UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF WISCONSIN

UNITED STATES OF AMERICA, and THE STATE OF WISCONSIN,
ex rel. DR. TOBY TYLER WATSON,

Plaintiffs,

v. Case No. 11-CV-236-JPS

JENNIFER KING VASSEL, *et al.*,

Defendant.

RELATOR'S REPLY TO DEFENDANT JENNIFER KING VASSEL'S BRIEF IN OPPOSITION TO THE PLAINTIFF'S MOTION IN *LIMINE* REGARDING FALSE CLAIMS

Relator Dr. Toby Tyler Watson hereby submits his brief in reply to Defendant Jennifer King Vassel's Brief In Opposition To The Plaintiff's Motion In *Limine* Regarding False Claims, Docket No. 109. In an attempt to open the door to irrelevant evidence, Defendant Jennifer King Vassel ("Dr, King") makes the nonsensical argument that Medicaid coverage for outpatient drugs is not limited to "covered outpatient drugs." This argument is contrary to (A) the law of the case; (B) the text of the Medicaid statute; and (C) the position repeatedly taken by the U.S. Government. It should be rejected.

A. The Law of the Case Is That Prescriptions Presented to Medicaid Not for a Medically Accepted Indication Are False Claims

Dr. King improperly attempts to reopen an issue already decided against her by both this Court and the Court of Appeals. When a court decides upon a rule of law, that decision should continue to govern the same issues in subsequent stages in the same preceding, see, eg. *Creek v. Village of Westhaven*, 144 F.3d 441 (1998).

Dr. King's argument is that Medicaid coverage for outpatient drugs is not limited to "covered outpatient drugs." This has been soundly rejected by both this Court and the Court of Appeals. This Court held at page 11 of the Order granting summary judgment, Docket No. 59:

> A "false or fraudulent claim" occurs when Medicaid pays for drugs that are not used for an indication that is either approved by the Food, Drug, and Cosmetic Act (FDCA) or supported by a drug compendia.

The Court of Appeals in its remand opinion at page 16 affirmed:

> Medicaid can only provide reimbursement for "covered outpatient drugs." 42 U.S.C. §§ 1396b(i)(10), 1396r–8(a)(3). Covered drugs do not include any drugs "used for a medical indication which is not a medically accepted indication." 42 U.S.C. § 1396r–8(k)(3). Watson's theory was that King–Vassel prescribed medication to N.B. for reasons that were not medically accepted indications. Helpfully, "medically accepted indication" is a statutorily-defined term that refers to a prescription purpose approved by the Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 et seq., or "supported by" any of several identified "compendia," 42 U.S.C. § 1396r–8(k)(6), § 1396r–8(g)(1)(B)(i) (listing as approved "compendia" the American Hospital Formulary Service Drug Information, the United States Pharmacopeia–Drug Information (or its successor publications), and the DRUGDEX Information System). The prescriptions at issue are "off-label" and so the parties agree that the drugs were not prescribed for an indication covered under the FDCA.

Under the law of the case doctrine, this issue should not be reopened.

B. States Cannot Expand Medicaid Coverage Beyond Congress's Limitation to Covered Outpatient Drugs

1. The Statutory Provisions Cited By Dr. King Allow Further Restriction of Medicaid Coverage, Not Expansion

Dr. King cites to a *limiting* section of the code in her attempt to support her proposition that states can *expand* Medicaid coverage for outpatient drugs beyond "covered outpatient drugs," ignoring the statutory framework, and misstating the case she cites in the process.

a. 42 U.S.C. §1396r-8(d) Does Not Allow the States to Expand Coverage Beyond Covered Outpatient Drugs

42. U.S.C. §1396r-8(k)(2) is titled "Covered outpatient drug" and sets forth what can be roughly characterized as most legally prescribed drugs. The statute then provides a limiting

definition, and states in pertinent part that "[t]he term 'covered outpatient drug' does not include any . . . drug . . . used for a medical indication which is not a medically accepted indication." 42. U.S.C. §1396r-8(k)(3). The statute defines "medically accepted indication," as follows:

> The term "medically accepted indication" means any use for a covered outpatient drug which is approved under the Federal Food, Drug, and Cosmetic Act [21 U.S.C.A. § 301 et seq.], or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in subsection (g)(1)(B)(i) of this section.

42 U.S.C. §1396r-8(k)(6). The compendia referenced are American Hospital Formulary Service Drug Information, United States Pharmacopeia-Drug Information (or its successor publications) and the DRUGDEX Information System. 42 U.S.C. §1396r-8(g)(1)(B)(i)(I-III).

Those drugs that are covered – i.e., those drugs whose use is approved under the FDCA or supported by one of the compendia – may be further restricted: There are 6 categories of "Limitations on coverage of drugs," set forth in §1396r-8(d)(1-6). One of those 6 categories is titled "permissible restrictions," and lists five permissible restrictions. 42 U.S.C. §1396r-8(d)(1)(B)(i-v).

Despite the clear statutory framework that mandates one begin the limitation analysis with only drugs that are "covered outpatient drugs," Dr. King cites two of the five permissible restrictions in 42 U.S.C. §1396r-8(d)(1)(B) for the proposition that Congress did not limit coverage for outpatient drugs to what it defined as covered outpatient drugs.

b. Dr. King Misstates the Authority and Purpose of §1396r-8(d)(1)(B)(iv) Formularies and Drug Utilization Review Boards

In her analysis, Dr. King cites 42 U.S.C. §1396r-8(d)(1)(B)(iv) for the proposition that states can expand coverage through the establishment of formularies beyond medically accepted indications. She further cites the "requirements for formularies" found in 42 U.S.C. §1396r-

8(d)(4) to grant upon drug utilization review (DUR) boards the authority to expand coverage. However, the statutory framework only allows formularies and DUR boards to further *restrict* coverage, not expand it. See 42 U.S.C. §1396r(d)(1) and discussion above.

This is in fact how the DUR process is to be utilized in practice. The Centers for Medicare and Medicaid Services (CMS), the Government agency charged with administering the Medicaid program at the federal level, describes the role of the DUR as follows:

> The Medicaid Drug Utilization Review (DUR) Program promotes patient safety through state-administered utilization management tools and systems that interface with CMS' Medicaid Management Information Systems (MMIS). Medicaid DUR is a two-phase process that is conducted by the Medicaid state agencies. In the first phase (prospective DUR) the state's Medicaid agency's electronic monitoring system screens prescription drug claims to identify problems such as therapeutic duplication, drug-disease contraindications, incorrect dosage or duration of treatment, drug allergy and clinical misuse or abuse. The second phase (retrospective DUR) involves ongoing and periodic examination of claims data to identify patterns of fraud, abuse, gross overuse, or medically unnecessary care and implements corrective action when needed.

http://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Drug-Utilization-Review.html (Exhibit 1.)

c. Dr. King's Interpretation of 42 U.S.C. §1396r-8(d)(1)(B)(i) is Nonsensical

Dr. King also cites 42 U.S.C. §1396r-8(d)(1)(B)(i) for the proposition that states can expand coverage beyond medically accepted indications as defined in the statute. This coverage-limiting provision states:

> (B) A State may exclude or otherwise restrict coverage of a covered outpatient drug if--
>
> (i) the prescribed use is not for a medically accepted indication (as defined in subsection (k)(6) of this section);

42 U.S.C. §1396r-8(d)(1)(B)(i).

This provision is circular, because "covered outpatient drug" is defined in 42 USC 1396R-8(k)(3) to "not include any . . . drug . . . used for a medical indication which is not a medically accepted indication." Thus, substituting the definition of "medically accepted indication," the statutory provision relied upon by the Defendant states,

> A State may exclude or otherwise restrict coverage of a covered outpatient drug to a covered outpatient drug.

or, substituting the definition of "covered outpatient drug:"

> A State may exclude or otherwise restrict coverage of drugs prescribed for a medically accepted indication to drugs prescribed for a medically accepted indication.

It is apparent there are two provisions to restrict coverage to medically accepted indications. One is universal and the other is at the option of the states, but both have been enacted, leaving superfluous the state option, §1396r-8(d)(1)(B)(i). The whole structure of the statute with respect to covered outpatient drugs is that it is restricted to medically accepted indications, defined as uses approved under the FDCA or supported by at least one of the compendia. Section1396r-8(d)(1)(B)(i) cannot be read to override Congress' explicit limitation of Medicaid coverage for outpatient drugs to medically accepted indications.

2. Drug Utilization Review Board Action Does Not Negate Knowledge Under the False Claims Act

At p. 2 of her Opposition Dr. King cites *United States ex rel. Rost v. Pfizer, Inc.*, 253 F.R.D. 11, 16 (D. Mass. 2008) for the proposition that "States can choose to reimburse for off-label use of prescription medication."[1] This is not true. What *Rost* actually says is that a Drug

[1] Deliberately or not, Dr. King consistently misstates that Dr. Watson is asserting that all off-label prescriptions are false claims. If a prescription is not for a use approved under the FDCA, it is called "off-label." Congress did not disallow all off-label coverage; instead it disallowed coverage if it was not supported by any of the compendia. This makes perfect sense, both in terms of controlling unwarranted costs, but also to protect the health of Medicaid recipients.

Utilization Review Board approval of reimbursement for drugs that are not for a medically accepted indication "would 'negate the intent requirement under the FCA as a matter of law.' "[2] However, this is an incorrect statement of the law. The United States Supreme Court has held such an *estoppel* does not apply when government funding is involved.

> Protection of the public fisc requires that those who seek public funds act with scrupulous regard for the requirements of law; respondent could expect no less than to be held to the most demanding standards in its quest for public funds. This is consistent with the general rule that *those who deal with the Government are expected to know the law and may not rely on the conduct of Government agents contrary to law*.

Heckler v. Community Health Services, 467 U.S. 51, 63, 104 S.Ct. 2218, 2225 (1984), emphasis added.

C. The United States Government Has Repeatedly Taken the Position that Claims Presented to Medicaid That Are Not for a Medically Accepted Indication Are False Claims

Just as has this Court and the Court of Appeals, the United States Government has taken the position that drugs not for a medically accepted indication, i.e., drugs that are neither approved under the F.D.C.A. nor supported by one of the compendia, are false claims.

For example, the Department of Justice's September 2, 2009, news release titled *Justice Department Announces Largest Health Care Fraud Settlement In Its History* related to exactly this type of false claim, as explained in the news release:

> Pfizer . . . caused false claims to be submitted to government health care programs for uses that were not medically accepted indications and therefore not covered by those programs.

Exhibit 2, page 1.

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[2] It can also be noted that *Rost* succinctly stated, "Medicaid can only pay for drugs that are used for a 'medically accepted indication, meaning one that is either approved by the FDA or 'supported by citations' in one of three drug compendia, including DRUGDEX." See *id*. At 13. (citations omitted)

Similarly, in its Statement of Interest in *United States of America ex rel Polansky v. Pfizer, Inc.*, EDNY, Case No. 1:04-cv-0074-ERK-ALC attached hereto as Exhibit 3, citing to 42 U.S.C. § 1396r-8(k)(2), (3) and (6), the United States Government walked through the statutory provisions that a "covered outpatient drug . . does not include a drug . . . used for a medical indication which is not a medically accepted indication."[3] *Polansky* involved the drug Lipitor and thus the United States said with respect to it:

> Prescription claims for Lipitor would be "false" if they were prescribed for unapproved uses that were not supported by a citation in one of the statutorily-identified compendia.[4]

This is precisely the type of false claim at issue here. In *Polansky*, the United States explained why Congress prohibited coverage of drugs that were not for a medically accepted indication:

> It . . . would undermine the gatekeeping role of the federal government in protecting public health as well as the public fisc in ensuring that, based on the information available at the time, only indications that have been FDA-approved or are sufficiently supported by scientific literature as safe and effective are reimbursed.[5]

Indeed, the settlement in *United States of America, ex rel James Wetta v. Astrazeneca Corp.*, Case No. 04-3479, ED Pennsylvania, is based on prescriptions to Medicaid patients and other federal health care programs that are not for a medically accepted indication constituting false claims. Exhibit 4. Thus, in ¶II.G.(1), the settlement agreement recites that the unapproved uses [under the FDCA] that were the subject of the lawsuit "were not medically accepted indications for which the United States and the Medicaid programs provided coverage for Seroquel," concluding ¶II.G. with:

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[3] *Id.* pp. 3-4.

[4] *Id.*, pp. 7-8.

[5] *Id.* p. 8.

> As a result of the foregoing conduct, the United States contends that AstraZeneca knowingly caused false or fraudulent claims for Seroquel to be submitted to, or caused purchases by, Medicaid, Medicare and the other Federal Health Care Programs.[6]

This is not just a position taken in litigation. In May of 2011, the Inspector General of the Department of Health and Human Services issued a report, titled, "Medicare Atypical Antipsychotic Drug Claims for Elderly Nursing Home Residents, Exhibit 5. The Executive Summary Background section at page i, includes the statement:

> Medicare requires that drugs be used for medically accepted indications supported by one or more of three compendia to be eligible for reimbursement.

And at page 5, it states:

> For drugs to qualify for Medicare Part D reimbursement, the Medicare Benefit Policy Manual and the Prescription Drug Benefit Manual require that drugs be used for medically accepted indications.[16]
>
> These indications include both the uses approved by FDA and those uses, including off-label, supported by one or more of three compendia: (1) the American Society of Health System Pharmacists, Inc.'s, *American Hospital Formulary Service Drug Information*; (2) the *United States Pharmacopeia-Drug Information* (or its successor publications); and (3) Thomson Reuters' DrugDEX Information System. Hereinafter these are collectively referred to as the compendia.
>
> [16] The Social Security Act (the Act) § 1927(g)(1)(B)(i). 42 U.S.C. 1396r-8(g)(1)(B)(i). The compendia described at the Act § 1927(g)(1)(B)(i) are incorporated into the Part D definition of "medically accepted indication" through the Act § 1860D-2(e)(4)(A)(ii), 42 U.S.C. 1395w-102(e)(4)(A)(ii), which refers to the Act § 1927(k)(6), which, in turn, refers to the Act § 1927(g)(1)(B)(i).

(footnotes, except 16, omitted).

In other words, Medicare Part D drug coverage incorporates the Medicaid restriction to medically accepted indications, which is limited to uses approved under the FDCA or supported

[6] Exhibit 4, p. 3.

by one of the compendia. This is an explicit, official statement of the coverage restriction by the Inspector General of the United States Department of Health and Human Services.

D. ONLY RELEVANT TESTIMONY SHOULD BE ALLOWED

Dr. King is attempting to get before the jury irrelevant evidence to draw attention away from Congress' explicit restriction of outpatient drug coverage under Medicaid to statutorily defined "medically accepted indications." At page 6 of her brief, Dr. King states she "will present expert testimony regarding her off-label use of prescription medications and Wisconsin's formulary permitting reimbursement beyond the compendia,"[7] citing the Court of Appeals remand Opinion for the proposition that "[t]he district court may very well be correct that Watson requires an expert to explain some number of the prescriptions he charges constitute false claims." By its very words, this quote from the Court of Appeals discusses whether Dr. Watson, not Dr. King, requires an expert. It does not authorize Dr. King to present irrelevant testimony.

E. CONCLUSION

Previously, Dr. King led this Court astray by asserting expert testimony on behalf of Dr. Watson was required to establish that a false claim was caused by Dr. King's off-label prescription to a known Medicaid patient that did not have support in any of the compendia. Here, Dr. King is attempting to again lead this Court astray by asserting, contrary to the rulings of both this Court and the Court of Appeal in its remand Opinion, that she should be allowed to present expert testimony that coverage for outpatient drugs is not limited to covered outpatient drugs. This question is not one for an expert, or any other witness. It is a statutory construction issue -- a statutory construction issue that has already been decided against Dr. King.

[7] Then, in the next paragraph, Dr. King says she will need to conduct discovery to determine if this representation to the Court is true.

