



September 6, 2011

TO: Donald M. Berwick, M.D.
Administrator
Centers for Medicare & Medicaid Services

FROM: /Daniel R. Levinson/
Inspector General

SUBJECT: Review of Medicare Part B Avastin and Lucentis Treatments for Age-Related Macular Degeneration (A-01-10-00514)

The attached final report provides the results of our review of Medicare Part B Avastin and Lucentis treatments for age-related macular degeneration.

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If you have any questions or comments about this report, please do not hesitate to call me, or your staff may contact Brian P. Ritchie, Assistant Inspector General for the Centers for Medicare & Medicaid Audits, at (410) 786-7104 or through email at Brian.Ritchie@oig.hhs.gov. We look forward to receiving your final management decision within 6 months. Please refer to report number A-01-10-00514 in all correspondence.

Attachment

Department of Health and Human Services

**OFFICE OF
INSPECTOR GENERAL**

**REVIEW OF
MEDICARE PART B
AVASTIN AND LUCENTIS
TREATMENTS FOR AGE-RELATED
MACULAR DEGENERATION**



Daniel R. Levinson
Inspector General

September 2011
A-01-10-00514

Office of Inspector General

<http://oig.hhs.gov>

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The designation of financial or management practices as questionable, a recommendation for the disallowance of costs incurred or claimed, and any other conclusions and recommendations in this report represent the findings and opinions of OAS. Authorized officials of the HHS operating divisions will make final determination on these matters.

EXECUTIVE SUMMARY

BACKGROUND

Medicare Part B provides limited coverage for drugs and biologicals that are furnished incident to a physician's service and that are not usually self-administered. Biologicals are medications that are made from living organisms or their products. In general, to meet coverage requirements, drugs and biologicals must be safe and effective and otherwise reasonable and necessary. Medicare considers drugs and biologicals that the Food and Drug Administration (FDA) has approved for marketing to be safe and effective when used for indications specified on the labeling.

Physicians sometimes prescribe drugs and biologicals for indications not specified on their labels. Such uses are referred to commonly as "off-label." Medicare may cover off-label use of FDA-approved drugs and biologicals if it determines the use to be medically accepted. While off-label prescribing by physicians is not prohibited, manufacturers may not promote drugs and biologicals for uses that have not been approved by FDA.

Wet age-related macular degeneration (wet AMD) is the leading cause of severe vision loss in people over the age of 65 in the United States. Avastin and Lucentis are currently the most commonly administered Part B biologicals used to treat wet AMD. FDA originally approved Avastin as a colorectal cancer treatment in 2004, but physicians administer it off-label to treat wet AMD.¹ FDA approved Lucentis for the treatment of wet AMD in 2006. These biologicals are antibodies that inhibit the abnormal blood vessel growth and leakage in the eyes that cause vision loss. The number of Medicare beneficiaries treated with Avastin and Lucentis increased from 198,000 in calendar year (CY) 2008 to 218,000 in CY 2009.

The National Eye Institute of the National Institutes of Health has acknowledged the widespread use of Avastin to treat wet AMD and has recognized the lack of any large, carefully controlled clinical trial to evaluate its effectiveness and safety for this use. The National Eye Institute funded a series of studies called the Comparison of Age-Related Macular Degeneration Treatment Trials (CATT). The first of the studies is a 2-year Lucentis-Avastin trial to compare the efficacy and safety of the two biologicals for the treatment of wet AMD. In April 2011, researchers reported that the trial's first year results showed that Avastin and Lucentis had equivalent effects on visual acuity when administered on the same dosing schedule.

Our audit covered 936,382 line items of service for potential Avastin treatments and 696,927 line items of service for potential Lucentis treatments furnished during CYs 2008 and 2009. We reviewed random samples of potential Avastin and Lucentis treatments to verify the biological used, the number of treatments furnished, and the payment amounts for those treatments.

¹ Because Avastin is packaged in 100- and 400-milligram vials that exceed the 1.25-milligram dose commonly used for treating wet AMD, physicians often use compounding pharmacies to repackage it into single-use syringes that contain the smaller intravitreal dose. On August 30, 2011, in response to a cluster of eye infections traced to patients who had received Avastin repackaged by a pharmacy in Florida, FDA alerted health care professionals of infection risk from repackaged Avastin intravitreal injections. Available online at <http://www.fda.gov/Drugs/DrugSafety/ucm270296.htm>.

OBJECTIVES

Our objectives were (1) to determine the number of and payments for Avastin and Lucentis treatments administered to Medicare Part B beneficiaries for wet AMD during CYs 2008 and 2009 and (2) to calculate the extent to which the exclusive use of either Avastin or Lucentis for the treatment of wet AMD would have impacted Medicare Part B and beneficiary expenditures.

