

United States Senate  
**Committee on Finance**  
Washington, D.C. 20510

For Immediate Release

Wednesday, May 30, 2007

Grassley seeks additional information about pricing and marketing of anti-anemia drugs

WASHINGTON --- Sen. Chuck Grassley is asking a leading drug maker to cooperate with his ongoing inquiry into the pricing and marketing of anti-anemia drugs given to kidney and cancer patients and the Food and Drug Administration's access to data from the drug maker's studies of such drugs.

The text of the letter Grassley sent today to Johnson & Johnson is below, along with the text of inquiries he made earlier this month and in April of the Food and Drug Administration, Amgen Inc. and the Centers for Medicare and Medicaid Services.

Grassley is Ranking Member of the Senate Committee on Finance.

May 30, 2007

Mr. William C. Weldon  
Chairman and Chief Executive Officer  
Johnson & Johnson  
One Johnson & Johnson Plaza  
New Brunswick, NJ 08933

Mr. Joaquin Duato  
President  
Ortho Biotech Products, L.P.  
430 Route 22 East  
P.O. Box 6914  
Bridgewater, NJ 08807-0914

Dear Messrs. Weldon and Duato:

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 beneficiaries receive drugs that are both safe and effective.

On May 10, 2007, the Food and Drug Administration's (FDA) 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. In 2005, Medicare alone spent more than \$770 million on the anti-anemia drug Procrit marketed by Johnson & Johnson's subsidiary Ortho Biotech Products, L.P. (Ortho Biotech).

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.<sup>[1]</sup> In particular, *The New York Times* reported on profits that doctors can make through rebates they receive from purchasing the drugs directly from Amgen Inc. and Johnson & Johnson and collecting payments from Medicare and private insurers, which are often above the purchase price. In addition, it is my understanding that the rebates are based on the amount of drugs purchased—the more a doctor buys, the higher the rebate.

I also read with great concern *The Wall Street Journal* article dated May 10, 2007, regarding allegations by two former Ortho Biotech salesmen that the company engaged in questionable pricing practices and “pushed” doctors to prescribe a higher dose of Procrit before FDA had approved that dose for cancer patients. Overuse of ESAs is not only a financial concern to the Committee, but also a major patient safety concern because recent clinical studies identified increased risks of death, blood clots, strokes, heart attacks, and tumor growths when ESAs are given in higher than recommended doses.

In addition, I was troubled by a *Bloomberg* article, dated May 11, 2007, which reported that the FDA was given **limited** access to results from company studies.<sup>[2]</sup> Although the article did not discuss the details of this so-called “limited” access, I believe 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 Johnson & Johnson and Ortho Biotech cooperate with the Committee's review of the marketing and pricing allegations reported in *The Wall Street Journal* on May 10, 2007. In addition, I request that Johnson & Johnson and Ortho Biotech arrange a briefing for my Committee staff by June 13, 2007, to discuss the issues and concerns that have been reported in the media over the last several weeks regarding, among other things, Johnson & Johnson's and/or Ortho Biotech's pricing and marketing practices and the safety of ESAs. In particular, please be prepared, at a minimum, to address the following questions at the briefing:

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<sup>[1]</sup> Marilyn Chase, “Amgen's Star Fades Amid Safety Questions,” *The Wall Street Journal*, April 10, 2007; “Dialysis Profits May Put Patients At Risk,” *Associated Press*, April 19, 2007; Alex Berenson and Andrew Pollack, “Doctors Reap Millions for Anemia Drugs,” *The New York Times*, May 9, 2007; Heather Won Tesoriero and Avery Johnson, “Suit Details How J&J Pushed Sales of Procrit,” *The Wall Street Journal*, May 10, 2007.

<sup>[2]</sup> Luke Timmerman, “Amgen Shares Fall on Downgrades, Anemia Drug Concern,” *Bloomberg*, May 11, 2007.