Under F.R.E. 401 & 402, Dr. King is not allowed to present testimony of no consequence in determining the action. Therefore, it is respectfully suggested *Relator's* Motion In *Limine* Re: False Claims, Docket No. 102, should be **GRANTED**.

Dated this 22nd day of September, 2013.

LAW PROJECT FOR PSYCHIATRIC RIGHTS, INC.

s/ James B. Gottstein
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Exhibit 1

to

Relator's Reply To Defendant Jennifer King Vassel's Brief In Opposition To The Plaintiff's Motion In Limine Regarding False Claims

Drug Utilization Review

Medicaid Drug Utilization Review (DUR) Program

The Medicaid Drug Utilization Review (DUR) Program promotes patient safety through state-administered utilization management tools and systems that interface with CMS' Medicaid Management Information Systems (MMIS) (/Medicaid-CHIP-Program-Information/By-Topics/Data-and-Systems/MMIS.html). Medicaid DUR is a two-phase process that is conducted by the Medicaid state agencies. In the first phase (prospective DUR) the state's Medicaid agency's electronic monitoring system screens prescription drug claims to identify problems such as therapeutic duplication, drug-disease contraindications, incorrect dosage or duration of treatment, drug allergy and clinical misuse or abuse. The second phase (retrospective DUR) involves ongoing and periodic examination of claims data to identify patterns of fraud, abuse, gross overuse, or medically unnecessary care and implements corrective action when needed.

On an annual basis, states are required to report on their state's prescribing habits, cost savings generated from their DUR programs and their program's operations, including adoption of new innovative DUR practices via the Medicaid Drug Utilization Review Annual Report Survey (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/DURSurvey.pdf) . For states' convenience in filling out the DUR annual report, an NDC and Drug Category file (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/MedicaidRebateDrugSourceFile4Q2012-DUR.zip) extracted from the fourth quarter 2012 Medicaid Drug product data file (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Medicaid-Drug-Rebate-Program-Data.html) is provided.

42 CFR Subpart K – Drug Use Review (DUR) Program and Electronic Claims Management System for Outpatient Drug Claims, Section 456.700-456.725 (http://www.access.gpo.gov/nara/cfr/waisidx_10/42cfr456_10.html), provides the requirements for the DUR program.

Medicaid Drug Utilization Review (DUR) Annual Reports

To view each State's Medicaid DUR Annual report, please visit the Medicaid Drug Programs Data and Resources (http://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Medicaid-Drug-Programs-Data-and-Resources.html?filterBy=Drug Utilization Review (DUR)) page. The most recently posted annual reports are for FFY 2012.

The fee-for-service data from the FFY 2011 DUR reports has been compiled and presented in several sections to allow interested parties to see a comparison of the findings. The first section is a Comparison Report [ZIP] (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/DURSurvey2011-ComparisonReport-02262013.zip) , detailing state-by-state listing of each state's response to the questions in the survey. The second section is a Summary Report [ZIP] (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/DURSurvey2011-SummaryReportUpdated01152013.zip) of all states' responses to individual questions. The third section is a compilation of the unedited Executive Summary Reports [PDF] (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/DURSurvey2011-StateXIIExecutiveSummarySurvey01152013.pdf) submitted at the state's option, depicting an overview of DUR activities during the FFY 2011.

2011 Drug Utilization Review (DUR) Innovative Practices

The Centers for Medicare and Medicaid Services (CMS) has reviewed the

Prescription Drug Content

- Branded Prescription Drug Fee Program (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Branded-Prescription-Drug.html)
- Covered Outpatient Drugs Policy (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Covered-Outpatient-Drugs-Policy.html)
- Drug Utilization Review (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Drug-Utilization-Review.html)
- Federal Upper Limits (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Federal-Upper-Limits.html)
- Medicaid Drug Rebate Program (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Medicaid-Drug-Rebate-Program.html)
- Medicaid Drug Rebate Program Data (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Medicaid-Drug-Rebate-Program-Data.html)
- Medicaid Drug rebate Program Dispute Resolution (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-

Innovative Practices that the states submitted in their 2011 DUR Annual Reports. In an effort to share useful information on the activities states are performing to improve the quality of care and prudent delivery of their programs. We have provided examples of those activities below. Please note that the examples provided do not reflect all the different approaches that states may be using as these were submitted at state option. The detailed descriptions of specific state programs were taken directly from the 2011 DUR reports submitted by the states. CMS did not edit the material submitted.

All state pharmacy programs have reported on various pre-authorization requirements. Some states reported specific practices, e.g., AK, AR, NC - increased oversight for specific drug therapies; FL, ME, NV - new electronic systems and protocols recently implemented to enhance their existing programs. For details please click on this link for Prior Authorization (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/DUR-PreAuthorization.pdf) .

The misuse of antipsychotic drugs is prevalent throughout the country. Generally each state Medicaid pharmacy program is actively monitoring the prescribing of antipsychotic drugs with edits when the prescription is submitted to be filled, unless restricted by state law. We have highlighted the initiatives of CA, NV, PA, VA, and WV. For details please click on this link Antipsychotic Drug Monitoring (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/DUR-AntipsychoticDrugMonitor.pdf) .

The treatment of hemophilia is costly to all states. Utah has provided an example of how it reduces unnecessary waste and improved care by using case management control. For details please click on this link: Hemophilia Case Management (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/DUR-CaseManagement.pdf) .

All states have techniques to educate providers to improve the quality of their prescribing practices. California and Colorado shared their methods for disseminating educational information to prescribers in a timely fashion. For details please click on this link RetroDUR/Education (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/DUR-RetroDUR.pdf) .

Fraud, waste, misuse and abuse continues to be high priority for each state Medicaid program. States utilize a variety of tools to combat these issues including CT - Fraud Hotlines, MD - Corrective Case Management programs and DE, MT and, NJ - Chronic Pain Management. For details please click on this link Fraud, Waste, Abuse (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/DUR-WI-STCsFinal.pdf) .

Please note: The information found at the links above were taken unedited from the 2011 DUR reports sent in by states. If you would like additional information about any of these programs, please contact the person listed in the contact information in the individual 2011 state report found at this link Medicaid Drug Programs Data and Resources (http://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Medicaid-Drug-Programs-Data-and-Resources.html?filterBy=Drug Utilization Review (DUR)).

Psychotropic Medication Use in Children in Foster Care

Much attention has been focused on monitoring the prescribing of psychotropic medications to children in foster care since the passage of the Child and Family Services Improvement and Innovation Act of 2011 (P.L.112-34). Children in state custody often have emotional and behavioral challenges as a result of maltreatment and trauma. Creating, coordinating and implementing monitoring protocols across various agencies (state child welfare, Medicaid and mental health systems) to ensure appropriate prescribing and monitoring of medication therapy requires careful planning. While there is no single way to create a perfect system, state DUR programs can develop and share effective strategies for building creative and collaborative methods for promoting quality care for these vulnerable individuals. To that end, we are providing a brief summary (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/CIB-Posting.pdf) of different actions various states have taken to address this issue, along with a list of resources.

Drugs/Medicaid-Drug-Rebate-Program-Dispute-Resolution.html)

- National Drug Rebate Agreement (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/National-Drug-Rebate-Agreement.html)
- Program Releases (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Program-Releases.html)
- State Prescription Drug Resources (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/State-Prescription-Drug-Resources.html)
- Survey of Retail Prices (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Survey-of-Retail-Prices.html)
- Medicaid Drug Programs Data & Resources (/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Medicaid-Drug-Programs-Data-and-Resources.html)

Questions on the Drug Utilization Review Program? Email DURPolicy@cms.hhs.gov (mailto:DURPolicy@cms.hhs.gov).

Page last updated on July 30, 2013

Exhibit 2

to

Relator's Reply To Defendant Jennifer King Vassel's Brief In Opposition To The Plaintiff's Motion In Limine Regarding False Claims

Department of Justice

FOR IMMEDIATE RELEASE
Wednesday, September 2, 2009
WWW.USDOJ.GOV

AAG
(202) 514-2007
TDD (202) 514-1888

Justice Department Announces Largest Health Care Fraud Settlement in Its History

Pfizer to Pay $2.3 Billion for Fraudulent Marketing

WASHINGTON – American pharmaceutical giant Pfizer Inc. and its subsidiary Pharmacia & Upjohn Company Inc. (hereinafter together "Pfizer") have agreed to pay $2.3 billion, the largest health care fraud settlement in the history of the Department of Justice, to resolve criminal and civil liability arising from the illegal promotion of certain pharmaceutical products, the Justice Department announced today.

Pharmacia & Upjohn Company has agreed to plead guilty to a felony violation of the Food, Drug and Cosmetic Act for misbranding Bextra with the intent to defraud or mislead. Bextra is an anti-inflammatory drug that Pfizer pulled from the market in 2005. Under the provisions of the Food, Drug and Cosmetic Act, a company must specify the intended uses of a product in its new drug application to FDA. Once approved, the drug may not be marketed or promoted for so-called "off-label" uses – *i.e.*, any use not specified in an application and approved by FDA. Pfizer promoted the sale of Bextra for several uses and dosages that the FDA specifically declined to approve due to safety concerns. The company will pay a criminal fine of $1.195 billion, the largest criminal fine ever imposed in the United States for any matter. Pharmacia & Upjohn will also forfeit $105 million, for a total criminal resolution of $1.3 billion.

In addition, Pfizer has agreed to pay $1 billion to resolve allegations under the civil False Claims Act that the company illegally promoted four drugs – Bextra; Geodon, an anti-psychotic drug; Zyvox, an antibiotic; and Lyrica, an anti-epileptic drug – and caused false claims to be submitted to government health care programs for uses that were not medically accepted indications and therefore not covered by those programs. The civil settlement also resolves allegations that Pfizer paid kickbacks to health care providers to induce them to prescribe these, as well as other, drugs. The federal share of the civil settlement is $668,514,830 and the state Medicaid share of the civil settlement is $331,485,170. This is the largest civil fraud settlement in history against a pharmaceutical company.

As part of the settlement, Pfizer also has agreed to enter into an expansive corporate integrity agreement with the Office of Inspector General of the Department of Health and Human Services. That agreement provides for procedures and reviews to be put in place to avoid and promptly detect conduct similar to that which gave rise to this matter.

Whistleblower lawsuits filed under the *qui tam* provisions of the False Claims Act that are pending in the District of Massachusetts, the Eastern District of Pennsylvania and the Eastern District of Kentucky triggered this investigation. As a part of today's resolution, six whistleblowers will receive payments totaling more than $102 million from the federal share of the civil recovery.

The U.S. Attorney's offices for the District of Massachusetts, the Eastern District of Pennsylvania, and the Eastern District of Kentucky, and the Civil Division of the Department of Justice handled these cases. The U.S. Attorney's Office for the District of Massachusetts led the criminal investigation of Bextra. The investigation was conducted by the Office of Inspector General for the Department of Health and Human Services (HHS), the FBI, the Defense Criminal Investigative Service (DCIS), the Office of Criminal Investigations for the Food and Drug Administration (FDA), the Veterans' Administration's (VA) Office of Criminal Investigations, the Office of the Inspector General for the Office of Personnel Management (OPM), the Office of the Inspector General for the United States Postal Service (USPS), the National Association of Medicaid Fraud Control Units and the offices of various state Attorneys General.

"Today's landmark settlement is an example of the Department of Justice's ongoing and intensive efforts to protect the American public and recover funds for the federal treasury and the public from those who seek to earn a profit through fraud. It shows one of the many ways in which federal government, in partnership with its state and local allies, can help the American people at a time when budgets are tight and health care costs are increasing," said Associate Attorney General Tom Perrelli. "This settlement is a testament to the type of broad, coordinated effort among federal agencies and with our state and local partners that is at the core of the Department of Justice's approach to law enforcement."

"This historic settlement will return nearly $1 billion to Medicare, Medicaid, and other government insurance programs, securing their future for the Americans who depend on these programs," said Kathleen Sebelius, Secretary of Department of Health and Human Services**.** "The Department of Health and Human Services will continue to seek opportunities to work with its government partners to prosecute fraud wherever we can find it. But we will also look for new ways to prevent fraud before it happens. Health care is too important to let a single dollar go to waste."

"Illegal conduct and fraud by pharmaceutical companies puts the public health at risk, corrupts medical decisions by health care providers, and costs the government billions of dollars," said Tony West, Assistant Attorney General for the Civil Division. "This civil settlement and plea agreement by Pfizer represent yet another example of what penalties will be faced when a pharmaceutical company puts profits ahead of patient welfare."

"The size and seriousness of this resolution, including the huge criminal fine of $1.3 billion, reflect the seriousness and scope of Pfizer's crimes," said Mike Loucks, acting U.S. Attorney for the District of Massachusetts. "Pfizer violated the law over an extensive time period. Furthermore, at the very same time Pfizer was in our office negotiating and resolving the allegations of criminal conduct by its then newly acquired subsidiary, Warner-Lambert, Pfizer was itself in its other operations violating those very same laws. Today's enormous fine demonstrates that such blatant and continued disregard of the law will not be tolerated."

"Although these types of investigations are often long and complicated and require many resources to achieve positive results, the FBI will not be deterred from continuing to ensure that pharmaceutical companies conduct business in a lawful manner," said Kevin Perkins, FBI Assistant Director, Criminal Investigative Division.

"This resolution protects the FDA in its vital mission of ensuring that drugs are safe and effective. When manufacturers undermine the FDA's rules, they interfere with a doctor's judgment and can put patient health at risk," commented Michael L. Levy, U.S. Attorney for the Eastern District of Pennsylvania. "The public trusts companies to market their drugs for uses that FDA has approved, and trusts that doctors are using independent judgment. Federal health dollars should only be spent on treatment decisions untainted by misinformation from manufacturers concerned with the bottom line."

"This settlement demonstrates the ongoing efforts to pursue violations of the False Claims Act and recover taxpayer dollars for the Medicare and Medicaid programs," noted Jim Zerhusen, U.S. Attorney for the Eastern District of Kentucky.

"This historic settlement emphasizes the government's commitment to corporate and individual accountability and to transparency throughout the pharmaceutical industry," said Daniel R. Levinson, Inspector General of the United States Department of Health and Human Services. "The corporate integrity agreement requires senior Pfizer executives and board members to complete annual compliance certifications and opens Pfizer to more public scrutiny by requiring it to make detailed disclosures on its Web site. We expect this agreement to increase integrity in the marketing of pharmaceuticals."

"The off-label promotion of pharmaceutical drugs by Pfizer significantly impacted the integrity of TRICARE, the Department of Defense's healthcare system," said Sharon Woods, Director, Defense Criminal Investigative Service. "This illegal activity increases patients' costs, threatens their safety and negatively affects the delivery of healthcare services to the over nine million military members, retirees and their families who rely on this system. Today's charges and settlement demonstrate the ongoing commitment of the Defense Criminal Investigative Service and its law enforcement partners to investigate and prosecute those that abuse the government's healthcare programs at the expense of the taxpayers and patients."

"Federal employees deserve health care providers and suppliers, including drug manufacturers, that meet the highest standards of ethical and professional behavior," said Patrick E. McFarland, Inspector General of the U.S.

Office of Personnel Management. "Today's settlement reminds the pharmaceutical industry that it must observe those standards and reflects the commitment of federal law enforcement organizations to pursue improper and illegal conduct that places health care consumers at risk."

"Health care fraud has a significant financial impact on the Postal Service. This case alone impacted more than 10,000 postal employees on workers' compensation who were treated with these drugs," said Joseph Finn, Special Agent in Charge for the Postal Service's Office of Inspector General. "Last year the Postal Service paid more than $1 billion in workers' compensation benefits to postal employees injured on the job."