SUMMARY OF RESULTS

Based on statistical sampling, we estimated that for wet AMD treatments, Medicare Part B paid physicians \$40 million for 936,382 Avastin treatments and \$1.1 billion for 696,927 Lucentis treatments furnished during the period of our review. We calculated that if Medicare reimbursement for all beneficiaries treated with Avastin or Lucentis for wet AMD had been paid at the Avastin rate during calendar years (CY) 2008 and 2009, Medicare Part B would have saved approximately \$1.1 billion and beneficiaries would have saved approximately \$275 million in copayments. Conversely, we calculated that if Medicare reimbursement for all beneficiaries treated with Avastin or Lucentis for wet AMD had been paid at the Lucentis rate, Medicare Part B would have increased spending by approximately \$1.5 billion and beneficiaries would have paid approximately \$370 million more in copayments.

There is a significant difference in Medicare Part B reimbursement for the two products. However, addressing expenditures for the treatment of an increasing number of beneficiaries with wet AMD with Avastin or Lucentis presents several challenges for the Medicare program. Any action CMS takes to encourage the use of Avastin to treat wet AMD could be controversial. In addition, CMS is required to reimburse most Part B covered drugs and biologicals at 106 percent of the average sales price. Thus, there is little pressure for Genentech, the manufacturer of Avastin and Lucentis, to lower the sales price of Lucentis. CMS's authority to limit reimbursement for the treatment of wet AMD to the rate of the least costly alternative is questionable. Finally, despite the magnitude of Medicare expenditures for biologicals such as Lucentis, CMS does not have the authority to require price concessions or rebates from the manufacturers of such products under the Part B program.

RECOMMENDATIONS

We recommend that CMS:

- consider the results of this report when evaluating coverage and reimbursement policies related to Avastin and Lucentis, as well as broader strategies to control Part B drug expenditures, and
- evaluate its current authorities and seek additional authorities as necessary to control Part B drug and biological expenditures more effectively.

CENTERS FOR MEDICARE & MEDICAID SERVICES COMMENTS

In written comments on our draft report, CMS stated that, with regard to our first recommendation, its existing coverage policies accurately reflect the available evidence on the use of Avastin and Lucentis. CMS also stated that it would implement changes to its policies based on new evidence, if appropriate. CMS concurred with our second recommendation. CMS's comments are included in their entirety as Appendix E.

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INTRODUCTION

BACKGROUND

The Medicare program, established by Title XVIII of the Social Security Act (the Act) in 1965, provides health insurance coverage to people aged 65 and over, people with disabilities, and people with end-stage renal disease. The Centers for Medicare & Medicaid Services (CMS) administers the program.

CMS contracts with entities called Medicare administrative contractors (MAC) to process and pay Medicare Part B claims from physicians. Each contractor is responsible for processing claims submitted by physicians within 1 of 15 designated regions, or jurisdictions, of the United States and its territories.¹

Medicare Part B Drug Coverage

Pursuant to CMS's *Medicare Benefits Policy Manual*, Pub. No. 100-02, ch. 15, § 50, Part B provides limited coverage for drugs and biologicals that are furnished incident to a physician's service and are not usually self-administered. Biologicals are medications that are made from living organisms or their products. In general, to meet coverage requirements, drugs and biologicals must be safe and effective and otherwise reasonable and necessary for patient care. Medicare considers drugs and biologicals that the Food and Drug Administration (FDA) has approved for marketing to be safe and effective when used for indications specified on the labeling.

Pursuant to the *Medicare Benefits Policy Manual*, Pub. No. 100-02, ch. 15, § 50.4.2, FDA-approved drugs and biologicals used for indications other than those specified on the label may be covered if a Medicare contractor determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature, and/or accepted standards of medical practice. Such uses are referred to commonly as "off-label."

Off-label prescribing may allow for innovation in clinical practice based on emerging clinical evidence. While off-label prescribing by physicians is not prohibited, manufacturers may not promote or market drugs and biologicals for uses that have not been approved by FDA.² The United States has entered into settlement agreements with numerous pharmaceutical manufacturers to resolve allegations that they promoted their drugs for uses that FDA did not approve and that the nonapproved uses of the drugs were not reimbursable under Federal health care programs. The Federal law enforcement community continues to focus on industry promotion of drugs for off-label uses.

¹ Section 911 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, P.L. No. 108-173, requires CMS to transfer the functions of fiscal intermediaries and carriers to MACs between October 2005 and October 2011. Most, but not all, of the MACs are fully operational; for jurisdictions where the MACs are not fully operational, the fiscal intermediaries and carriers continue to process claims. For purposes of this report, the term "Medicare contractor" means the fiscal intermediary, carrier, or MAC, whichever is applicable.

² Manufacturers are permitted to promote and market their products only for the indications (uses) specified in the FDA-approved labeling. See, e.g., 21 U.S.C. § 352(f)(1) and 21 U.S.C. § 331(a).