1. As mentioned in this letter, *Bloomberg* reported that FDA was given limited access to results from company studies. Did Johnson & Johnson and/or Ortho Biotech limit FDA's access to any study results? If so, please explain why complete results were withheld from the FDA and identify the studies from which the results were withheld. In addition, did Johnson & Johnson and/or Ortho Biotech withhold any other information or data requested by the FDA related to the safety and/or efficacy of ESAs?
2. Please identify all safety and efficacy trials of ESAs sponsored either directly or indirectly by Johnson & Johnson and/or Ortho Biotech whether conducted within or outside the U.S. from January 2002 through May 2007 in a table according to the following format. If Johnson & Johnson and/or Ortho Biotech have in their possession information from post-marketing studies or clinical trials conducted by independent investigators, please also include that information in the table.

Title	Trial Phase	Trial Purpose	Trial Population and Size	Trial Location	Description of Primary and Secondary Outcome Measures (including quality of life outcomes)	Summary of Results	Trial Status

3. In its proposed coverage decision memorandum,<sup>[3]</sup> CMS expressed concern that a number of clinical trials of ESA treatment have been terminated, suspended, and/or otherwise not completed. Did Johnson & Johnson and/or Ortho Biotech sponsor any trials of ESA treatment from January 2002 through May 2007 that were terminated, suspended, and/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 those trial results were withheld from the FDA and identify the trials from which the results were withheld. Please provide information regarding the trials in a table according to the following format:

Title	Trial Phase	Trial Purpose	Trial Population and Size	Trial Location	Description of Primary and Secondary Outcome Measures (including quality of life outcomes)	Summary of Results (including findings regarding serious adverse effects)	Trial Status

<sup>[3]</sup> Available on the CMS Web site at <http://www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?id=203>.

4. *The Wall Street Journal* reported on May 10, 2007, that Johnson & Johnson “urged” doctors to enroll patients in “mini” trials using a once-a-week 40,000-unit dose instead of three 10,000-unit doses a week. What were the findings of those trials? Did Johnson & Johnson and/or Ortho Biotech submit any reports and data to the FDA related to these “mini” trials? Please provide the Committee with a copy of any reports prepared by Johnson & Johnson and/or Ortho Biotech and/or any of the companies’ consultants, including third party contractors regarding the findings and conclusions of these so-called “mini” trials, in particular findings related to the safety of Procrit.
5. Please provide the total and average amounts and range of rebate payments to physicians and group practices that purchased Procrit from Johnson & Johnson and/or Ortho Biotech in calendar years 2004, 2005, and 2006 by state. How many physicians and group practices in each state received rebates from Johnson & Johnson and/or Ortho Biotech for Procrit in calendar years 2004, 2005, and 2006? As a preliminary response to this request, please identify the five physicians and/or group practices that received the highest rebate payments in each state in calendar years 2004, 2005, and 2006.
6. In light of the reported increased risk of serious adverse effects, including death, associated with the use of ESAs in cancer patients no longer on chemotherapy, what actions, if any, have Johnson & Johnson and/or Ortho Biotech taken to ensure that doctors and patients are informed of the new safety risks? Please provide a detailed timeline of Johnson & Johnson’s and/or Ortho Biotech’s actions regarding Procrit beginning with the date on which the company first became aware of potential, increased risks related to the use and/or overuse of ESAs in cancer patients.

Any documents responsive to the issues and questions to be discussed at the briefing should be sent prior to the briefing via electronic transmission in PDF searchable format to [thomas\\_novelli@finance-rep.senate.gov](mailto:thomas_novelli@finance-rep.senate.gov) or via facsimile to (202) 228-2131 and original by U.S. mail in accordance with the attached instructions and general definitions. 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 Johnson & Johnson/Ortho Biotech during the Committee’s review by no later than June 4, 2007.

Sincerely,  
Charles E. Grassley  
Ranking Member  
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 erythropoiesis-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 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 Epopen 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  
Ranking Member  
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  
Ranking Member  
Committee on Finance