized the importance of providing FDA's advisory committees with the relevant and truthful information they need to perform their advisory function. It is even more essential that the FDA works with a full deck of cards because it decides what safety actions to take based on the data and information available to the agency.

In light of the concerns raised during the Advisory Committee meeting on ESAs, it appears that the FDA may need tools that will enable the agency to obtain access to additional data and information from manufacturers so that informed decisions can be made about a drug's safety and efficacy. The U.S. Senate passed the Food and Drug Administration Revitalization Act last week, but the House of Representatives has not yet acted, which gives Congressional leaders another opportunity to consider new and important measures to strengthen the hand of the FDA in looking out for American consumers.

Accordingly, I am requesting that the FDA arrange a meeting with my Committee staff by no later than May 31, 2007, to discuss ways to ensure that the FDA receives all of the relevant and truthful information that it requires to perform its duties. Please have your staff prepared to discuss FDA's data needs and the issues and concerns raised in this letter. In particular, they should be prepared to respond to the following questions:

1. What data or information that is not already available to the FDA does the agency believe should be available for purposes of evaluating a drug's safety or efficacy or the integrity of the data that is submitted to the FDA?

2. Please describe the type(s) of data that the FDA requested from Amgen regarding ESAs and discuss the manufacturer's explanation for not providing that data to the FDA and submitting incomplete responses. What is the relevance of the data to FDA's assessment of the safety of ESAs?

3. The FDA announced that its Cardiovascular and Renal Drugs Advisory Committee would meet this fall to discuss the safety of ESAs in the ESRD setting. Given the reported incomplete responses to the FDA's data request, do you anticipate similar problems with obtaining data from the manufacturer for the Cardiovascular and Renal Drugs Advisory Committee meeting?

4. Last month, the Wall Street Journal reported that Amgen may have promoted use of Aranesp and Epogen to improve a patient's quality of life and that the manufacturer had conducted some studies in that area. When did the manufacturer inform the FDA of those studies? Has the FDA requested data from the manufacturer regarding those studies, and if so, has the manufacturer submitted the data as requested to the FDA?

I look forward to your cooperation and assistance on this important matter. Please have

your staff contact my Committee staff to schedule a meeting.

Sincerely,
Charles E. Grassley
Ranking Member
Committee on Finance

May 16, 2007

Mr. Kevin Sharer
Chairman, Chief Executive Officer
and President
Amgen Inc.
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

Dear Mr. Sharer:

The United States Senate Committee on Finance (Committee) has jurisdiction over the Medicare and Medicaid programs and, accordingly, a responsibility to the more than 80 million Americans who receive health care coverage under those programs to oversee the proper administration of the programs, including the payment for prescription drugs regulated by the Food and Drug Administration (FDA).

Last Thursday, FDA's Oncologic Drugs Advisory Committee (Advisory Committee) met to discuss the use of erythropoiesis-stimulating agents (ESAs) in cancer patients. As you know, the Advisory Committee recommended new restrictions on prescribing information for ESAs and additional clinical trials to assess the drugs' safety. In addition, on May 14, 2007, the Centers for Medicare and Medicaid Services (CMS) released its proposed coverage decision memorandum regarding the clinical conditions for Medicare reimbursement for ESAs.

Several news articles have raised concerns not only about Medicare's payment system creating incentives for using higher doses of ESAs than are necessary, but also the impact of marketing and supply contracts between ESA manufacturers and dialysis providers on the utilization of ESAs. The Wall Street Journal reported that Amgen Inc. (Amgen) may have promoted the use of Aranesp and Epogen for improving a patient's quality of life without sufficient evidence for the claim. The New York Times reported on profits that doctors make through rebates they may receive from purchasing the drugs from Amgen and Johnson & Johnson and collecting payments from Medicare and private insurers, which are often above the purchase price.

In addition, I read with great concern the Los Angeles Times article, dated May 11, 2007, which noted that some members of the Advisory Committee suggested that Amgen "was not being upfront about all the drug's risks." What further troubled me was a Bloomberg article, also dated May 11, 2007, which reported that the FDA was given limited access to results from

company studies and Amgen did not provide complete responses to the FDA's requests for data. It is essential that the FDA receive complete and accurate information in order for the agency to take appropriate and timely actions in response to emerging safety concerns.

Accordingly, I am requesting that Amgen arrange a briefing for my Committee staff by May 31, 2007, to discuss the issues and concerns that have been reported in the media over the last several weeks regarding the marketing and safety of ESAs. In addition, please be prepared to address the following questions:

1. Please describe the type(s) of data that the FDA requested from Amgen. Were the data related to the safety and/or efficacy of the ESAs?

2. Did Amgen provide complete responses to FDA's data requests? If not, please provide an explanation for submitting incomplete responses.

3. In its proposed coverage decision memorandum, CMS expressed concern that a number of trials of ESA treatment have been terminated, suspended, or otherwise not completed. Has Amgen sponsored any trials of ESA treatment that have been terminated, suspended, or otherwise not completed that showed evidence of serious adverse effects? If so, have the results from those trials been made available to the FDA? If not, please explain why study results were withheld from the FDA.