Medicare Part B Reimbursement for Covered Drugs

Medicare Part B determines reimbursement for most covered drugs and biologicals using the average sales price (ASP) methodology.³ Under this methodology, the Medicare allowance is 106 percent of the ASP. Part B reimburses physicians 80 percent of the allowance, and beneficiaries are responsible for the remaining 20 percent.

Compounded⁴ drugs and biologicals are exceptions to ASP-based reimbursement. Pursuant to the *Medicare Claims Processing Manual*, Pub. No. 100-04, ch. 17, § 20.1.2, reimbursement for compounded drugs and biologicals is determined by local Medicare contractors. Part B reimburses physicians 80 percent of the contractor-determined price, and beneficiaries are responsible for the remaining 20 percent.

Alternative Treatments for Wet Age-Related Macular Degeneration

Wet age-related macular degeneration (wet AMD) is the leading cause of severe vision loss in people over the age of 65 in the United States.⁵ Avastin (bevacizumab) and Lucentis (ranibizumab) are currently the most commonly administered Part B drugs or biologicals used to treat wet AMD. Genentech, Inc. (Genentech), a subsidiary of Roche, manufactures both biologicals.⁶ The number of beneficiaries treated for wet AMD with Avastin or Lucentis was 198,000 in calendar year (CY) 2008 and 218,000 in CY 2009.

FDA originally approved Avastin as a colorectal cancer treatment in 2004; physicians use it off-label to treat wet AMD. Lucentis received FDA approval in 2006 as a treatment for wet AMD. These biologicals are antibodies that inhibit the abnormal blood vessel growth and leakage in the eyes that cause vision loss. According to the National Eye Institute, Avastin and Lucentis are molecularly similar but not identical; Lucentis is a modified fragment of the Avastin

³ Section 1847A(c) of the Act defines an ASP as the value of a manufacturer's sales of a drug to all purchasers (with certain exceptions) in the United States in a calendar quarter, net of any price concessions, divided by the total number of units of the drug sold by the manufacturer in that same quarter.

Section 1847A(c)(2) of the Act excludes from the ASP calculation any sales at a nominal charge and any sales excluded from the determination of "best price" as defined under section 1927(c)(1)(C)(i). For example, the Act specifically excludes from the ASP calculation sales to certain Government entities able to obtain discounted prices by statute or contract, such as the Departments of Defense and Veterans Affairs and the Public Health Service.

⁴ The International Academy of Compounding Pharmacists defines the term "compounded" as follows: a compounded drug or biological is the "... customized preparation of a medicine that is not otherwise commercially available" Available online at <http://www.iacprx.org/site/PageServer?pagename=FAQs>. Accessed April 4, 2011.

⁵ National Eye Institute, *Comparison of Age-Related Macular Degeneration Treatments Trials (CATT): Lucentis—Avastin Trial Manual of Procedures*, §1.1 (May 2010).

⁶ For CY 2008, three Genentech products—including Avastin and Lucentis—accounted for almost 21 percent of total Part B drug expenditures for physician-administered drugs or biologicals.

antibody. Physicians administer these biologicals via intravitreal injection. Neither medication cures wet AMD, and physicians administer both at regular or varying intervals.⁷

In June 2010, FDA approved Lucentis for the treatment of a different ophthalmic condition, macular edema following retinal vein occlusion. Physicians also use Avastin off-label to treat that condition and other ophthalmic conditions.

Avastin

Physicians have prescribed Avastin widely for off-label treatment of wet AMD for several years because of its availability, low cost, and evidence about its effectiveness.⁸ Physicians began using Avastin intravitreally before FDA approved Lucentis.⁹ Even after Lucentis received FDA approval, doctors continued to use Avastin.¹⁰ Genentech has stated that it “does not interfere with physicians’ prescribing choices” but that it believes Lucentis “is the most appropriate treatment for patients with [wet AMD] because it was specifically designed, formally studied, approved by the ... [FDA] and manufactured for intraocular delivery for the treatment of wet AMD.”¹¹

Genentech has not applied for FDA approval of Avastin for the treatment of wet AMD. The company states that it developed Lucentis specifically for that indication.¹² Our analysis of ASP data showed that Genentech does not appear to have a financial incentive to apply for FDA approval for the use of Avastin as a treatment for wet AMD. For CYs 2008 and 2009, we calculated that the ASP for a dose of Lucentis was approximately \$1,915; the ASP associated with an intravitreal dose of Avastin was approximately \$7.

During the period of our review, all Medicare contractors reimbursed physicians for the off-label use of Avastin to treat wet AMD. However, contractors had issued varying instructions on how to bill for Avastin used to treat wet AMD. Some contractors directed physicians to submit claims using the billing code for Avastin, while others required the use of “unclassified” drug billing codes. In addition, each contractor established locally determined reimbursement

⁷ National Eye Institute, *Comparison of Age-Related Macular Degeneration Treatments Trials (CATT): Lucentis—Avastin Trial Manual of Procedures*, §§ 1.4.6, 1.4.7.3, and 1.5 (May 2010).