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09-900

Exhibit 3

to

Relator's Reply To Defendant Jennifer King Vassel's Brief In Opposition To The Plaintiff's Motion In Limine Regarding False Claims

UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NEW YORK

UNITED STATES OF AMERICA ex rel. DR. JESSE POLANSKY,	)	
Plaintiff,	)	No. 04-cv-0704 (ERK)(ALC)
v.	)	
PFIZER, INC.,	)	
Defendants	)	

UNITED STATES' STATEMENT OF INTEREST
IN RESPONSE TO DEFENDANT'S MOTION TO DISMISS
COUNTS I AND III THROUGH XIX OF THE FIFTH AMENDED COMPLAINT

The United States, real party in interest in this action, hereby moves to submit this Statement of Interest (Statement) pursuant to 28 U.S.C. § 517 to respond to certain arguments raised in defendant's Motion to Dismiss relator Polansky's Fifth Amended Complaint. The United States remains a real party in interest in this matter, even where it has not intervened in the action. *United States ex rel. Karvelas v. Melrose-Wakefield Hosp.*, 360 F.3d 220, 231 (1st Cir. 2004). The False Claims Act (FCA), 31 U.S.C. § 3729 *et seq.*, is the United States' primary tool used to redress fraud on the government. As such, the statute should be read broadly to reach all fraudulent attempts to cause the government to pay out sums of money. *United States v. Neifert-White*, 390 U.S. 228, 233 (1968). Thus, the United States has a keen interest in the development of the law in this area and in the correct application of the law in this and similar cases.

The United States submits this Statement to clarify the legal basis for an FCA claim predicated on allegations of off-label marketing by pharmaceutical manufacturers. First, claims for payment of items or services that are not eligible for reimbursement by federal health programs are "false claims." Second, a drug manufacturer may cause a provider to submit a false claim for reimbursement if that false claim was a reasonably foreseeable consequence of the drug manufacturer's conduct. Third, the identification of specific false claims is not an absolute prerequisite to satisfying the particularity requirement of Rule 9(b) in FCA cases. So long as the complaint as a whole is sufficiently particular to strengthen the inference of fraud beyond possibility, a court may conclude that Rule 9(b) is satisfied. Nonetheless, the United States submits that if the Court finds that relator's complaint fails to meet that test and is subject to dismissal under Rule 9(b), then it need not reach the other issues addressed herein.[1] The United States takes no position on whether relator has adequately plead facts that would state a cognizable claim under the FCA as properly interpreted.

I. CLAIMS FOR OFF-LABEL, NON-COVERED USES ARE FALSE CLAIMS.

Physicians are free to prescribe drugs for off-label uses. Nonetheless, as defendant concedes, federal health care programs do not cover *all* uses of *all* drugs. *See* Defendant's Brief in support of its Motion to Dismiss (Def. Br.) at 12. Rather, the programs at issue here generally cover drugs for "medically accepted indications," which, by statute, are defined as indications

[1] The United States does request that should the Court decide to dismiss Relator's Fifth Amended Complaint for failure to plead fraud with particularity, the dismissal should be without prejudice as to the United States. *See United States ex rel. Williams v. Bell Helicopter Textron Inc.*, 417 F.3d 450, 455 (5th Cir. 2005).

that are FDA-approved or that are "supported by a citation" in a statutorily-recognized compendium. 42 U.S.C. § 1396r-8(k)(6).

By way of background, in order to participate in the Medicaid program, a State must have a plan for medical assistance that has been approved by the Centers for Medicare and Medicaid Services (CMS), which administers the program on behalf of the Secretary of Health and Human Services. If the plan is approved by the Secretary, the State thereafter is eligible for federal financial participation, *i.e.*, reimbursement by the federal government for a specified percentage of the amounts that qualify as medical assistance under the state plan. 42 U.S.C. §§ 1396b(a)(1), 1396d(b).

Under the Medicaid Drug Rebate Statute, federal financial participation is prohibited for a drug manufacturer's covered outpatient drugs unless there is a rebate agreement between the manufacturer and the Secretary under the statute. *See* 42 U.S.C. §§ 1396b(i)(10)(A) and 1396r-8(a)(1). Once a drug manufacturer has entered into a rebate agreement for a covered outpatient drug, a State is generally required to cover that drug under the state plan. However, there are several provisions of the Medicaid Act that permit a State to exclude or restrict coverage. 42 U.S.C. § 1396r-8(d).[2]

Under the statute, a "covered outpatient drug" includes a drug dispensed by prescription and approved as safe and effective under the Federal Food, Drug, and Cosmetic Act (FDCA), 21

[2] A State may restrict from coverage or exclude altogether certain drugs or classes of drugs or certain medical uses where "the prescribed use is not for a medically accepted indication." 42 U.S.C. § 1396r-8(d)(1)(B)(i). In addition, a State also may adopt a prior authorization program, maintain a formulary, impose limits on prescription quantities to discourage waste, and address instances of fraud or abuse by individuals. 42 U.S.C. § 1396r-8(d)(4)-(6).

U.S.C. §§ 355 and 357, but does not include "a drug or biological used for a medical indication which is not a medically accepted indication." 42 U.S.C. § 1396r-8(k)(2), (3). The statute defines "medically accepted indication" as a use that is FDA-approved or a use that is "supported by a citation" in certain statutorily-identified compendia. *Id.* at § 1396r-8(k)(6).[3] Thus, under this statutory scheme, an off-label use that is not "supported by a citation" in the compendia falls outside the definition of a covered outpatient drug under Medicaid, and Medicaid is free to deny payment for resulting claims for such an off-label use.[4]

Courts have held that when a drug is prescribed for a use that is not covered by federal programs, the resulting claim for reimbursement of that prescription is "false" under the FCA. *See United States ex rel. Rost v. Pfizer, Inc*., 253 F.R.D. 11, 13-14 (D. Mass. 2008); *United States ex rel. Franklin v. Parke-Davis*, 2003 WL 22048255, at *2 (D. Mass. Aug. 22, 2003) (*Parke-Davis II)* ; *United States ex rel. Franklin v. Parke-Davis*, 147 F. Supp. 2d 39, 51-53 (D. Mass. 2001) (*Parke-Davis I*) ("[T]he alleged FCA violation arises - not from unlawful off-label marketing activity itself - but from the submission of Medicaid claims for uncovered off-label uses induced by Defendant's fraudulent conduct."); *Strom ex rel. U.S. v. Scios, Inc.*, 676 F. Supp. 2d 884, 891 (N.D. Cal. 2009) ("Because the [Medicare] statute permits reimbursement only for 'reasonable and necessary' treatments, [an off-label prescription] in a context where it is not 'reasonable' or 'necessary' would be statutorily ineligible for reimbursement. This satisfies the

[3] The three compendia described in subsection (g)(1)(B)(i) are the American Hospital Formulary Service Drug Information, the United States Pharmacopeia-Drug Information, and the Drugdex Information System. Id. at § 1396r-8(g)(1)(B)(i).

[4] Medicare Part D incorporates by reference the provisions of the Medicaid Drug Rebate Statute pertaining to "covered outpatient drugs." 42 U.S.C. § 1395w-102(e).

FCA's requirement of a 'false' statement."). Court have similarly found in other contexts that claims for services not covered by Medicare are false under the FCA. *See Peterson v. Weinberger*, 508 F.2d 45, 52 (5th Cir. 1975).

This principle is consistent with a host of other situations in which courts have found FCA liability even though there may be nothing false on the face of the claims in question. *See United States ex rel. Marcus v. Hess*, 317 U.S. 537, 543-44 (1943) (bid rigging to obtain a contract renders the claims submitted under the fraudulently procured contract false); *United States v. Rogan*, 517 F.3d 449, 452 (7th Cir. 2008) (claim may be ineligible for payment where physician received a kickback for the billed service); *United States v. McLeod*, 721 F.2d 282, 284 (9th Cir. 1983) (deposit of a facially valid check to which defendant was not entitled is a false claim); *Scolnick v. United States*, 331 F.2d 598, 599 (1st Cir. 1964) (same); *United States v. Incorporated Village of Island Park,* 888 F. Supp. 419, 440 (E.D.N.Y. 1995) (facially-accurate claims resulting from conduct that violated fair housing and non-discrimination provisions in HUD program were false within the meaning of the FCA).

When a claim is false because it is for a non-reimbursable item (*e.g.,* an off-label indication that is not otherwise covered by federal health programs), an analysis under a "certification theory" is simply inapposite. *See* Def. Br. at 19 (discussing false certification theory of liability). Whether the provider "certified" on the claim for payment that the prescribed usage was on-label or otherwise reimbursable is irrelevant. Rather, the core question for "falsity" under the FCA is whether the government received a bill from a healthcare provider for an item or service that was not legally reimbursable. This is an objective question and is not, as defendant argues, a "subjective interpretation of defendant's legal duties" that preclude a finding

of falsity. Def. Br. at 13. For that same reason, contrary to defendant's suggestion (Def. Br. at 11, 22), whether other information on the claim form is "truthful," such as the identity of the patient or the name of the drug used, has no bearing on the fact that a prescription was for a non-covered, non-reimbursable use and thus constitutes a false claim within the meaning of the FCA.

Accordingly, defendant also is incorrect in suggesting that the claim must contain a separate "conscious and deliberate 'lie'" in order to be a false claim. Def. Br. at 10. As is clear from the language of the statute, the FCA does not require proof of double falsity – a false claim *and* a false statement. The first two sections of the FCA provide independent and distinct bases for FCA liability. *Compare* 31 U.S.C. § 3729(a)(1) (liability for false claims) *with* (a)(2) (liability for false statements).[5] By its very terms, Section 3729(a)(1) only requires that the defendant presented or caused the presentment of a false claim, not that the defendant made a false statement or lied on the claim itself. *See United States ex rel. Rost v. Pfizer, Inc.*, 507 F.3d 720, 731-33 (1st Cir. 2007) (separately analyzing false statement allegations under Section 3729(a)(2)); *United States ex rel. Franklin v. Parke-Davis*, 2003 WL 22048255, at *2 (D. Mass. Aug. 22, 2003) (same). Accordingly, a case cited by Pfizer, *United States ex rel. Hess v. Sanofi-Synthelabo, Inc.*, 2006 WL 1064127, at *7 (E.D. Mo. Apr. 21, 2006), was wrongly decided because it demanded a showing of "extra" false statements and failed all together to consider liability under Section (a)(1), which does not require proof of any false statement at all. The *Hess* court also erred on the issue of materiality, as the question as to whether a claim is even eligible for payment is obviously material to the Government's decision to pay that claim.

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[5] The FCA was recently amended and these sections were recodified as 31 U.S.C. §§ 3729(a)(1)(A) & (a)(1)(B).

Furthermore, in order for a statement to be "false" under section 3729(a)(2), it need not be an affirmative misrepresentation; a material omission will suffice: "[H]alf the truth may obviously amount to a lie, if it is understood to be the whole." *W. Page Keeton, Prosser & Keeton on the Law of Torts* § 106, at 738 (5th ed. 1984); *see Luckey v. Baxter Healthcare Corp.*, 183 F.3d 730, 732 (7th Cir. 1999) (observing that a half-truth may amount to a false statement under the FCA in certain circumstances); *United States ex rel. Schwedt v. Planning Research Corp.*, 59 F.3d 196, 199 (D.C. Cir. 1995) (finding that false progress reports may constitute false statements under the FCA). Thus, a statement urging a physician to prescribe a drug for an unapproved use could well amount to a half-truth and satisfy the false statement requirement of section (a)(2), where, for example, the drug sales representative fails to mention evidence that does not support the drug's safety or efficacy for the unapproved use or that the FDA has specifically denied approval for that indication.

Relator here has alleged that promoting Lipitor therapy for patients outside the risk categories and cutpoints set forth in the National Cholesterol Education Program Guidelines is unlawful off-label promotion, and that resulting claims outside those Guidelines did not qualify for reimbursement under federal health care programs. This court has already observed that advocacy by Pfizer for an off-label use of Lipitor may well have violated the FDCA, but the fact that Pfizer may have done so does not automatically translate into FCA liability if the resulting claims for such prescriptions are not false under the FCA. *United States ex rel. Polansky v. Pfizer, Inc.*, 2009 WL 1456582, at *6-7 (E.D.N.Y. May 22, 2009). Prescriptions claims for

Lipitor would be "false" if they were prescribed for unapproved uses that were not supported by a citation in one of the statutorily-identified compendia.[6]

The United States takes no position as to whether relator has adequately alleged facts to support his claim that the Lipitor claims at issue here are false; however, Pfizer's reliance on the fact that the label for Lipitor was changed in 2009 clearly is misplaced. Def Br. at 3. If a claim was false when it was submitted in 2004, a label change five years later does not transform that false claim into a reimbursable one. To hold otherwise would be to render federal health care program restrictions on coverage meaningless. It also would undermine the gatekeeping role of the federal government in protecting public health as well as the public fisc in ensuring that, based on the information available at the time, only indications that have been FDA-approved or are sufficiently supported by scientific literature as safe and effective are reimbursed.

II. FCA Pleading Requirements

Of course, if a relator is claiming that the defendant drug company *caused* the providers to submit these false claims, the relator must adequately allege such causation. The relator need not allege an express false statement to satisfy the causation element, though such evidence would be one way the relator could do so. Assuming that a relator has supported his allegations with sufficient facts, courts analyze causation based on general tort law principles when determining whether the company may be liable for causing the submission of false claims based on off-label marketing conduct. *See United States ex rel. Cantekin v. Univ. of Pittsburgh*, 192

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[6] As noted, the statutory definition of "medically accepted indication" refers to off-label indications that are supported (as opposed to listed) in the compendia. *United States ex rel. Rost v. Pfizer, Inc.*, 253 F.R.D. 11, 16 (D. Mass. 2008) (citing CMS Release No. 141); *see* 42 U.S.C. § 1396r-8(k)(6).

F.3d 402, 415 (3d Cir. 1999) (discussing principles of causation); *Parke-Davis II*, 2003 WL 22048255 at *4-6. In *Parke-Davis II*, the court found that causation is satisfied where (a) the drug manufacturer's alleged off-label marketing was a "substantial factor" in producing the false claims and (b) it was "foreseeable" that the off-label marketing would result in false claims. 2003 WL 22048255 at *4-6. That court, like others presented with FCA cases based on allegations of off-label marketing, also found that the actions of health care providers are not an intervening force that breaks the chain of legal causation, particularly because influencing those actions is the goal of off-label promotion. *Id.* at *5 ("[T]he participation of doctors and pharmacists in the submission of false Medicaid claims was not only foreseeable, it was an intended consequence of the alleged scheme of fraud."); *see also Scios*, 676 F. Supp. 2d at 891 (denying a motion to dismiss and finding that the independent actions of physicians "only breaks the causal connection when it is unforeseeable" that a particular drug would be billed to a federal health care program). Indeed, the pharmaceutical industry would not employ the army of sales representatives who promote their products if these sales efforts had no effect on physician practices. Thus, the relevant question here is whether relator has sufficiently alleged that it was foreseeable that Pfizer's conduct would result in some false claims being submitted to federal health care programs.

Likewise, under the FCA, courts have held that a false claim is material if it "has a natural tendency to influence agency action or is capable of influencing agency action." *Harrison v. Westinghouse Savannah River Co.*, 176 F.3d 776, 785 (4th Cir. 1999).[7] Pfizer's argument that

[7] The FCA has also been recently amended to expressly define "materiality" in this fashion. *See* 31 U.S.C. § 3729(b)(4) (2009) (defining "material" as "having a natural tendency to influence, or be capable of influencing, the payment or receipt of money or property").

federal health care programs do not require certain information on claims forms that may have allowed the programs to prevent the payment of non-covered claims should be rejected because it runs counter to the courts' long-standing recognition that those who deal with the Government must "turn square corners" and cannot take advantage of government officials who may have too few resources to catch attempted fraud at its inception. *See, e.g., Rock Island, Arkansas & Louisiana R.R. v. United States*, 254 U.S. 141, 143 (1920); *Rogan*, 517 F.3d at 452 ("The United States is entitled to guard the public fisc against schemes designed to take advantage of overworked, harried, or inattentive disbursing officers"). The Government processes millions of claims for payment by federal health programs each year, and requiring it, as Pfizer apparently suggests, to examine every claim it pays for potential underlying misconduct is patently unreasonable.