4. On April 10, 2007, The Wall Street Journal reported that Amgen conducted some studies related to the use of Aranesp and Epogen to improve a patient's quality of life. When did Amgen inform the FDA of those studies? Has the FDA requested data regarding those studies? If so, did Amgen submit the data as requested?

5. The Wall Street Journal also reported $500 million a year in sales from doctors who prescribed Aranesp "off label" to treat anemia in cancer patients who were no longer receiving chemotherapy. In light of the increased risk of serious adverse effects, including death, associated with the use of ESAs in this patient population, what actions, if any, has Amgen taken to ensure that doctors and patients are informed of the new safety risks?

Any documents responsive to the issues and questions to be discussed at the briefing should be sent to the Committee prior to the briefing via electronic transmission in PDF format. In cooperating with the Committee's review, no documents, records, data or information related to these matters shall be destroyed, modified, removed or otherwise made inaccessible to the Committee.

I look forward to your cooperation and assistance on this important matter. Thank you in advance for providing the name and contact information, including an e-mail address, for a person who will act as the point of contact for Amgen during the Committee's review by no later than May 22, 2007.

Sincerely,

Charles E. Grassley
United States Senator
Ranking Member of the Committee on Finance

April 10, 2007

Leslie Norwalk
Acting Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Acting Administrator Norwalk:

The United States Senate Committee on Finance (Committee) has jurisdiction over the Medicare and Medicaid programs and, accordingly, a responsibility to ensure that drugs and services provided to the 80 million beneficiaries of these programs are safe and effective and are purchased in a fiscally responsible manner.

The Centers for Medicare and Medicaid Services (CMS) is responsible for making coverage determinations for a wide variety of drugs, biologics, devices, and medical services. One of the most significant expenditures within the Medicare program is for end-stage renal disease (ESRD) related care. ESRD spending accounted for nearly $7.9 billion of total Medicare spending in 2005. One of the central services within the ESRD program is the administration of erythropoiesis-stimulating agents (ESAs) for the treatment of anemia in patients with chronic kidney failure. Outside of the ESRD program, Medicare and Medicaid also make significant expenditures on ESAs for chemotherapy-induced anemia in cancer patients. According to the Government Accountability Office (GAO), Medicare spent $2 billion in 2005 for Epogen alone, an ESA manufactured by Amgen, Inc. (Amgen). Amgen also manufactures two other ESAs, Aranesp and Procrit, the latter of which is marketed by Ortho Biotech Products, L.P., a subsidiary of Johnson & Johnson.

Although ESAs have improved the quality of life for thousands of kidney patients, the GAO report cites concerns that the Medicare payment system has created incentives for using more doses of ESAs than are necessary. Medicare pays one rate for dialysis and other ESRD services; however, it pays for ESAs separately on a per service basis. According to the GAO, bundling all ESRD drugs and services under a single rate would encourage more prudent use of ESAs. The Medicare Payment Advisory Commission (MedPAC) also recommends that payment be bundled to control costs and promote quality care. In addition, MedPAC has recommended implementation of a quality incentive payment policy for providers of outpatient dialysis services.

An overuse or inefficient use of ESAs is not only a financial concern to the Committee, but also a major patient safety concern. I am troubled by the findings in recent clinical studies of

increased risks of death, blood clots, strokes, heart attacks, and tumor growths when ESAs are given in higher than recommended doses. As a result of these studies, on March 9, 2007, the FDA issued a public health advisory to inform doctors and patients of the new safety information regarding Aranesp, Epogen, and Procrit. Furthermore, the product labeling for ESAs have been revised to include new warnings and modifications to the dosing instructions.

Accordingly, I am requesting that CMS arrange a briefing for my Committee staff by no later than April 27, 2007, to address the following questions, among other things:

1. In light of new warnings from the FDA regarding ESAs, CMS announced that it would closely review all Medicare policies related to the administration of ESAs. What is the status of CMS's review and what specific actions are being considered to ensure the safety of Medicare and Medicaid beneficiaries and prevent the overuse of ESAs?

2. Medicare Part B currently requires that physicians report hemoglobin or hematocrit levels for certain chronic kidney disease patients, but not for cancer patients. Section 110 of the Tax Relief and Health Care Act of 2006 requires that all Part B claims submitted for drugs that are furnished to individuals on or after January 1, 2008, in connection with chemotherapy include the hemoglobin or hematocrit levels for those individuals. What is the status of implementation of this new requirement?

3. On April 1, 2006, CMS implemented a national monitoring policy for use of ESAs in Medicare beneficiaries with ESRD. According to information posted on CMS's website, the previous methodology for monitoring ESA claims "was implemented with limited scientific analysis." What was the scientific support for CMS's current monitoring policy? Did CMS consider the funding source of the studies and/or other scientific support upon which the agency relied in developing the current monitoring policy? Did CMS review the validity and impartiality of the scientific evidence?

4. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 required CMS to issue a report and conduct a demonstration of a system for bundling payment of ESAs with other ESRD items and services under a single rate. CMS's report was due in October 2005, but according to GAO testimony dated December 6, 2006, both the report and the demonstration testing of the feasibility of a bundled rate have been delayed. What is the status of the report and demonstration? What are the reasons for the delays?

Thank you for your prompt attention to this matter.

Sincerely,
Charles E. Grassley
United States Senator
Ranking Member of the Committee on Finance