⁸ National Eye Institute, *Comparison of Age-Related Macular Degeneration Treatments Trials (CATT): Lucentis—Avastin Trial Manual of Procedures*, §1.4.7.1 (May 2010).

⁹ National Eye Institute, *Comparison of Age-Related Macular Degeneration Treatments Trials (CATT): Lucentis—Avastin Trial Manual of Procedures*, §1.4.7.1 (May 2010).

¹⁰ National Eye Institute, *Comparison of Age-Related Macular Degeneration Treatments Trials (CATT): Lucentis—Avastin Trial Manual of Procedures*, §1.4.7.1 (May 2010).

¹¹ Genentech, Inc., “Avastin Distribution Update: December 20th (2007) Press Statement.” Available online at <http://www.gene.com/gene/features/avastin/press-statement.html>. Accessed December 15, 2010.

¹² Genentech, Inc., “Avastin Distribution Update: December 20th (2007) Press Statement.” Available online at <http://www.gene.com/gene/features/avastin/press-statement.html>. Accessed December 15, 2010.

amounts for off-label Avastin. As a result, we could not readily identify Avastin treatments for wet AMD in Medicare claims data.

Because Avastin is packaged in 100- and 400-milligram vials that exceed the 1.25-milligram dose commonly used for treating wet AMD, physicians often use compounding pharmacies to repackage it into single-use syringes that contain the smaller intravitreal dose.¹³

Lucentis

As a biological used to treat wet AMD, Lucentis meets Medicare Part B coverage requirements. It is packaged in a single-use vial designed to provide an individual dose to a single eye. Genentech holds patents for Lucentis, which expire in 2017 and 2019,¹⁴ and has additional exclusivity rights, which expire in 2018.¹⁵ Because of the complexity of biologicals and their manufacture, the future availability of generic versions of Lucentis and new competing drugs or biologicals is not known.

Because wet AMD is a disease that typically affects elderly patients, Medicare beneficiaries represent a significant portion of the total market for Lucentis.¹⁶ We calculated that Medicare Part B paid for at least 72 percent of the treatments that were used to calculate the ASP for Lucentis during CYs 2008 and 2009.

It has been reported that recently Genentech may have begun to offer rebates based on both volume and increased use of Lucentis.¹⁷ Under the rebate program, physicians apparently may qualify for rebates of up to 3 percent of the wholesale price of Lucentis. In addition to offering the rebate program, Genentech offers free samples of Lucentis for new wet AMD patients or patients with macular edema following retinal vein occlusion.¹⁸ Genentech also provides

¹³ On August 30, 2011, in response to a cluster of eye infections traced to patients who had received Avastin repackaged by a pharmacy in Florida, FDA alerted health care professionals of infection risk from repackaged Avastin intravitreal injections. Available online at <http://www.fda.gov/Drugs/DrugSafety/ucm270296.htm>.

¹⁴ Genentech, “Form 10-K for the Fiscal Year Ended December 31, 2007,” p. 8. Available online at http://www.sec.gov/Archives/edgar/data/318771/000031877108000004/form10-k_2007.htm. Accessed May 4, 2011.

¹⁵ Under 42 U.S.C. 262(k)(7)(A), FDA approval of an application for a “biosimilar” product may not be made effective until 12 years after the date on which the reference product was first licensed. Lucentis was first licensed in 2006.

¹⁶ The total market for Lucentis may include individuals who are not Medicare beneficiaries, such as individuals who receive health insurance benefits through an employer.

¹⁷ Andrew Pollack, “Genentech Offers Secret Rebates for Eye Drug,” *New York Times*, November 3, 2010. Available online at http://www.nytimes.com/2010/11/04/business/04eye.html?_r=2&ref=genentech_inc. Accessed March 22, 2011.

¹⁸ Genentech, “About Lucentis Direct: Lucentis Sampling Program.” Available online at <http://www.lucentisdirect.com/LucentisDirect/directNews-samplingProgram.html>. Accessed March 16, 2011.

assistance for eligible patients who do not have insurance coverage or cannot afford out-of-pocket copayments.¹⁹

Comparison of Age-Related Macular Degeneration Treatments Trials Study

The National Eye Institute of the National Institutes of Health has acknowledged the widespread use of Avastin to treat wet AMD and has recognized the lack of any large, carefully controlled clinical trial to evaluate its effectiveness and safety for this use. To meet the need for research, the National Eye Institute funded a series of studies called the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT). The first of the studies is a 2-year Lucentis-Avastin trial²⁰ to compare the efficacy and safety of the two biologicals for the treatment of wet AMD. The primary outcome to be measured is mean change in visual acuity, while secondary outcomes include the number of treatments and the incidence of adverse events.²¹