III. Rule 9(b) Pleading Requirements

Defendant further asserts that relator has failed to identify specific claims and that regardless of whether relator has identified specific claims submitted to federal health care programs, he has failed to provide sufficient details about those claims. The United States takes no position on the sufficiency of relator's complaint; however, to the extent that defendant contends that relator's complaint must fail because it did not identify specific false claims or do so with sufficient particularity, defendant seeks to impose too rigid a pleading standard in FCA cases.

The allegation of a specific false claim is not an absolute prerequisite to pleading a viable FCA claim. Although FCA liability attaches to the claim for payment, whether specific claims must be identified for a complaint to satisfy Rule 9(b)'s particularity requirement will depend on

the circumstances of each case. *See Ebeid ex rel. U.S. v. Lungwitz*, 2010 WL 3092637, at *4-5 (9th Cir. Aug. 9, 2010); *United States ex rel. Duxbury v. Ortho Biotech Products, L.P.*, 579 F.3d 13, 31-32 (1st Cir. 2009); *United States ex rel. Grubbs v. Kanneganti*, 565 F.3d 180, 188 (5th Cir. 2009); *United States ex rel. Lusby v. Rolls-Royce Corp.*, 570 F.3d 849 (7th Cir. 2009); *United States ex rel. Rost v. Pfizer, Inc.*, 507 F.3d 720, 732 (1st Cir. 2007); *In re Pharm. Indus. Average Wholesale Price Litig.*, 538 F. Supp. 2d 367, 390-91 (D. Mass. 2008). Thus, in off-label cases, where the alleged false claims were submitted not by the defendant, but instead by a third party, a relator "need not allege the details of particular claims, so long as 'the complaint as a whole is sufficiently particular to pass muster under the FCA.'" *See In re Pharm. Indus. Average Wholesale Price Litig.*, 538 F. Supp. 2d at 390 (quoting *Rost*, 507 F.3d at 732). As this court has considered in examining relator's prior complaint in this action, in evaluating such matters on a case-by-case basis, the strength of the inference of fraud on the government may be measured by, for example, factual or statistical evidence tending to show fraud beyond possibility. *See Polansky*, 2009 WL 1456582, at *9; *see, e.g., In re Pharm. Indus. Average Wholesale Price Litig.*, 538 F. Supp. 2d at 390.

CONCLUSION

The United States submits this Statement regarding how to interpret and apply certain aspects of the Medicaid Act and the FCA. The United States takes no position on the sufficiency of the complaint herein.

Respectfully submitted,

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Dated: September 24, 2010

Exhibit 4

to

Relator's Reply To Defendant Jennifer King Vassel's Brief In Opposition To The Plaintiff's Motion In Limine Regarding False Claims

FILED UNDER SEAL

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA, ex rel. JAMES WETTA,	)	
Plaintiff,	)	C.A. No. 04-3479
v.	)	Filed Under Seal
ASTRAZENECA CORPORATION,	)	
Defendant.	)	

UNITED STATES' NOTICE OF INTERVENTION FOR PURPOSES OF SETTLEMENT

The United States of America, by and through its undersigned attorneys, provides this written notice to the Court that it is intervening in the above-captioned action pursuant to 31 U.S.C. §3730(b) for the purposes of settlement and dismissal.

The United States, relator James Wetta and defendant AstraZeneca have reached an amicable resolution of these matters. A copy of the Settlement Agreement is attached as Exhibit A. The parties agree that, upon receipt of the Settlement Amount as defined in the Settlement Agreement, the United States and relator will file a Stipulation of Dismissal in accordance with

the terms of the Settlement Agreement.

Respectfully submitted,

MICHAEL L. LEVY
United States Attorney

VIRGINIA A. GIBSON
First Assistant United States Attorney

COLIN M. CHERICO
Assistant United States Attorney

SETTLEMENT AGREEMENT

I. PARTIES

This Settlement Agreement (Agreement) is entered into among the United States of America, acting through the United States Department of Justice and the United States Attorney's Office for the Eastern District of Pennsylvania, the Office of Inspector General of the United States Department of Health and Human Services ("OIG-HHS"), the TRICARE Management Activity ("TMA"), and the United States Office of Personnel Management ("OPM") (collectively the "United States"); James Wetta ("Wetta"); Stephan Kruszewski, M.D. ("Kruszewski"); and Astra Zeneca LP and AstraZeneca Pharmaceuticals LP (collectively, "AstraZeneca"), through their authorized representatives. Collectively, all of the above will be referred to as "the Parties."

II. PREAMBLE

As a preamble to this Agreement, the Parties agree to the following:

A. AstraZeneca LP and AstraZeneca Pharmaceuticals LP are Delaware limited partnerships with their principal places of business in Wilmington, Delaware. At all relevant times herein, AstraZeneca distributed, marketed and sold pharmaceutical products in the United States, including a drug sold under the trade name of Seroquel.

B. On July 24, 2004, Wetta filed a qui tam action in the United States District Court for the Eastern District of Pennsylvania captioned United States of America ex rel. James Wetta v. AstraZeneca Corporation, Civil Action No. 04-3479 (hereinafter "Civil Action I").

C. On September 8, 2006, Kruszewski filed a qui tam action in the United States District Court for the Eastern District of Pennsylvania captioned United States of America ex rel. Stephan Kruszewski v. AstraZeneca Pharmaceuticals LP, Civil Action No. 06-4004

(hereinafter "Civil Action II"). Civil Action I and Civil Action II hereinafter may be referred to collectively as the "Civil Actions."

D. AstraZeneca has entered or will be entering into separate settlement agreements, described in Paragraph 1(b), below (hereinafter referred to as the "Medicaid State Settlement Agreements") with certain states and the District of Columbia in settlement of the Covered Conduct. States with which AstraZeneca executes a Medicaid State Settlement Agreement in the form to which AstraZeneca and the National Association of Medicaid Fraud Control Units ("NAMFCU") Negotiating Team have agreed, or in a form otherwise agreed to by AstraZeneca and an individual State, shall be defined as "Medicaid Participating States."

E. The United States and the Medicaid Participating States allege that AstraZeneca caused claims for payment for Seroquel to be submitted to the Medicaid Program, Title XIX of the Social Security Act, 42 U.S.C. §§ 1396-1396v (the Medicaid Program).

F. The United States further alleges that AstraZeneca caused claims for payment for Seroquel to be submitted to the Medicare Program, Title XVIII of the Social Security Act, 42 U.S.C. § 1395-1395hhh; the TRICARE program, 10 U.S.C. §§ 1071-1109; the Federal Employees Health Benefits Program ("FEHBP"), 5 U.S.C. §§ 8901-8914; the Federal Employees Compensation Act Program, 5 U.S.C. § 8101 et seq; and caused purchases of Seroquel by the Department of Veterans' Affairs ("DVA"), Department of Defense, and the Bureau of Prisons ("BOP") (collectively, the "other Federal Health Care Programs").

G. The United States contends that it has certain civil claims, as specified in Paragraph 2, below, against AstraZeneca for engaging in the following conduct during the period January 1, 2001 through December 31, 2006 (hereinafter referred to as the "Covered Conduct"):

(1) AstraZeneca promoted the sale and use of Seroquel to psychiatrists, other physicians (including primary care physicians) and other health care professionals in pediatric and primary care physician offices, in long-term care facilities and hospitals and in prisons for certain uses that were not approved by the Food and Drug Administration as safe and effective for those uses (including aggression, Alzheimer's disease, anger management, anxiety, attention deficit hyperactivity disorder, bipolar maintenance, dementia, depression, mood disorder, post-traumatic stress disorder, and sleeplessness) ("unapproved uses"). AstraZeneca also promoted the unapproved uses by engaging in the following conduct: AstraZeneca improperly and unduly influenced the content of and speakers in company-sponsored Continuing Medical Education programs; engaged doctors to give promotional speaker programs it controlled on unapproved uses for Seroquel; engaged doctors to conduct studies on unapproved uses of Seroquel; recruited doctors to serve as authors of articles largely prepared by medical literature companies about studies they did not conduct on unapproved uses of Seroquel; and, used those studies and articles as the basis for promotional messages about unapproved uses of Seroquel. These unapproved uses were not medically accepted indications for which the United States and the state Medicaid programs provided coverage for Seroquel.

(2) AstraZeneca offered and paid illegal remuneration to doctors: (a) it recruited to conduct studies for unapproved uses, (b) it recruited to serve as authors of articles written by AstraZeneca and its agents about these unapproved uses of Seroquel, (c) to travel to resort locations to "advise" AstraZeneca about marketing messages for unapproved uses of Seroquel, and (d) it recruited to give promotional lectures to other health care professionals about unapproved and unaccepted uses of Seroquel. The United States contends that these payments were intended to induce the doctors to promote and/or prescribe Seroquel for unapproved uses in violation of the Federal Anti-Kickback Statute, 42 U.S.C. § 1320-7b(b).

As a result of the foregoing conduct, the United States contends that AstraZeneca knowingly caused false or fraudulent claims for Seroquel to be submitted to, or caused purchases by, Medicaid, Medicare and the other Federal Health Care Programs.

H. The United States also contends that it has certain administrative claims against AstraZeneca, as set forth in Paragraphs 4 through 6, below, for engaging in the Covered Conduct.

I. This Agreement is made in compromise of disputed claims. This Agreement is neither an admission of facts or liability by AstraZeneca nor a concession by the United States that its claims are not well founded. AstraZeneca expressly denies the allegations of the United States, the Medicaid Participating States, Wetta and Kruszewski as set forth herein and in Civil Action I and Civil Action II and denies that it has engaged in any wrongful conduct. Neither this Agreement, its execution, nor the performance of any obligation under it, including any payment, nor the fact of settlement, are intended to be, or shall be understood as, an admission of liability or wrongdoing, or other expression reflecting on the merits of the dispute by AstraZeneca.

J. To avoid the delay, uncertainty, inconvenience, and expense of protracted litigation of the above claims, the Parties reach a full and final settlement pursuant to the Terms and Conditions below.

III. TERMS AND CONDITIONS

NOW, THEREFORE, in reliance on the representations contained herein and in consideration of the mutual promises, covenants, and obligations in this Agreement, and for good and valuable consideration, receipt of which is hereby acknowledged, the Parties agree as follows:

1. AstraZeneca agrees to pay to the United States and the Medicaid Participating States, collectively, the sum of Five Hundred and Twenty Million Dollars ($520,000,000), plus

accrued interest at the rate of 3% per annum from December 1, 2009, and continuing until and including the date of payment (the "Settlement Amount"). Payments shall be made as follows:

(a) AstraZeneca shall pay to the United States the sum of $301,907,007, plus accrued interest as set forth above ("Federal Settlement Amount"). The Federal Settlement Amount shall be paid by electronic funds transfer pursuant to written instructions from the United States no later than ten (10) business days after the Effective Date of this Agreement.

(b) AstraZeneca shall pay to the Medicaid Participating States the sum of $218,092,993, plus accrued interest as set forth above ("Medicaid State Settlement Amount") pursuant to written instructions from the NAMFCU Negotiating Team and under the terms and conditions of the Medicaid State Settlement Agreements that AstraZeneca will enter into with the Medicaid Participating States.

(c) Contingent upon the United States receiving the Federal Settlement Amount from AstraZeneca, the United States agrees to pay, as soon as feasible after receipt, to Wetta $45,286,051, plus a pro rata share of the actual accrued interest paid to the United States by AstraZeneca, as set forth in Paragraph 1(a), above, ("Relator's Share") as relator's share of the proceeds pursuant to 31 U.S.C. § 3730(d). No other relator payments of any sort shall be made by the United States to Wetta and/or Kruszewski with respect to the matters covered by this Agreement.

(d) Wetta and Kruszewski have entered into a separate agreement under which Kruszewski will receive a portion of the Relator's Share.

2. Subject to the exceptions in Paragraph 7, below, in consideration of the obligations of AstraZeneca in this Agreement, conditioned upon AstraZeneca's full payment of

the Settlement Amount, the United States (on behalf of itself, its officers, agents, agencies, and departments) agrees to release AstraZeneca, together with AstraZeneca's predecessors, current and former parents, affiliates, direct and indirect subsidiaries, brother or sister entities, divisions, transferees, successors and assigns, and all of their current or former directors, officers and employees (hereinafter, collectively "AstraZeneca Releasees") from any civil or administrative monetary claim the United States has or may have for the Covered Conduct under the False Claims Act, 31 U.S.C. §§ 3729-3733; the Civil Monetary Penalties Law, 42 U.S.C. § 1320a-7a; the Program Fraud Civil Remedies Act, 31 U.S.C. §§ 3801-3812; any statutory provision for which the Civil Division of the Department of Justice has actual and present authority to assert and compromise pursuant to 28 C.F.R. Part O, Subpart I, Section 0.45(D); or the common law theories of payment by mistake, unjust enrichment, fraud, disgorgement of illegal profits, and, if applicable, breach of contract.

3. In consideration of the obligations of AstraZeneca in this Agreement, conditioned upon AstraZeneca's full payment of the Settlement Amount, Wetta and Kruszewski, for themselves and for their heirs, successors, attorneys, agents, and assigns, fully and finally release the AstraZeneca Releasees from any claim the United States has, may have or could have asserted related to the Covered Conduct, and from all liability, claims, demands, actions or causes of action whatsoever existing as of the Effective Date of this Agreement, whether known or unknown, fixed or contingent, in law or in equity, in contract or in tort, under any federal or state statute or regulation or that they or their heirs, successors, attorneys, agents and assigns otherwise would have standing to bring, including any liability arising from the filing of the Civil Actions, except for any claims they may have under 31 U.S.C. § 3730(d) and/or 31 U.S.C.

§ 3730(h).

4. In consideration of the obligations of AstraZeneca in this Agreement and the Corporate Integrity Agreement ("CIA"), entered into between OIG-HHS and AstraZeneca, conditioned upon AstraZeneca's full payment of the Settlement Amount, OIG-HHS agrees to release and refrain from instituting, directing, or maintaining any administrative action seeking exclusion from Medicare, Medicaid, and other Federal health care programs (as defined in 42 U.S.C. § 1320a-7b(f)), against AstraZeneca under 42 U.S.C. § 1320a-7a (Civil Monetary Penalties Law) or 42 U.S.C. § 1320a-7(b)(7) (permissive exclusion for fraud, kickbacks, and other prohibited activities) for the Covered Conduct, except as reserved in Paragraph 7 below, and as reserved in this Paragraph. The OIG-HHS expressly reserves all rights to comply with any statutory obligations to exclude AstraZeneca from Medicare, Medicaid, and other Federal health care programs under 42 U.S.C. § 1320a-7(a) (mandatory exclusion) based upon the Covered Conduct. Nothing in this Paragraph precludes the OIG-HHS from taking action against entities or persons, or for conduct and practices, for which claims have been reserved in Paragraph 7, below.

5. In consideration of the obligations of AstraZeneca set forth in this Agreement, conditioned upon AstraZeneca's full payment of the Settlement Amount, TMA agrees to release and refrain from instituting, directing, or maintaining any administrative action seeking exclusion from the TRICARE Program, against AstraZeneca under 32 C.F.R. § 199.9 for the Covered Conduct, except as reserved in Paragraph 7, below, and as reserved in this Paragraph. TMA expressly reserves authority to exclude AstraZeneca under 32 C.F.R. §§ 199.9 (f)(1)(i)(A), (f)(1)(i)(B), and (f)(1)(iii), based upon the Covered Conduct. Nothing in this Paragraph

precludes TMA or the TRICARE Program from taking action against entities or persons, or for conduct and practices, for which claims have been reserved in Paragraph 7, below.