In April 2011, researchers reported that the trial's first year results showed that Avastin and Lucentis had equivalent effects on visual acuity when administered on the same dosing schedule. The instances of deaths, heart attacks, and strokes were low and similar for both biologicals during the first year of the study. However, the rate of serious adverse events (primarily hospitalizations) was 24 percent for patients treated with Avastin and 19 percent for patients treated with Lucentis. The number of patients in the Lucentis-Avastin trial is not large enough to determine whether there is an association between a particular adverse event and treatment. Differences in the rates of serious adverse events will require further study. Researchers will continue to follow patients through a second year of treatment.²²

OBJECTIVES, SCOPE, AND METHODOLOGY

Objectives

Our objectives were (1) to determine the number of and payments for Avastin and Lucentis treatments administered to Medicare Part B beneficiaries for wet AMD during CYs 2008 and 2009 and (2) to calculate the extent to which the exclusive use of either Avastin or Lucentis for the treatment of wet AMD would have impacted Medicare Part B and beneficiary expenditures.

¹⁹ Genentech, "Lucentis Access Solutions: What We Do." Available online at <http://www.genentechaccesssolutions.com/portal/site/AS/menuitem.7ef3b8542d7c63460313edacd79c23a0/?vgnexto id=26394dd658127210VgnVCM1000007dc9320aRCRD&vgnnextchannel=7f105465a5c07210VgnVCM1000007dc9320aRCRD>. Accessed March 16, 2011.

²⁰ National Eye Institute, *Comparison of Age-Related Macular Degeneration Treatments Trials (CATT): Lucentis — Avastin Trial Manual of Procedures*, §§ 1.4.7.1, 1.4.7.4, 1.5, and 2.1 (May 2010).

²¹ National Eye Institute, *Comparison of Age-Related Macular Degeneration Treatments Trials (CATT): Lucentis — Avastin Trial Manual of Procedures*, § 2.2, Table 2-1 (May 2010).

²² The CATT Study Group, "Ranibizumab and Bevacizumab for Neovascular Age-Related Macular Degeneration," *The New England Journal of Medicine*, April 28, 2011. Available online at <http://www.nejm.org/doi/full/10.1056/NEJMoa1102673#t=article>. Accessed April 29, 2011.

Scope

Our audit covered 936,382 line items of service for potential Avastin treatments and 696,927 line items of service for potential Lucentis treatments furnished during CYs 2008 and 2009. Our objectives did not require that we identify or review any internal controls. The marketing of Avastin and Lucentis was outside the scope of our review.

The objectives of our review did not require that we determine whether the Medicare reimbursement amounts for Avastin and Lucentis were appropriate. The Office of Inspector General is conducting a separate inspection to compare physician-acquisition costs to Medicare payment amounts for Avastin and Lucentis.

Methodology

To accomplish our objectives, we:

- reviewed applicable Medicare laws, regulations, and guidance;
- reviewed literature from various sources (e.g., the National Institutes of Health and medical and professional journals) on the two biologicals;
- interviewed CMS officials;
- reviewed local coverage determinations and articles issued by various Medicare contractors relating to coverage of and payment for Avastin;
- analyzed Medicare billing and reimbursement requirements to determine identifying characteristics for Avastin and Lucentis treatments (Appendix A);
- used these characteristics to identify potential Avastin and Lucentis treatments in CMS's National Claims History data for CYs 2008 and 2009;
- selected random samples of 100 potential Avastin treatments and 100 potential Lucentis treatments (Appendix A);
- obtained medical and payment records from physicians who provided the sampled services to verify the biological used, the number of treatments furnished, and the payment amount for those treatments;
- estimated the total number of and Part B payments for Avastin and Lucentis treatments for CYs 2008 and 2009 using our two random samples (Appendix B);
- calculated the average Medicare and beneficiary payments per treatment (Appendixes C and D);

- calculated the savings if Medicare reimbursement for all beneficiaries treated with Avastin or Lucentis for wet AMD had been paid at the Avastin rate (Appendixes C and D); and
- calculated the increased expenditure if Medicare reimbursement for all beneficiaries treated with Avastin or Lucentis for wet AMD had been paid at the Lucentis rate (Appendixes C and D).

We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

RESULTS OF REVIEW

Based on statistical sampling, we estimated that for wet AMD treatments, Medicare Part B paid physicians \$40 million for 936,382 Avastin treatments and \$1.1 billion for 696,927 Lucentis treatments furnished during the period of our review.

We calculated that if Medicare reimbursement for all beneficiaries treated with Avastin or Lucentis for wet age-related macular degeneration (wet AMD) had been paid at the Avastin rate during calendar years (CY) 2008 and 2009, Medicare Part B would have saved approximately \$1.1 billion and beneficiaries would have saved approximately \$275 million in copayments. Conversely, we calculated that if Medicare reimbursement for all beneficiaries treated with Avastin or Lucentis for wet AMD had been paid at the Lucentis rate, Medicare Part B would have increased spending by approximately \$1.5 billion and beneficiaries would have paid approximately \$370 million more in copayments.

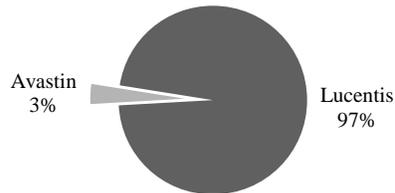
ESTIMATED NUMBER OF TREATMENTS AND AVERAGE PAYMENTS

Based on our sample results, we estimated that physicians administered 936,382 Avastin treatments and 696,927 Lucentis treatments during the period of our review. Although the majority of treatments used Avastin, we estimated that Medicare Part B paid physicians \$1.1 billion for Lucentis treatments and only \$40 million for Avastin treatments in our 2-year audit period (Appendix B). The percentages are shown in Figures 1 and 2.

Fig. 1: Estimated Number of Treatments Paid by Medicare Part B in CYs 2008 and 2009



Fig. 2: Estimated Medicare Part B Expenditures in CYs 2008 and 2009



For our sample, we calculated that the average Medicare Part B physician payment during CYs 2008 and 2009 was \$43 for Avastin and \$1,624 for Lucentis, a difference of \$1,582 per treatment. We calculated that the average beneficiary copayment (coinsurance and/or deductible) was \$11 for Avastin and \$406 for Lucentis, a difference of \$395 per treatment (Appendix D). The average Part B payment for an Avastin treatment was almost 38 times less than the average payment for a Lucentis treatment.

IMPACT OF POTENTIAL UTILIZATION CHANGES

For CYs 2008 and 2009, we calculated savings of approximately \$1.1 billion to Medicare Part B and \$275 million to beneficiaries had only Avastin been used for the treatment of wet AMD. Conversely, we calculated additional expenditures of approximately \$1.5 billion to Medicare Part B and \$370 million to beneficiaries had only Lucentis been used (Appendix D). These calculations show the possible impact of the CATT study results, which may influence physicians' use of the two biologicals for the treatment of wet AMD and result in a more concentrated use of one biological.

CONCLUSION

We recognize that the scenario in which physicians would exclusively use either Avastin or Lucentis to treat all beneficiaries with wet AMD is highly unlikely. However, we designed the calculations set forth in this report to inform future policy discussions.

There is a significant difference in the Medicare reimbursement amounts for the two products. However, addressing expenditures for the treatment of an increasing number of beneficiaries with wet AMD presents several challenges for the Medicare program.

Any action CMS takes to encourage the use of Avastin to treat wet AMD could be controversial. In addition, CMS is required to reimburse most Part B covered drugs and biologicals at 106 percent of ASP. Thus, there is little pressure for Genentech to lower the price of Lucentis. A 2009 court ruling invalidated CMS's application of its Least Costly Alternative (LCA) policy and calls into question CMS's authority to limit reimbursement for the treatment of wet AMD to the rate of the LCA.²³ Finally, despite the magnitude of Medicare expenditures for biologicals such as Lucentis, CMS does not have the authority to require price concessions or rebates for drugs or biologicals covered under Part B. This is in contrast to the Medicaid program, which requires manufacturers to pay rebates for covered outpatient drugs.²⁴

²³ In a case involving inhalation drugs, CMS was prohibited from implementing the LCA policy to control Medicare expenditures. Under this policy, CMS gave Medicare contractors the discretion to limit reimbursement for an item to the price of the least costly substitute that was reasonably feasible and medically appropriate. However, in December 2009, the U.S. Court of Appeals for the District of Columbia Circuit affirmed a lower court decision and ruled that the Secretary of Health & Human Services lacked the authority under the Act to apply the LCA policy for the drugs at issue (*Hays v. Sebelius*, 589 F. 3d 1279 (D.C. Cir. 2009)). Given that the Court evaluated the LCA policy in the context of a specific reimbursement methodology, the broader implications of the *Hays* decision in other situations are unclear.

²⁴ The Omnibus Budget Reconciliation Act of 1990, P.L. No. 101-508, established the Medicaid drug rebate program effective January 1, 1991. The program is outlined in section 1927 of the Act.

Medicare coverage and reimbursement for Part B drugs and biologicals is a complex issue. We are planning future work on drug reimbursement methodology.

RECOMMENDATIONS

We recommend that CMS:

- consider the results of this report when evaluating coverage and reimbursement policies related to Avastin and Lucentis, as well as broader strategies to control Part B drug expenditures, and
- evaluate its current authorities and seek additional authorities as necessary to control Part B drug and biological expenditures more effectively.

CENTERS FOR MEDICARE & MEDICAID SERVICES COMMENTS

In written comments on our draft report, CMS stated that, with regard to our first recommendation, its existing coverage policies accurately reflect the available evidence on the use of Avastin and Lucentis. CMS also stated that it would implement changes to its policies based on new evidence, if appropriate. CMS concurred with our second recommendation.

CMS's comments are included in their entirety as Appendix E.