6. In consideration of the obligations of AstraZeneca in this Agreement, conditioned upon AstraZeneca's full payment of the Settlement Amount, OPM agrees to release and refrain from instituting, directing, or maintaining any administrative action, against AstraZeneca under 5 U.S.C. § 8902a or 5 C.F.R. Part 919 or Part 970 for the Covered Conduct, except as reserved in Paragraph 7, below and except as required by 5 U.S.C. §8902a(b). Nothing in this Paragraph precludes OPM from taking action against entities or persons, or for conduct and practices, for which claims have been reserved in Paragraph 7, below.

7. Notwithstanding any term of this Agreement, the following claims of the United States are specifically reserved and excluded from the scope and terms of this Agreement as to any entity or person (including AstraZeneca, Wetta and/or Kruszewski):

(a) Any civil, criminal, or administrative liability arising under Title 26, U.S. Code (Internal Revenue Code);

(b) Any criminal liability;

(c) Except as explicitly stated in this Agreement, any administrative liability, including mandatory exclusion from Federal health care programs;

(d) Any liability to the United States (or its agencies) for any conduct other than the Covered Conduct;

(e) Any liability based upon such obligations as are created by this Agreement;

(f) Any liability for express or implied warranty claims or other claims for

defective or deficient products or services, including quality of goods and services;

(g) Any liability for personal injury or property damage or for other consequential damages arising from the Covered Conduct; and

(h) Any liability for failure to deliver goods or services due.

8. Wetta and Kruszewski and their heirs, successors, attorneys, agents, and assigns agree not to object to this Agreement and agree and confirm that this Agreement is fair, adequate, and reasonable under all the circumstances, pursuant to 31 U.S.C. § 3730(c)(2)(B) and, conditioned upon the United States' payment of the Relator's Share, as set forth in Paragraph 1(c), above, Wetta and Kruszewski, for themselves individually, and for their heirs, successors, agents, and assigns, fully and finally release, waive, and forever discharge the United States, and its officers, agents, and employees, from any claims arising from or relating to 31 U.S.C. § 3730; from any claims arising from the filing of Civil Action I and/or Civil Action II; and from any other claims for a share of the Settlement Amount or payment of any sort from the United States relating to the Settlement Agreement or the filing of Civil Action I and/or Civil Action II; and in full settlement of any claims Wetta and/or Kruszewski may have under this Agreement. This Agreement does not resolve or in any manner affect any claims the United States has or may have against Wetta and/or Kruszewki arising under Title 26, U.S. Code (Internal Revenue Code), or any claims arising under this Agreement.

9. AstraZeneca waives and shall not assert any defenses AstraZeneca may have to any criminal prosecution or administrative action relating to the Covered Conduct that may be based in whole or in part on a contention that, under the Double Jeopardy Clause in the Fifth

Amendment of the Constitution, or under the Excessive Fines Clause in the Eighth Amendment of the Constitution, this Agreement bars a remedy sought in such criminal prosecution or administrative action. Nothing in this paragraph or any other provision of this Agreement constitutes an agreement by the United States concerning the characterization of the Settlement Amount for purposes of the Internal Revenue laws, Title 26 of the United States Code.

10. AstraZeneca fully and finally releases the United States, its agencies, employees, servants, and agents from any claims (including attorney's fees, costs, and expenses of every kind and however denominated) that AstraZeneca has asserted, could have asserted, or may assert in the future against the United States, its agencies, employees, servants, and agents, related to the Covered Conduct and the United States' investigation and prosecution thereof.

11. Conditioned upon Wetta and Kruszewski's compliance with their obligations under this Agreement, AstraZeneca fully and finally releases Wetta and Kruszewski from any claims (including attorney's fees, costs, and expenses of every kind and however denominated) that AstraZeneca has asserted, could have asserted, or may assert in the future against Wetta and/or Kruszewksi, related to the Covered Conduct and Wetta and/or Kruszewski's investigation and prosecution thereof, except to the extent related to claims Wetta or Kruszewski may have under 31 U.S.C. § 3730(d) and/or 31 U.S.C. § 3730(h).

12. The Settlement Amount shall not be decreased as a result of the denial of claims for payment now being withheld from payment by any Medicare carrier or intermediary or any other state or Federal payer, related to the Covered Conduct; and AstraZeneca agrees not to resubmit to any Medicare carrier or intermediary or any other state or Federal payer any previously denied claims related to the Covered Conduct, and agrees not to appeal any such

denials of claims.

13. AstraZeneca agrees to the following:

(a) Unallowable Costs Defined: that all costs (as defined in the Federal Acquisition Regulation, 48 C.F.R. § 31.205-47; and in Titles XVIII and XIX of the Social Security Act, 42 U.S.C. §§ 1395-1395hhh and 1396-1396v; and the regulations and official program directives promulgated thereunder) incurred by or on behalf of AstraZeneca, its present or former officers, directors, employees, shareholders and agents in connection with the following shall be "Unallowable Costs" on government contracts and under the Medicare Program, Medicaid Program, TRICARE Program, and FEHBP:

(i) the matters covered by this Agreement;

(ii) the United States' audit(s) and civil and any criminal investigation(s) of the matters covered by this Agreement;

(iii) AstraZeneca's investigation, defense, and corrective actions undertaken in response to the United States' audit(s) and civil and any criminal investigation(s) in connection with the matters covered by this Agreement (including attorney's fees);

(iv) the negotiation and performance of this Agreement;

(v) the payment AstraZeneca makes to the United States pursuant to this Agreement and any payments that AstraZeneca may make to Wetta and/or Kruszewski, including costs and attorneys fees; and

(vi) the negotiation of, and obligations undertaken pursuant to the CIA to:

(a) retain an independent review organization to perform annual reviews as described in Section III of the CIA; and

(b) prepare and submit reports to the OIG-HHS.

However, nothing in this paragraph 13(a)(vi) that may apply to the obligations undertaken pursuant to the CIA affects the status of costs that are not allowable based on any other authority applicable to AstraZeneca. (All costs described or set forth in this Paragraph 13(a) are hereafter "Unallowable Costs.")

(b) Future Treatment of Unallowable Costs: If applicable, these Unallowable Costs shall be separately determined and accounted for by AstraZeneca, and AstraZeneca shall not charge such Unallowable Costs directly or indirectly to any contracts with the United States or any State Medicaid program, or seek payment for such Unallowable Costs through any cost report, cost statement, information statement, or payment request submitted by AstraZeneca or any of its subsidiaries or affiliates to the Medicare, Medicaid, TRICARE, or FEHBP Programs.

(c) Treatment of Unallowable Costs Previously Submitted for Payment: If applicable, AstraZeneca further agrees that within 90 days of the Effective Date of this Agreement, it shall identify to applicable Medicare and TRICARE fiscal intermediaries, carriers, and/or contractors, and Medicaid and FEHBP fiscal agents, any Unallowable Costs (as defined in this Paragraph) included in payments previously sought from the United States, or any State Medicaid program, including, but not limited to, payments sought in any cost reports, cost statements, information reports, or payment requests already submitted by AstraZeneca or any of its subsidiaries or affiliates, and shall request, and agree, that such cost reports, cost statements, information reports, or payment requests, even if already settled, be adjusted to account for the

effect of the inclusion of the unallowable costs. AstraZeneca agrees that the United States, at a minimum, shall be entitled to recoup from AstraZeneca any overpayment plus applicable interest and penalties as a result of the inclusion of such Unallowable Costs on previously-submitted cost reports, information reports, cost statements, or requests for payment.

Any payments due after the adjustments have been made shall be paid to the United States pursuant to the direction of the Department of Justice and/or the affected agencies. The United States reserves its rights to disagree with any calculations submitted by AstraZeneca or any of its subsidiaries or affiliates on the effect of inclusion of Unallowable Costs (as defined in this Paragraph) on AstraZeneca or any of its subsidiaries or affiliates' cost reports, cost statements, or information reports.

(d) Nothing in this Agreement shall constitute a waiver of the rights of the United States to audit, examine, or re-examine AstraZeneca's books and records to determine that no Unallowable Costs have been claimed in accordance with the provisions of this Paragraph.

14. This Agreement is intended to be for the benefit of the Parties only. The Parties do not release any claims against any other person or entity, except to the extent provided for above or in Paragraph 15 (waiver for beneficiaries paragraph), below.

15. AstraZeneca agrees that it waives and shall not seek payment for any of the health care billings covered by this Agreement from any health care beneficiaries or their parents, sponsors, legally responsible individuals, or third party payors based upon the claims defined as Covered Conduct.

16. AstraZeneca warrants that it has reviewed its financial situation and that it

currently is solvent within the meaning of 11 U.S.C. §§ 547(b)(3) and 548(a)(1)(B)(ii)(I), and shall remain solvent following payment to the United States of the Settlement Amount. Further, the Parties warrant that, in evaluating whether to execute this Agreement, they (a) have intended that the mutual promises, covenants, and obligations set forth constitute a contemporaneous exchange for new value given to AstraZeneca, within the meaning of 11 U.S.C. § 547(c)(1); and (b) have concluded that these mutual promises, covenants, and obligations do, in fact, constitute such a contemporaneous exchange. Further, the Parties warrant that the mutual promises, covenants, and obligations set forth herein are intended to and do, in fact, represent a reasonably equivalent exchange of value that is not intended to hinder, delay, or defraud any entity to which AstraZeneca was or became indebted to on or after the date of this transfer, within the meaning of 11 U.S.C. § 548(a)(1).

17. Upon receipt of the payments described in Paragraph 1, above, the United States and Wetta shall promptly sign and file in Civil Action I a Notice of Intervention and Joint Stipulation of Dismissal with prejudice as to all federal counts in Civil Action I pursuant to the terms and conditions of the Agreement. Upon receipt of the payments described in Paragraph 1, above, Kruszewski shall promptly sign and file in Civil Action II a Notice of Dismissal with prejudice as to all federal counts in Civil Action II pursuant to the terms and conditions of the Agreement.

18. Except as expressly provided to the contrary in this Agreement, each Party shall bear its own legal and other costs incurred in connection with this matter, including the preparation and performance of this Agreement.

19. AstraZeneca represents that this Agreement is freely and voluntarily entered into

without any degree of duress or compulsion whatsoever.

20. Wetta and Kruszewski represent that this Agreement is freely and voluntarily entered into without any degree of duress or compulsion whatsoever.

21. This Agreement is governed by the laws of the United States. The Parties agree that the exclusive jurisdiction and venue for any dispute arising between and among the Parties under this Agreement is the United States District Court for the Eastern District of Pennsylvania, except that disputes arising under the CIA shall be resolved exclusively under the dispute resolution provisions in the CIA.

22. For purposes of construction, this Agreement shall be deemed to have been drafted by all Parties to this Agreement and shall not, therefore, be construed against any Party for that reason in any subsequent dispute.

23. This Agreement constitutes the complete agreement between the Parties. This Agreement may not be amended except by written consent of the Parties.

24. The individuals signing this Agreement on behalf of AstraZeneca represent and warrant that they are authorized by AstraZeneca to execute this Agreement. The individual(s) signing this Agreement on behalf of Wetta and Kruszewski represent and warrant that they are authorized by Wetta and Kruszewski to execute this Agreement. The United States signatories represent that they are signing this Agreement in their official capacities and that they are authorized to execute this Agreement.

25. This Agreement may be executed in counterparts, each of which constitutes an original and all of which constitute one and the same Agreement.

26. This Agreement is binding on AstraZeneca's successors, transferees, heirs, and

assigns.

27. This Agreement is binding on Wetta and Kruszewski's successors, transferees, heirs, and assigns.

28. All parties consent to the United States' disclosure of this Agreement, and information about this Agreement, to the public.

29. This Agreement is effective on the date of signature of the last signatory to the Agreement (Effective Date of this Agreement). Facsimiles of signatures shall constitute acceptable, binding signatures for purposes of this Agreement.

THE UNITED STATES OF AMERICA

DATED: 4-27-10 BY: _____
MICHAEL L. LEVY
United States Attorney
United States Attorney's Office
Eastern District of Pennsylvania

DATED: 4-27-10 BY: _____
VIRGINIA A. GIBSON
First Assistant
United States Attorney's Office
Eastern District of Pennsylvania

DATED: 4-27-10 BY: _____
MARGARET L. HUTCHINSON
Chief, Civil Division
United States Attorney's Office
Eastern District of Pennsylvania

DATED: 4-27-10 BY: _____
COLIN CHERICO
Assistant U.S. Attorney
United States Attorney's Office
Eastern District of Pennsylvania

DATED: _____ BY: _____
PATRICIA L. HANOWER
Trial Attorney
Commercial Litigation Branch
Civil Division
United States Department of Justice

THE UNITED STATES OF AMERICA

DATED:_____ BY: _____
MICHAEL L. LEVY
United States Attorney
United States Attorney's Office
Eastern District of Pennsylvania

DATED:_____ BY: _____
VIRGINIA A. GIBSON
First Assistant
United States Attorney's Office
Eastern District of Pennsylvania

DATED:_____ BY: _____
MARGARET L. HUTCHINSON
Chief, Civil Division
United States Attorney's Office
Eastern District of Pennsylvania

DATED:_____ BY: _____
COLIN CHERICO
Assistant U.S. Attorney
United States Attorney's Office
Eastern District of Pennsylvania

DATED: 4/27/10 BY: _____
PATRICIA L. HANOWER
Trial Attorney
Commercial Litigation Branch
Civil Division
United States Department of Justice

DATED: 4/27/10

BY: _____

GREGORY E. DEMSKE
Assistant Inspector General for Legal Affairs
Office of Counsel to the Inspector General
Office of Inspector General
United States Department of Health and Human Services

DATED: _____

BY: _____

LAUREL C. GILLESPIE
Deputy General Counsel
TRICARE Management Activity
United States Department of Defense

DATED: _____

BY: _____

SHIRLEY R. PATTERSON
Acting Deputy Associate Director Insurance Operations
Center for Retirement & Insurance Services
United States Office of Personnel Management

DATED: _____

BY: _____

DAVID COPE
Debarring Official
Office of the Assistant Inspector General for Legal Affairs
United States Office of Personnel Management

DATED:_____ BY: _____
GREGORY E. DEMSKE
Assistant Inspector General for Legal Affairs
Office of Counsel to the Inspector General
Office of Inspector General
United States Department of Health and Human Services

DATED: April 23, 2010 BY: Rhonda L. Bershok, Acting Deputy General Counsel
For: LAUREL C. GILLESPIE
Deputy General Counsel
TRICARE Management Activity
United States Department of Defense

DATED:_____ BY: _____
SHIRLEY R. PATTERSON
Acting Deputy Associate Director Insurance Operations
Center for Retirement & Insurance Services
United States Office of Personnel Management

DATED:_____ BY: _____
DAVID COPE
Debarring Official
Office of the Assistant Inspector General for Legal Affairs
United States Office of Personnel Management

DATED:_____ BY: _____
GREGORY E. DEMSKE
Assistant Inspector General for Legal Affairs
Office of Counsel to the Inspector General
Office of Inspector General
United States Department of Health and Human Services

DATED:_____ BY: _____
LAUREL C. GILLESPIE
Deputy General Counsel
TRICARE Management Activity
United States Department of Defense

DATED: 4/26/10 BY: Shirley R Patterson
SHIRLEY R. PATTERSON
Acting Deputy Associate Director Insurance Operations
Center for Retirement & Insurance Services
United States Office of Personnel Management

DATED: 4/26/2010 BY: _____
DAVID COPE
Debarring Official
Office of the Assistant Inspector General for Legal Affairs
United States Office of Personnel Management

ASTRAZENECA

DATED: 4/27/10 BY: _____

Glenn M. Engelmann
Vice President and General Counsel
AstraZeneca LP
AstraZeneca Pharmaceuticals LP

DATED: 4/27/10 BY: _____

JOHN C. DODDS, ESQ.
Morgan, Lewis and Bockius, LLP

RELATOR JAMES WETTA

DATED:_____ BY: _____
JAMES WETTA

DATED:_____ BY: _____
STEPHEN A. SHELLER, ESQ.