APPENDIXES

APPENDIX A: SAMPLE DESIGN AND METHODOLOGY

PURPOSE

The objective of our samples was to estimate the number of and payments for Avastin and Lucentis treatments administered to Medicare Part B beneficiaries for the treatment of wet age-related macular degeneration (wet AMD) during calendar years 2008 and 2009.

POPULATIONS

The populations consisted of Medicare Part B line items of service with characteristics of Avastin or Lucentis treatments billed by physicians nationwide on behalf of beneficiaries being treated for wet AMD during calendar years 2008 and 2009.

SAMPLING FRAMES

The Avastin sampling frame was a database of 936,382 line items of service with the characteristics of Avastin treatments. Those 936,382 line items totaled \$39,643,347 in Medicare Part B payments to providers. We determined that Avastin treatments shared the following characteristics:

- Healthcare Common Procedure Coding System (HCPCS) codes J3490 (not otherwise classified drug), J3590 (not otherwise classified biologic), or J9035 (Avastin);
- diagnosis code 362.52 (wet AMD);
- provider specialty code 18 (ophthalmologist); and
- allowed payment amounts between \$35 and \$65.

The Lucentis sampling frame was a database of 696,927 line items of service with the characteristics of Lucentis treatments. Those 696,927 line items totaled \$1,134,862,853 in Medicare Part B payments to providers. We determined that Lucentis treatments shared the following characteristics:

- HCPCS code J2778 (Lucentis),
- diagnosis code 362.52,
- provider specialty code 18, and
- allowed payment amounts between \$1,900 and \$4,100.

SAMPLE UNIT

The sample unit was a Part B claim line item of service that represented potential Avastin or Lucentis treatment(s) furnished to a beneficiary diagnosed with wet AMD.

SAMPLE DESIGN

We used a simple random sample from each sampling frame.

SAMPLE SIZE

We selected 100 line items of service from each sampling frame.

SOURCE OF RANDOM NUMBERS

We used the Office of Inspector General, Office of Audit Services (OIG/OAS), statistical sampling software, RAT-STATS 2007, version 2, to generate the random numbers.

METHOD OF SELECTING SAMPLE ITEMS

We consecutively numbered the sample units in the Avastin frame from 1 to 936,382. We consecutively numbered the sample units in the Lucentis frame from 1 to 696,927. After generating the random numbers, we selected the corresponding sample units from each frame.

ESTIMATION METHODOLOGY

We used the OIG/OAS statistical software variable appraisal program to estimate the number of Avastin and Lucentis treatments and the dollar value of Avastin and Lucentis treatments paid for by Medicare Part B.

APPENDIX B: SAMPLE RESULTS AND ESTIMATES

Avastin Sample Results						
	Frame Size	Value of Frame	Sample Size	Value of Sample	Number of Avastin Treatments	Value of Avastin Treatments
Part B	936,382	\$39,643,347	100	\$4,258	100	\$4,258
Copayments	-	-	-	-	100	\$1,122

**Estimated Number of Avastin Treatments and Expenditures
(Limits Calculated for a 90-Percent Confidence Level)**

Estimated Avastin Treatments

Point Estimate 936,382
 Lower Limit 936,382
 Upper Limit 936,382

Estimated Part B Avastin Expenditures

Point Estimate \$39,868,336
 Lower Limit \$38,905,096
 Upper Limit \$40,831,577

Lucentis Sample Results						
	Frame Size	Value of Frame	Sample Size	Value of Sample	Number of Lucentis Treatments	Value of Lucentis Treatments
Part B	696,927	\$1,134,862,853	100	\$164,061	100 ¹	\$162,434
Copayments	-	-	-	-	100 ¹	\$40,609

**Estimated Number of Lucentis Treatments and Expenditures
(Limits Calculated for a 90-Percent Confidence Level)**

Estimated Lucentis Treatments

Point Estimate 696,927
 Lower Limit 680,481
 Upper Limit 713,373

Estimated Part B Lucentis Expenditures

Point Estimate \$1,132,048,355
 Lower Limit \$1,105,390,640
 Upper Limit \$1,158,706,069

¹ Physicians provided documentation verifying 100 Lucentis treatments. We verified that 98 of the 100 sampled line items represented single treatments and 1 line item represented a bilateral treatment (2 treatments). One line item could not be verified.

APPENDIX C: CALCULATION DESIGN AND METHODOLOGY

DESCRIPTION OF CALCULATIONS

The audit included calculations of the potential increases or decreases in Medicare Part B and beneficiary expenditures based on changes in the utilization of Avastin and Lucentis as a possible result of the Comparison of Age-Related Macular Degeneration Treatment Trials.

CALCULATION METHODOLOGY

We used the OIG/OAS statistical software variable appraisal program for simple random samples of 100 potential Avastin and 100 potential Lucentis treatments to estimate the number of treatments of each biological. We used the same samples to calculate the average Medicare Part B and beneficiary copayments (coinsurance and/or deductible) for each biological.