(Counsel to Relator James Wetta)

RELATOR JAMES WETTA

DATED: 4/23/11

BY: James Wetta by Michael Mustokoff
JAMES WETTA

DATED: 4/23/11

BY: Stephen A. Sheller
STEPHEN A. SHELLER, ESQ.

(Counsel to Relator James Wetta)

BY: Michael Mustokoff
MICHAEL MUSTOKOFF
MARK LIPOWICZ
TERESA CAVENAGH
DUANE MORRIS, LLP

BY: Gary M. Farmer by Michael Mustokoff
GARY M. FARMER JR.
FARMER JAFFE WEISSING EDWARDS FISTOS and LEHRMAN

[illegible]
[illegible]

RELATOR STEPHAN KRUSZEWSKI

DATED: 4/23/2010 BY: _____
STEFAN KRUSZEWSKI

DATED: _____ BY: _____
WILLIAM LEONARD, ESQUIRE
(Counsel to Stephan Kruszewski)

RELATOR STEPHAN KRUSZEWSKI

DATED:_____ BY: _____
STEFAN KRUSZEWSKI

DATED: 4/23/10 BY: _____
WILLIAM LEONARD, ESQUIRE
(Counsel to Stephan Kruszewski)

Exhibit 5

to

Relator's Reply To Defendant Jennifer King Vassel's Brief In Opposition To The Plaintiff's Motion In Limine Regarding False Claims

Department of Health and Human Services

OFFICE OF INSPECTOR GENERAL

MEDICARE ATYPICAL ANTIPSYCHOTIC DRUG CLAIMS FOR ELDERLY NURSING HOME RESIDENTS

Daniel R. Levinson
Inspector General

May 2011
OEI-07-08-00150

OBJECTIVES

To determine the extent to which, from January 1 through June 30, 2007:

1. nursing home residents aged 65 and older had Medicare claims for atypical antipsychotic drugs,
2. Medicare claims for atypical antipsychotic drugs for nursing home residents aged 65 and older were associated with off-label conditions and/or the condition specified in the Food and Drug Administration's (FDA) boxed warning,
3. claimed atypical antipsychotic drugs for nursing home residents aged 65 and older complied with Medicare reimbursement criteria, and
4. claimed atypical antipsychotic drugs were administered in accordance with Centers for Medicare & Medicaid Services (CMS) standards regarding unnecessary drug use in nursing homes.

BACKGROUND

Senator Charles Grassley requested that the Office of Inspector General (OIG) evaluate the extent to which elderly nursing home residents receive atypical antipsychotic drugs and the associated cost to Medicare. Senator Grassley expressed concern about atypical antipsychotic drugs prescribed for elderly nursing home residents for off-label conditions (i.e., conditions other than schizophrenia and/or bipolar disorder) and/or for residents with the condition specified in the FDA boxed warning (i.e., dementia).

FDA has approved the use of eight atypical antipsychotic drugs for the treatment of schizophrenia and/or bipolar disorder. Side effects associated with these drugs include increased risk of death in elderly persons with dementia. Medicare requires that drugs be used for medically accepted indications supported by one or more of three compendia to be eligible for reimbursement. CMS sets standards to ensure that nursing home residents' drug therapy regimens are free from unnecessary drugs, such as drugs provided in excessive doses or for excessive durations.

We used Medicare claims data from Part B and Part D and the Minimum Data Set to identify Medicare claims and payments for atypical antipsychotic drugs for elderly (i.e., aged 65 and older) nursing

home residents from January 1 through June 30, 2007. Using medical record documentation, medical reviewers completed a medical record review instrument to determine the extent to which these drugs were provided to residents diagnosed with conditions that were off-label and/or specified in the boxed warning and whether Medicare erroneously paid for these drugs. Based on medical reviewers' responses, we also determined whether drugs associated with these claims were provided in compliance with CMS standards for drug therapy in nursing homes.

FINDINGS

Fourteen percent of elderly nursing home residents had Medicare claims for atypical antipsychotic drugs. Of the 2.1 million elderly nursing home residents, 304,983 had at least 1 Medicare claim for an atypical antipsychotic drug from January 1 through June 30, 2007. Claims for elderly nursing home residents accounted for 20 percent of the total 8.5 million claims for atypical antipsychotic drugs for all Medicare beneficiaries during the review period. Claims for these residents amounted to $309 million.

Eighty-three percent of Medicare claims for atypical antipsychotic drugs for elderly nursing home residents were associated with off-label conditions; 88 percent were associated with the condition specified in the FDA boxed warning. Using medical reviewers' responses, we determined that, during the review period, almost 1.4 million atypical antipsychotic drug claims were for elderly nursing home residents diagnosed with conditions that were off-label and/or were specified in the boxed warning. Physicians are not prohibited from prescribing drugs for off-label conditions or in the presence of the condition(s) specified in the FDA boxed warning.

Fifty-one percent of Medicare atypical antipsychotic drug claims for elderly nursing home residents were erroneous, amounting to $116 million. For the period of January 1 through June 30, 2007, we determined from medical record review that over 726,000 of the 1.4 million atypical antipsychotic drug claims for elderly nursing home residents did not comply with Medicare reimbursement criteria. The claimed drugs were either not used for medically accepted indications as supported by the compendia or not documented as having been administered to the elderly nursing home residents.

Twenty-two percent of the atypical antipsychotic drugs claimed were not administered in accordance with CMS standards regarding unnecessary drug use in nursing homes. For the 6-month review period, we determined using medical record review that 317,971 Medicare claims ($63 million) were associated with atypical antipsychotic drugs that were not administered according to CMS standards for drug regimens in nursing homes. Nursing homes' noncompliance with these standards (e.g., providing drugs in excessive doses or for excessive durations) does not cause Medicare payments for these drugs to be erroneous because the payments are made on behalf of the residents, not the nursing homes. However, failure to comply with CMS standards may affect nursing homes' participation with Medicare.

RECOMMENDATIONS

To ensure that payments for atypical antipsychotic drugs are correct and that elderly nursing home residents are free from unnecessary drugs, we recommend that CMS:

Facilitate access to information necessary to ensure accurate coverage and reimbursement determinations.

Assess whether survey and certification processes offer adequate safeguards against unnecessary antipsychotic drug use in nursing homes.

Explore alternative methods beyond survey and certification processes to promote compliance with Federal standards regarding unnecessary drug use in nursing homes.

Take appropriate action regarding the claims associated with erroneous payments identified in our sample.

AGENCY COMMENTS AND OFFICE OF INSPECTOR GENERAL RESPONSE

In its written comments on the draft report, CMS shared the concern of OIG and Congress over whether atypical antipsychotics and other drugs are being appropriately prescribed for elderly nursing home residents. CMS concurred with the second, third, and fourth recommendations; however, CMS did not concur with the first recommendation and expressed several general concerns with the report.

In response to the second recommendation, CMS concurred and stated that it has already assessed and made improvements to the survey and certification process. However, CMS acknowledged that other efforts are needed in combination with onsite surveys to achieve the progress desired to safeguard nursing home residents against unnecessary antipsychotic drug use.

Regarding the third recommendation, CMS concurred but did not believe the examples provided in the report to be practicable (excluding provider education). CMS stated that it continues to explore alternative strategies within its statutory authority that more directly address the financial incentives in contractual agreements among drug manufacturers, long term care (LTC) pharmacies, LTC facilities, and consultant pharmacists in nursing homes.

Regarding the fourth recommendation, CMS concurred and will consider what appropriate actions need to be taken when the claims data are received from OIG.

In response to the first recommendation, CMS did not concur, stating that diagnosis information is not a required data element of pharmacy billing transactions nor is it generally included on prescriptions. OIG recognizes that the industry has not developed a standardized way of collecting diagnosis information for prescription drugs. However, without access to diagnosis information, CMS cannot determine the indications for which drugs were used. For this reason, CMS is unable, absent a medical review, to determine whether claims meet payment requirements.

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INTRODUCTION

OBJECTIVES

To determine the extent to which, from January 1 through June 30, 2007:

1. nursing home residents aged 65 and older had Medicare claims for atypical antipsychotic drugs,
2. Medicare claims for atypical antipsychotic drugs for nursing home residents aged 65 and older were associated with off-label conditions and/or the condition specified in the Food and Drug Administration's (FDA) boxed warning,
3. claimed atypical antipsychotic drugs for nursing home residents aged 65 and older complied with Medicare reimbursement criteria, and
4. claimed atypical antipsychotic drugs were administered in accordance with Centers for Medicare & Medicaid Services (CMS) standards regarding unnecessary drug use in nursing homes.

BACKGROUND

Senator Charles Grassley requested that the Office of Inspector General (OIG) evaluate the extent to which elderly nursing home residents receive atypical antipsychotic drugs. For this evaluation, we are using the term "atypical antipsychotic drugs" for second-generation antipsychotic drugs developed to treat psychoses and/or mood disorders. Senator Grassley was specifically concerned about atypical antipsychotic drugs prescribed for elderly nursing home residents for off-label conditions (i.e., conditions other than schizophrenia and/or bipolar disorder) and/or for residents with the condition specified in the FDA boxed warning (i.e., dementia). Moreover, Senator Grassley was concerned about whether Medicare is paying for drugs that may not be in the best interest of elderly nursing home residents.

Atypical antipsychotic drug use by elderly nursing home residents has also been an issue in law enforcement activities. For example, in November 2009, the United States reached a $98 million settlement with Omnicare, Inc. (a long-term care (LTC) pharmacy), to resolve allegations that it received kickbacks to recommend drugs, including Risperdal (an atypical antipsychotic), for use in nursing homes. In January 2010, the Department of Justice filed suit against the manufacturer of Risperdal and two subsidiaries alleging that the

companies paid kickbacks to Omnicare, Inc., to induce it to purchase and recommend Risperdal and other drugs for use in nursing homes.[1] The United States has entered into settlements with the manufacturers of several other atypical antipsychotic drugs to resolve allegations that the manufacturers promoted their drugs for uses that were not approved by FDA and were not reimbursable under Federal health care programs. The marketing of atypical antipsychotic drugs was outside the scope of this evaluation.

The OIG mission is to protect the integrity of Department of Health & Human Services (HHS) programs and the health and welfare of the beneficiaries of those programs. In fulfilling this mission, OIG has conducted numerous studies examining the correctness of Medicare payments and the care of program beneficiaries residing in nursing homes. This study supports the OIG mission in that it seeks to identify vulnerabilities, detect waste and abuse, and promote efficiency and effectiveness in HHS programs. More specifically, this study addresses ongoing concerns regarding claims for atypical antipsychotic drugs prescribed for elderly nursing home residents for off-label conditions and/or in the presence of the condition specified in the FDA boxed warning. Further, this study seeks to address OIG-identified top management challenges for HHS with regard to the integrity of Federal health care program payment methodologies and quality of care by seeking to identify claims for atypical antipsychotic drugs that were paid in error or not in accordance with standards regarding their use in nursing homes.

FDA Drug Approval, Including Atypical Antipsychotic Drugs

FDA has approved eight atypical antipsychotic drugs: Aripiprazole, Clozapine, Olanzapine, Olanzapine/Fluoxetine, Paliperidone, Quetiapine, Risperidone, and Ziprasidone.[2] At the time of our review, FDA had approved all of these drugs for use in the psychiatric treatment of schizophrenia and/or bipolar disorder.[3]

All drugs have benefits and risks. Risks can range from less serious (e.g., an upset stomach) to permanent and potentially life threatening

[1] United States ex rel. Lisitza and Kammerer v. Johnson & Johnson, et al., Civil Action Nos. 07-10288-RGS and 05-11518 RGS (D. Mass.).

[2] These are the generic names for these drugs.

[3] FDA, *Drug Approvals List*. Accessed at http://www.fda.gov on February 22, 2008. At the time of our review, one of the eight atypical antipsychotic drugs was also approved to treat autism.

(e.g., liver damage).[4] If FDA determines that a drug's health benefits for its intended use outweigh its known risks, then FDA approves the drug for marketing for that use.[5]

Risks associated with the use of atypical antipsychotic drugs that apply to all persons and are included in product labeling include, but are not limited to: neuroleptic malignant syndrome, a life-threatening nervous system problem; tardive dyskinesia, a movement problem; high blood sugar and diabetes; and low blood pressure resulting in dizziness and possibly fainting. For a complete description of approved uses and risks of the eight FDA-approved atypical antipsychotic drugs at the time of our review, see Appendix A.

Off-Label Drug Use

After FDA approves a drug to be marketed for a specific use, physicians are permitted to prescribe that drug for other uses. This is commonly referred to as off-label use.

Off-label use is not uncommon. A 2006 study in the *Archives of Internal Medicine* found that off-label uses accounted for 21 percent of prescriptions written in 2001.[6] Specific to atypical antipsychotic drugs, a 2007 Agency for Healthcare Research and Quality (AHRQ) report listed the most common off-label uses: the treatment of agitation in dementia, depression, obsessive-compulsive disorder, posttraumatic stress disorder, personality disorders, Tourette's syndrome, and autism.[7] Additionally, a 2009 study examining antipsychotic drug use among patients in the Department of Veterans Affairs health care system found that 60.2 percent of the individuals who received an antipsychotic drug had no record of a diagnosis for which these drugs are FDA approved (i.e., the drug was used off-label).[8]

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[4] FDA, *Side Effects: Questions and Answers*. Accessed at http://www.fda.gov on November 12, 2009.

[5] FDA, *Approved Drugs: Questions and Answers*. Accessed at http://www.fda.gov on December 30, 2009.

[6] D.C. Radley, S.N. Finkelstein, and R.S. Stafford, "Off-Label Prescribing Among Office-Based Physicians," *Archives of Internal Medicine*, Vol. 166, 2006, pp. 1021–1026.

[7] AHRQ, *Efficacy and Comparative Effectiveness of Off-Label Use of Atypical Antipsychotics* (07-EHCOO3-EF), January 2007.

[8] D.L. Leslie, S. Mohamed, and R.A. Rosenheck, "Off-Label Use of Antipsychotic Medications in the Department of Veterans Affairs Health Care System," *Psychiatric Services,* Vol. 60, No. 9, 2009, pp. 1175–1181.

FDA's Boxed Warning

If drug manufacturers and/or FDA determine during the approval process or after a drug has been approved for marketing that the drug may produce severe or life-threatening risks, FDA requires that drug manufacturers include a boxed warning (also referred to as a black-box warning) on the product's labeling to warn prescribers and consumers of these risks.[9, 10] Physicians are not prohibited from prescribing a drug in the presence of the condition(s) specified in the boxed warning.

In April 2005, FDA issued a public health advisory for atypical antipsychotic drugs.[11] FDA required manufacturers of these drugs to include a boxed warning regarding the increased risk of mortality when these drugs are used for the treatment of behavioral disorders in elderly patients with dementia. See Figure 1 for an example of a boxed warning.

Figure 1. Example of a Boxed Warning

WARNING

Increased Mortality in Elderly Patients with Dementia-Related Psychosis — Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. [this drug] is not approved for the treatment of patients with dementia-related psychosis.

Boxed warning taken from an FDA-approved atypical antipsychotic drug label.
For the purposes of this report, OIG removed the name of the drug in this boxed warning.

Additionally in 2006, FDA revised its patient information sheets specific to each of the eight atypical antipsychotic drugs. These patient information sheets summarize the most important information specific

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[9] In 2006, FDA revised its regulations governing the content and format of labeling for drugs. 71 Fed. Reg. 3922 (Jan. 24, 2006). For categories of drugs described under 21 CFR § 201.56(b)(1), see the section entitled "boxed warnings" at 21 CFR § 201.57(c)(1) and the implementation schedule at 21 CFR § 201.56(c). For categories of drugs described under 21 CFR § 201.56(b)(2), see the section entitled "warnings" at 21 CFR § 201.80(e).

[10] FDA, *An FDA Guide to Drug Safety Terms*. Accessed at http://www.fda.gov on December 29, 2009.

[11] FDA noted that mortality for elderly demented patients with behavioral disorders treated with atypical antipsychotics increased 1.6–1.7 times compared to mortality for those treated with a placebo. FDA, *Public Health Advisory: Deaths With Antipsychotics in Elderly Patients With Behavioral Disturbances,* April 2005. Accessed at http://www.fda.gov on February 22, 2008.

to each drug, including risks and potential side effects. Among the risks and potential side effects listed for all eight atypical antipsychotic drugs is the increased chance of death in elderly persons. See Appendix B for an example of a patient information sheet for one of the eight atypical antipsychotic drugs.

Medicare Reimbursement Criteria for Drugs

Atypical antipsychotic drugs that are provided to Medicare beneficiaries, including those residing in nursing homes, are covered by both the Medicare Part D and Part B programs. Since January 1, 2006, most outpatient prescription drugs for Medicare beneficiaries and dually eligible beneficiaries (i.e., beneficiaries eligible for both Medicare and Medicaid) have been covered through Medicare Part D, which was created by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003.[12]

For drugs to qualify for Medicare Part D reimbursement, the Medicare *Benefit Policy Manual* and the *Prescription Drug Benefit Manual*[13] require that drugs be used for medically accepted indications.[14, 15]

These indications include both the uses approved by FDA and those uses, including off-label, supported by one or more of three compendia: (1) the American Society of Health System Pharmacists, Inc.'s, *American Hospital Formulary Service Drug Information*; (2) the *United States Pharmacopeia-Drug Information* (or its successor publications);

[12] Medicare Prescription Drug, Improvement, and Modernization Act of 2003, P.L. 108-173 (Dec. 8, 2003).

[13] CMS, *Medicare Benefit Policy Manual* (Internet-Only Manual), Pub. 100-02, ch. 15, § 50.4. CMS, *Medicare Prescription Drug Benefit Manual* (Internet-Only Manual), Pub. 100-18, ch. 6, § 10.6.

[14] CMS, State Medicaid Director Letter, *Release #141*, May 4, 2006.

[15] Medicare reimbursement criteria regarding medically accepted indications apply to all Part D drugs with the exception of anticancer drugs. The Medicare Improvements for Patients and Providers Act, or MIPPA, expanded the definition of medically accepted indications for anticancer drugs, effective January 1, 2009, to include drugs used in an anticancer chemotherapeutic regimen even if supported solely by peer-reviewed medical literature.

and (3) Thomson Reuters' *DrugDEX Information System*.[16,17] Hereinafter these are collectively referred to as the compendia.

For drugs to qualify for Medicare Part B reimbursement, the Medicare *Benefit Policy Manual*[18] specifies conditions for coverage of drugs that are administered in an outpatient setting (e.g., physician's office).

CMS Standards Regarding Drug Use in Nursing Homes

As a condition for participation in Medicare, nursing homes must comply with Federal nursing home quality and safety standards.[19] State agencies ensure that these standards are met through the State survey and certification process. For more information regarding the State survey and certification process, see Appendix C.[20, 21] One standard requires that nursing home residents' drug regimens be free from what CMS terms unnecessary drugs.[22] CMS defines unnecessary drugs as those that are used:

- in excessive dose,
- for excessive duration,
- without adequate monitoring,
- without adequate indications for use, and/or

[16] The Social Security Act (the Act) § 1927(g)(1)(B)(i). 42 U.S.C. 1396r-8(g)(1)(B)(i). The compendia described at the Act § 1927(g)(1)(B)(i) are incorporated into the Part D definition of "medically accepted indication" through the Act § 1860D-2(e)(4)(A)(ii), 42 U.S.C. 1395w-102(e)(4)(A)(ii), which refers to the Act § 1927(k)(6), which, in turn, refers to the Act § 1927(g)(1)(B)(i).

[17] Thomson Reuters' *DrugDEX Information System* is hereinafter referred to as *DrugDEX*.

[18] CMS, *Medicare Benefit Policy Manual* (Internet-Only Manual), Pub. 100-02, ch. 15, § 50.

[19] 42 CFR § 488.3(a)(2) (incorporating 42 CFR p.t. 483).

[20] The Act § 1864(a), 42 U.S.C. 1395aa, directs the Secretary of HHS to use the help of State health agencies or other appropriate agencies when determining whether health care entities meet Federal standards.

[21] CMS, *State Operations Manual* (Internet-Only Manual), Pub. 100-07, Appendix PP: Guidance to Surveyors for Long Term Care Facilities, F329, § 483.25(l), Unnecessary Drugs.

[22] 42 CFR § 483.25(l)(1).

- in the presence of adverse consequences[23] that indicate that the dosage should be reduced or discontinued.[24]

Nursing homes' failure to comply with Federal standards regarding unnecessary drugs may affect their participation in Medicare because they would not be meeting their conditions for participation.[25] However, Medicare drug reimbursement policy does not consider payments erroneous when claimed drugs are administered by nursing homes that fail to comply with standards regarding unnecessary drug regimens (e.g., providing drugs in excessive doses or for excessive durations), because drug claims are paid by or on behalf of individual residents, not nursing homes.[26]

CMS requires that nursing home residents who have not previously taken antipsychotic drugs, including atypical antipsychotic drugs, not be given these drugs unless the drug therapy is necessary to treat a specific condition as diagnosed and documented in the medical record.[27] CMS also requires that nursing homes administering antipsychotic drugs ensure that the residents receive gradual dose reductions and behavioral interventions in an effort to discontinue these drugs unless such measures are clinically contraindicated.[28, 29]

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[23] An adverse consequence is an unpleasant symptom or event that is due to or associated with a medication, such as impairment or decline in an individual's mental or physical condition or functional or psychosocial status. CMS, *State Operations Manual* (Internet-Only Manual), Pub. 100-07, Appendix PP: Guidance to Surveyors for Long Term Care Facilities.

[24] 42 CFR § 483.25(l)(1).

[25] Generally, see 42 CFR Part 488. More specifically, see 42 CFR § 488.406 listing available remedies in addition to termination of the provider agreement and 42 CFR § 488.414 describing actions that must be taken when there are repeated surveys with "substandard quality of care," as defined in CFR § 488.301.

[26] Medicare prescription drug insurance covers both brand-name and generic prescription drugs. As in other insurance policies, beneficiaries generally pay a monthly premium, which varies by plan, and a yearly deductible. Beneficiaries also pay a part of the cost of prescriptions, including a copayment or coinsurance. Everyone with Medicare is eligible for this coverage, regardless of income and resources, health status, or current prescription expenses. *Prescription Drug Coverage: Basic Information*, April 2, 2009. Accessed at http://www.medicare.gov on May, 10, 2010.

[27] 42 CFR § 483.25(l)(2)(i).

[28] 42 CFR § 483.25(l)(2)(ii).

[29] CMS, *State Operations Manual* (Internet-Only Manual), Pub. 100-07, Appendix PP: Guidance to Surveyors for Long Term Care Facilities, F329, §483.25(l) Unnecessary Drugs (describing circumstances under which gradual dose reduction is clinically contraindicated).

Related Studies

A 2001 OIG study assessed the extent and nature of psychotropic drug use in nursing homes; that study included four of the eight atypical antipsychotic drugs.[30] The study determined that psychotropic drug use in nursing homes was generally appropriate according to CMS guidelines.

A January 2007 AHRQ report assessed the off-label use of atypical antipsychotic drugs. AHRQ found that all of these drugs increase the risk of death for elderly persons with dementia.[31]

Additionally, CMS issued a data analysis brief in June 2009 reporting that 3 of the top 10 drugs paid for by Medicare Part D in 2006 were atypical antipsychotic drugs. The brief cautioned that Part D data do not provide information about the diagnosis associated with the claimed drug, only that a pharmacy indicated that the drug was dispensed.[32]

METHODOLOGY

Scope

This study included nursing home residents aged 65 or older, hereinafter referred to as elderly nursing home residents, with claims for atypical antipsychotic drugs billed to Medicare Part D and/or Part B from January 1 through June 30, 2007. This study excluded payments for atypical antipsychotic drugs provided under the Medicare Part A Prospective Payment System for short-term stays in skilled nursing facilities.[33]

We included elderly nursing home residents eligible for Medicare services, either as Medicare-only residents or those eligible for both Medicare and Medicaid services (i.e., dually eligible residents). Although we included dually eligible residents, we did not review Medicaid claims for atypical antipsychotic drugs. Elderly nursing home

[30] OIG, *Psychotropic Drug Use in Nursing Homes* (OEI-02-00-00490), November 2001.

[31] AHRQ, *Efficacy and Comparative Effectiveness of Off-Label Use of Atypical Antipsychotics* (07-EHCOO3-EF), January 2007.

[32] CMS, *Data Analysis Brief: Medicare Part D Utilization Trends for Atypical Antipsychotics: 2006–2008*, June 2009. Accessed at http://www.cms.hhs.gov on November 9, 2009.

[33] For skilled nursing facility stays of 100 days or less, prescription drug costs are included in the case-mix adjusted per diem Prospective Payment System rates covered by Part A. These costs were excluded from our analysis because they are not individually quantifiable based on claims data.

residents not eligible for Medicare benefits (i.e., Medicaid-eligible-only residents or those covered solely by private pay) were excluded from this study.

Further, while this study evaluated the extent to which claims for atypical antipsychotic drugs met Medicare reimbursement criteria and determined whether these drugs were provided in accordance with CMS standards regarding unnecessary drug use, this study did not evaluate the medical decisions used to determine each resident's treatment. This study did not evaluate the conduct of drug manufacturers and/or LTC pharmacies with regard to atypical antipsychotic drugs. This study also did not evaluate nursing home survey and certification processes, including those used to review nursing homes' compliance with standards regarding unnecessary drug use.

Data Sources

Identifying atypical antipsychotic drug claims. From CMS, we obtained Medicare Part D Prescription Drug Event (PDE) data and Part B program data containing only final action claims for the period January 1 through June 30, 2007.[34] We used drug codes[35] associated with atypical antipsychotic drugs from these data to identify claims for atypical antipsychotic drugs.

From each of these claims, we matched the Health Insurance Claim Number to the Medicare Enrollment Database to identify Social Security numbers (SSN) for all Medicare beneficiaries with claims for these drugs. Medicare allowed 8.5 million claims for atypical antipsychotic drugs for all Medicare beneficiaries from January 1 through June 30, 2007.

Identifying elderly nursing home residents with antipsychotic drug claims. From CMS, we obtained 2007 Minimum Data Set (MDS) data for all nursing home residents. We used the nursing home admission and discharge dates in the MDS to identify beneficiaries residing in nursing homes at any time during our 6-month review period. We then identified elderly nursing home residents by date of birth. We

[34] PDE records may be amended or deleted up to 6 months after the end of the payment year. After that point, CMS considers them to be final action claims. Final action claims data include all adjustments.

[35] Drug codes included in Part D are National Drug Codes and drug codes included in Part B are Healthcare Common Procedure Coding System codes. See Appendix D for detailed methodology regarding drug codes.

determined that 2,158,801 elderly beneficiaries resided in nursing homes at some time during our study period.

To identify elderly nursing home residents with atypical antipsychotic drug claims, we matched the SSNs from the data match described above when identifying atypical antipsychotic drug claims against the SSNs in MDS data. We identified 1,678,874 Part D and Part B claims for atypical antipsychotic drugs for elderly nursing home residents during the review period.[36]

Data Stratification and Sample Selection

We used available diagnosis codes[37] to identify diagnoses for each elderly nursing home resident with claims for atypical antipsychotic drugs.[38] Using these data, we stratified claims based on whether the data indicated that the beneficiaries lacked an FDA-approved condition[39] for the drug associated with each claim (i.e., the drug was used off-label) and/or whether the beneficiaries had been diagnosed with dementia (i.e., the drug was used in the presence of the condition specified in the boxed warning).

The four strata are as follows:

- an FDA-approved condition and no dementia (i.e., the drug was used neither for an off-label condition nor in the presence of the condition specified in the boxed warning);
- an FDA-approved condition and dementia (i.e., the drug was used in the presence of the condition specified in the boxed warning only);
- no FDA-approved condition and no dementia (i.e., the drug was used for an off-label condition only); and
- no FDA-approved condition and dementia (i.e., the drug was used for both an off-label condition and in the presence of the condition specified in the boxed warning).

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[36] We identified 1,678,441 Part D and 433 Part B claims for atypical antipsychotic drugs.

[37] Because Part D data do not include diagnosis codes, we used the following claims data from 2006 and 2007 to identify the diagnoses: MDS data; Medicare Part B physician and outpatient claims; and Medicare Part A home health, hospice, inpatient, and skilled nursing facility claims. See Appendix D for a more detailed methodology regarding diagnosis codes.

[38] We matched the beneficiaries' Health Insurance Claim Numbers and SSNs across MDS and Part A and Part B claims data to identify diagnosis codes.

[39] For the purposes of this report, an FDA-approved condition is a medical indication for which the FDA had approved the use of a drug at the time of our review period.

The intent of this stratification was to enable us to determine whether the presence or absence of the conditions indicated in the strata affected compliance with Medicare reimbursement criteria and CMS standards regarding unnecessary drug use in nursing homes.

We selected a random sample of 175 claims from each of the 4 strata, for a total of 700 claims. This included oversampling by 100 claims (25 in each stratum) to account for nursing homes we might choose not to contact because of ongoing OIG investigations and nonrespondent nursing homes. Table D-1 in Appendix D shows the sample size and corresponding population of claims for each stratum.

Medical Record Review and Data Analysis

We consulted with a medical record review contractor to select board-certified psychiatrists knowledgeable in the prescribing of atypical antipsychotic drugs for the elderly (hereinafter referred to as medical reviewers). The contractor hired the medical reviewers to review requested documentation from residents' medical records and complete a medical record review instrument for each record.

We developed a letter to request documentation from the nursing home in which each resident lived at the time of the sampled claim.[40] The contractor sent this letter to each nursing home up to three times at predetermined intervals to obtain the requested documentation. For information about the specific documentation requested, see Appendix D.

We instructed the medical record review contractor to provide to the medical reviewers the first 150 complete records received for each stratum, for a total of 600 records.[41] Therefore, our projections are based only on those claims for which medical review was conducted (600 of the 700 sampled claims) and will not equal the known universe of claims (1.7 million) during the study period. Although a nonresponse analysis showed statistically significant differences between the types of nursing homes from which claims were and were not reviewed, additional analysis found no statistically significant evidence that the results presented in our findings were biased because of nonresponse (see Appendix E).

[40] Nursing home contact information was obtained through MDS and Online Survey Certification and Reporting data.

[41] Appendix D explains requirements for a medical record to be considered complete.

Using the medical record documentation, medical reviewers completed a medical record review instrument for OIG to determine whether the claimed drug was used for an off-label condition and/or in the presence of the condition specified in the boxed warning, and whether the claim met Medicare reimbursement criteria. Based on medical reviewer responses, we also determined whether claimed drugs were administered in accordance with CMS standards regarding unnecessary drug use in nursing homes. We determined claims for drugs to be erroneously paid if they were undocumented[42] or did not meet Medicare reimbursement criteria regarding medically accepted indications supported by the compendia. For detailed information regarding the use of the compendia in this study, see Appendix D. Medicare claims for drugs not administered in accordance with CMS standards regarding unnecessary drug use in nursing homes were not considered erroneously paid.