To determine the potential savings at the level of 100-percent utilization of Avastin, we multiplied the difference in the average payments for the two biologicals by the point estimate of Lucentis treatments that we determined through statistical sampling.

To determine the potential increased expenditures at the level of 100-percent utilization of Lucentis, we multiplied the difference in the average payments for the two biologicals by the point estimate of Avastin treatments that we determined through statistical sampling.

SOURCE OF DATA

We extracted potential Avastin and Lucentis treatments from the Centers for Medicare & Medicaid Services' National Claims History data file to create sampling frames of 936,382 potential Avastin treatments and 696,927 potential Lucentis treatments. We determined whether each sample item represented a single treatment (i.e., one eye) or two treatments (i.e., two eyes) and the Medicare Part B and beneficiary payments for the treatment(s).

APPENDIX D: CALCULATION RESULTS

AVERAGE PAYMENT PER TREATMENT

	Medicare Part B		Copayment	
	Avastin	Lucentis	Avastin	Lucentis
Total Payments Identified	\$4,258	\$162,434	\$1,122	\$40,609
Divided by: Number of Treatments Identified	100	100	100	100
Average Payment Per Treatment	\$42.58	\$1,624.34	\$11.22	\$406.09

POTENTIAL EXPENDITURES INCREASE TO MEDICARE PART B AND BENEFICIARIES IF LUCENTIS REIMBURSEMENT RATES HAD BEEN USED FOR ALL WET AGE-RELATED MACULAR DEGENERATION TREATMENTS, CALENDAR YEARS 2008 AND 2009

	Medicare Part B	Copayment
Average Part B Payment for Lucentis	\$1,624.34	\$406.09
Less: Average Part B Payment for Avastin	\$42.58	\$11.22
Difference in Payment	\$1,581.76	\$394.87
Multiply by: Point Estimate of Avastin Treatments	936,382	936,382
Potential Expenditures Increase Using Lucentis	\$1,481,134,214	\$369,745,508

POTENTIAL SAVINGS TO MEDICARE PART B AND BENEFICIARIES IF AVASTIN REIMBURSEMENT RATES HAD BEEN USED FOR ALL WET AGE-RELATED MACULAR DEGENERATION TREATMENTS, CALENDAR YEARS 2008 AND 2009

	Medicare Part B	Copayment
Average Part B Payment for Avastin	\$42.58	\$11.22
Less: Average Part B Payment for Lucentis	\$1,624.34	\$406.09
Difference in Payment	(\$1,581.76)	(\$394.87)
Multiply by: Point Estimate of Lucentis Treatments	696,927	696,927
Potential Savings Using Avastin	\$1,102,373,342	\$275,195,564



DEPARTMENT OF HEALTH & HUMAN SERVICES

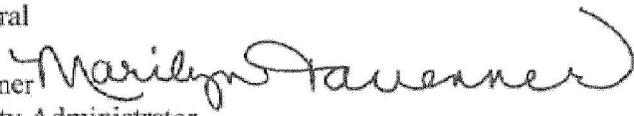
Centers for Medicare & Medicaid Services

Deputy Administrator

Baltimore, MD 21244-1850

DATE: JUL 15 2011

TO: Daniel Levinson
Inspector General

FROM: Marilyn Tavenner 
Principal Deputy Administrator

SUBJECT: Office of Inspector General (OIG) Draft Report: Review of Medicare Part B
Avastin and Lucentis Treatments for Age-Related Macular Degeneration
(A-01-10-00514)

The Centers for Medicare and Medicaid Services (CMS) appreciates the opportunity to review and comment on the OIG draft report entitled, "Review of Medicare Part B Avastin and Lucentis Treatments for Age-Related Macular Degeneration" (A-01-10-00514). We appreciate the OIG's efforts to examine payments made under the average sales price (ASP) methodology for these two drugs.

OIG RECOMMENDATION

The OIG recommends that CMS consider the results of this report when evaluating coverage and reimbursement policies related to Avastin and Lucentis, as well as broader strategies to control Part B drug expenditures.

CMS RESPONSE

We believe that our coverage policies accurately reflect the available published evidence on the use of these agents. We will continue to actively monitor the evidence and will, if appropriate, implement changes to our policies as the evidence base continues to grow.

OIG RECOMMENDATION

The OIG recommends that CMS evaluate its current authorities and seek additional authorities as necessary to control Part B drug and biological expenditures more effectively.

CMS RESPONSE

We concur with this recommendation. We appreciate the fact that the OIG quantified the range of payments that could occur if wet age-related macular degeneration (wet AMD) was treated exclusively with either Avastin or Lucentis. We are evaluating our current authorities and will seek additional authorities as necessary.

We thank the OIG for their thoughtful recommendations and we appreciate the OIG's constructive input. Additionally, we look forward to working in conjunction with OIG to facilitate continual improvement in administering the Medicare program.