In many cases, medical reviewers determined that documentation from the medical records supported diagnoses that were different from those listed in the data sources we used for stratification. For the purposes of our analyses and findings in this report, we used the diagnoses determined by medical reviewers and not the diagnoses indicated in claims data. See Table D-2 in Appendix D. Although we found no statistically significant differences in error rates among the strata, we did find differences in error rates among the diagnosis groups identified by medical reviewers. Appendix D explains these differences and error rates.

Limitations

Medical reviewers reviewed only the documentation provided by nursing homes. Medical reviewers did not conduct in-person observations of the residents, interview the residents or clinical staff, or conduct a pharmacist's medication regimen review.[43]

[42] Claims were undocumented if the medical record documentation provided by the nursing facility did not support the resident's receipt of the drug associated with the sampled claim.

[43] A pharmacist's medication regimen review is a thorough evaluation of a beneficiary's medication regimen, with the goal of promoting positive outcomes and minimizing adverse consequences associated with drugs. CMS, *State Operations Manual* (Internet-Only Manual), Pub. 100-07, Appendix PP: Guidance to Surveyors for Long Term Care Facilities, F329, § 483.25(l), Unnecessary Drugs.

DrugDEX is an electronically created and maintained system in which quarterly updates replace older versions. We consulted several sources to obtain historical copies of *DrugDEX*, including CMS, FDA, the Library of Congress, and the National Institutes of Health, but none of these sources possessed a version that covered our review period. Therefore, we used the 2008 version of *DrugDEX*, which was the version we could access that most closely covered our review period.

Standards

This study was conducted in accordance with the *Quality Standards for Inspection and Evaluation* issued by the Council of the Inspectors General on Integrity and Efficiency.

Fourteen percent of elderly nursing home residents had Medicare claims for atypical antipsychotic drugs

From January 1 through June 30, 2007, 304,983 (14 percent) of the 2.1 million elderly nursing home residents had at least 1 Medicare claim for an atypical antipsychotic drug. Claims for elderly nursing home residents accounted for 20 percent (1,678,874) of the 8.5 million atypical antipsychotic drug claims for all Medicare beneficiaries during the review period. Table 1 provides an overview of the number of Medicare claims and dollar amounts for elderly nursing home residents by atypical antipsychotic drug from January 1 through June 30, 2007.

Table 1: Number of Medicare Claims and Amount for Each Atypical Antipsychotic Drug (January 1 through June 30, 2007)

Generic Drug Name	Claims	Amount
Quetiapine	627,661	$85,847,131
Risperidone	536,600	$87,161,507
Olanzapine	356,695	$94,055,067
Aripiprazole	83,756	$29,565,887
Ziprasidone	44,681	$10,067,477
Clozapine	27,294	$1,691,718
Olanzapine/Fluoxetine	1,521	$431,799
Paliperidone	666	$207,731
Total	**1,678,874**	**$309,028,317**

Source: OIG analysis of Medicare Part B and Part D claims data, 2009.

The total dollar amount for atypical antipsychotic drug claims for elderly nursing home residents during the review period was $309 million, with an average dollar amount of $184 per claim. The average dollar amount for a 1-day supply of these drugs was $7.26. Dollar amounts ranged from $4.53 to $13.28 per claimed drug, depending on the drug. Further, 17 percent of elderly nursing home residents with claims for atypical antipsychotic drugs had claims for more than one of these drugs during the review period.

Eighty-three percent of Medicare claims for atypical antipsychotic drugs for elderly nursing home residents were associated with off-label conditions; 88 percent were associated with the condition specified in the FDA boxed warning

For the 6-month review period, we determined through medical record review that 83 percent (1,197,442) of atypical antipsychotic drug claims were for elderly nursing home residents diagnosed with conditions for which the drugs' use was not approved by FDA (i.e., the drugs were used off-label). Eighty-eight percent (1,263,641) of the drug claims were for residents diagnosed with dementia (the condition specified in the FDA boxed warning). In total, 95 percent (nearly 1.4 million) of Medicare claims for atypical antipsychotic drugs were for elderly nursing home residents diagnosed with off-label conditions and/or the condition specified in the boxed warning. Physicians are not prohibited from prescribing drugs for off-label conditions or in the presence of the condition(s) specified in the boxed warning.

Table 2 provides an overview of the number and percentage of Medicare claims for atypical antipsychotic drugs used for off-label conditions and/or in the presence of the condition specified in the boxed warning. For point estimates and confidence intervals for selected statistics, see Appendix F.

Table 2: Number and Percentage of Medicare Claims for Atypical Antipsychotic Drugs (January 1 Through June 30, 2007)

Indication for Use of Claimed Drug	Number of Claims	Percentage of Reviewed Claims
For off-label conditions	1,197,442	83.1%
In the presence of the condition specified in the FDA boxed warning	1,263,641	87.7%
For off-label conditions and in the presence of the condition specified in the FDA boxed warning	(1,088,260)	(75.5%)
For off-label conditions and/or in the presence of the condition specified in the FDA boxed warning	1,372,823	95.3%
Neither for off-label conditions nor in the presence of the condition specified in the FDA boxed warning	68,277	4.7%
Total reviewed (net)	**1,441,100***	**100.0%**
Records not reviewed	237,744	n/a
Total claims	**1,678,874**	**n/a**

Source: OIG medical record review analysis, 2009.

*Projection is based only on reviewed records for reviewed claims and will therefore not equate with the population size listed in Table 1.

Medical reviewers determined that elderly nursing home residents who were prescribed atypical antipsychotic drugs for off-label conditions and/or in the presence of the condition specified in the FDA boxed warning commonly had mental health conditions that required treatment, such as depression, dementia, psychosis not otherwise specified, and/or Alzheimer's disease. Additionally, 89 percent (1,216,823) of these residents exhibited symptoms that presented one or more of the following: a danger to themselves or others, significant inconsolable or persistent distress, a significant decline in functioning, or substantial difficulty in receiving needed care. Medical reviewers also expressed that it is not uncommon for atypical antipsychotic drugs to be used in nursing homes off-label for troublesome emotions or behaviors (e.g., anxiety, depression, complaining, or mild agitation) that may also exist in normal life.

Fifty-one percent of Medicare atypical antipsychotic drug claims for elderly nursing home residents were erroneous, amounting to $116 million

For the 6-month review period, we determined using medical record review that over 726,000 of the 1.4 million claims for atypical antipsychotic drugs did not comply with Medicare reimbursement criteria. The claimed drugs were either not used for medically accepted indications as supported by the compendia (50.2 percent of claims) or not documented as having been administered to elderly nursing home residents (0.3 percent of claims). Using the results of the medical record review, we evaluated only the extent to which claimed drugs met Medicare reimbursement criteria; we did not evaluate the clinical appropriateness of these drugs. Table 3 outlines the number and percentage of Medicare claims with dollar amounts for atypical antipsychotic drugs paid in error.

Table 3: Erroneous Medicare Claims for Atypical Antipsychotic Drugs (January 1 Through June 30, 2007)

Reason for Error	Number of Claims	Percentage of Claims	Amount
Claimed drug not documented*	3,808	0.3%	$559,333
Claimed drug not for medically accepted indications	722,975	50.2%	$115,919,685
Total errors	**726,783**	**50.5%**	**$116,479,018**

Source: OIG medical record review analysis of nursing home records, 2009.

*Undocumented claims are included only for the purposes of completing the table. There were only three undocumented claims in the sample, which is too few to calculate a 95-percent confidence interval for the projections.

Twenty-two percent of the atypical antipsychotic drugs claimed were not administered in accordance with CMS standards regarding unnecessary drug use in nursing homes

For the 6-month review period, we determined from medical record review that 317,971 of the 1.4 million claims were associated with drugs that were not administered according to CMS standards for drug therapy in nursing homes, which CMS terms unnecessary drug use. Claims for these drugs represent approximately $63 million. Nursing homes' failure to comply with CMS standards for drug therapy in nursing homes may affect their participation in Medicare. However, nursing homes' noncompliance with these standards does not cause Medicare payments for these drugs to be erroneous. Forty-two percent of claimed drugs did not comply with CMS standards for more than one reason (e.g., the drug was in an excessive dose and for an excessive duration). Table 4 outlines the number and percentage of Medicare claims with dollar amounts for atypical antipsychotic drugs that did not meet CMS standards.

Table 4: Medicare Claims for Atypical Antipsychotic Drugs Determined Unnecessary According to CMS Standards (January 1 Through June 30, 2007)

Reason Drug Did Not Meet CMS Standards	Number of Claims	Percentage of Claims	Amount
In excessive dose	150,106	10.4%	$36,050,851
For excessive duration	135,199	9.4%	$29,369,213
Without adequate indication(s) for use	115,818	8.0%	$21,396,226
Without adequate monitoring	110,949	7.7%	$18,150,616
In the presence of adverse consequences that indicate that the dosage should be reduced or discontinued	67,923	4.7%	$11,479,869
Total (gross)*	**579,994**	**40.2%**	**$116,446,775**
(Overlapping)	(262,023)	(18.2)%	($53,251,792)
Total (net)*	**317,971**	**22.1%**	**$63,194,984**

Source: OIG medical review analysis of nursing home records, 2009.

*Totals may not sum exactly because of rounding.

Medical reviewers noted that some nursing homes that failed to comply with CMS standards regarding unncecessary drugs may not adequately ensure nursing home residents' health and safety. For example, a medical reviewer noted the following for a beneficiary who received an atypical antipsychotic drug without adequate indications for use: "It clearly seems like [the antipsychotic drug] was ineffective in treating her agitation. Since her agitation was associated with infection and pain, more efforts could have been placed on treating those conditions."

We evaluated Medicare claims for atypical antipsychotic drugs from January 1 through June 30, 2007, and found that 14 percent of the 2.1 million elderly nursing home residents had at least 1 claim for these drugs. We determined through medical record review that 83 percent of claims were associated with atypical antipsychotic drugs used for off-label conditions and 88 percent with those used in the presence of the condition specified by the FDA boxed warning. While physicians are not prohibited from prescribing drugs for off-label conditions or in the presence of conditions specified in an FDA boxed warning, Medicare will pay only for drugs that are used for medically accepted indications approved by FDA or supported by the compendia. Using medical record review, we also determined that 50 percent of claims did not meet these conditions, amounting to $116 million. We further determined through medical record review that 22 percent of the atypical antipsychotic drugs associated with the sampled claims did not comply with CMS standards regarding unnecessary drugs in nursing homes, amounting to $63 million. Nursing homes' failure to comply with these standards may affect their participation in Medicare. However, nursing homes' noncompliance with these standards does not cause Medicare payments for the individual drug claims to be erroneous.

To ensure that payments for atypical antipsychotic drugs are correct and that elderly nursing home residents are free from unnecessary drugs, we recommend that CMS:

Facilitate access to information necessary to ensure accurate coverage and reimbursement determinations

Enhanced claims data could improve CMS's ability to enforce criteria for Medicare drug coverage and reimbursement and to determine whether a drug is covered by Medicare. For Part D claims, expansion of the required data elements to include diagnosis codes could help drug plan sponsors and CMS ensure that a drug meets the definition of a Part D-covered drug (i.e., is used for an FDA-approved indication or a medically accepted indication supported by the compendia). CMS should also consider what other claims data enhancements would facilitate ensuring accurate claims processing and program oversight.

Assess whether survey and certification processes offer adequate safeguards against unnecessary antipsychotic drug use in nursing homes

If any survey and certification processes are determined ineffective, CMS should develop improved mechanisms to ensure that all elderly nursing home residents are protected from unnecessary drugs.

Explore alternative methods beyond survey and certification processes to promote compliance with Federal standards regarding unnecessary drug use in nursing homes

Possible methods include provider education and incentive programs. Moreover, CMS should consider strategies to prevent Medicare payments for drugs by the Part D program and beneficiaries when those drugs were administered in violation of Federal standards. For example, CMS may want to consider making nursing homes responsible for reimbursing the Part D program when claimed drugs violate the CMS standards regarding unnecessary drug use.

Take appropriate action regarding the claims associated with erroneous payments identified in our sample

We will forward information on these claims to CMS in a separate memorandum.

AGENCY COMMENTS AND OFFICE OF INSPECTOR GENERAL RESPONSE

In its written comments on the draft report, CMS shared the concern of OIG and Congress over whether atypical antipsychotics and other drugs are being appropriately prescribed for elderly nursing home residents. CMS concurred with the second, third, and fourth recommendations; however, CMS did not concur with the first recommendation and expressed several general concerns with the report.

In response to the second recommendation, CMS concurred and stated that it had already assessed and made improvements to the survey and certification process. However, CMS acknowledged that other efforts are needed in combination with onsite surveys to achieve the progress desired to safeguard nursing home residents against unnecessary antipsychotic drug use, including efforts to address the financial incentives for unnecessary drug use. OIG recognizes CMS's previous efforts to improve the detection of unnecessary drug use through the survey and certification processes; however, OIG recommends that CMS

use its authority through the survey and certification processes to hold nursing homes accountable when unnecessary drug use is detected.

Regarding the third recommendation, CMS concurred but did not believe the examples provided in the report to be practicable (excluding provider education). CMS stated that although it can improve provider education in this area, establishing incentive programs and preventing Medicare drug payments and nursing home reimbursement are beyond its statutory authority. However, CMS stated that it continues to explore alternative strategies within its statutory authority that more directly address the financial incentives in contractual agreements among drug manufacturers, LTC pharmacies, facilities, and consultant pharmacists in nursing homes. OIG suggests that CMS either use its existing authority or seek new statutory authority to prevent payment and hold nursing homes responsible for submitting claims for drugs that are not administered according to CMS's standards regarding unnecessary drug use in nursing homes.

Regarding the fourth recommendation, CMS concurred and will consider what appropriate actions need to be taken when the claims data are received from OIG.

In response to the first recommendation, CMS did not concur, stating that diagnosis information is not a required data element of pharmacy billing transactions nor is it generally included on prescriptions. OIG recognizes that the industry has not developed a standardized way of collecting diagnosis information for prescription drugs. However, without access to diagnosis information, CMS cannot determine the indications for which drugs were used. For this reason, CMS is unable, absent a medical review, to determine whether claims meet payment requirements.

CMS also expressed a number of concerns regarding the report background and findings. Specifically, CMS was concerned about the nature of the contractual arrangements involving LTC facilities, LTC pharmacies, LTC consultant pharmacies, and drug manufacturers and/or distributors and the incentives such arrangements provide for inappropriate prescribing practices that may adversely affect the health and safety of LTC residents. CMS expressed the opinion that the report's combining of off-label uses cited in the compendia and uses in contraindication of the boxed warning overstates inappropriate use of atypical antipsychotic drugs. Finally, CMS requested that Part D

formulary policies relating to antipsychotic medications be included in the final report.

In response, although we evaluated the extent to which atypical antipsychotic drugs were prescribed for off-label conditions and/or in the presence of the condition specified in the FDA boxed warning, we did not examine the medical decisionmaking regarding why elderly nursing home residents were prescribed these drugs. Our report is based on a medical record review. We did not examine the influence of arrangements between various actors in the nursing home market on the use of atypical antipsychotic drugs. Therefore, our report cannot comment on the relationship, if any, between atypical antipsychotic drug use and contractual agreements involving LTC facilities, LTC pharmacies, LTC consultant pharmacies, and drug manufacturers and/or distributors. However, based on CMS's comments, we did add background information regarding law enforcement issues with atypical antipsychotic drugs.

In regard to CMS's concern that the report was overstating inappropriate drug use, the report states that off-label prescribing is permissible and not uncommon and that evaluating the medical appropriateness of prescribed drugs was outside the scope of this study. The report does not make any statements regarding inappropriate drug use, although it does identify erroneous payments for atypical antipsychotic drug claims that were erroneous because the claims did not comply with the Medicare payment policy (i.e., claimed drugs were not used for medically accepted indications as supported by the compendia or were not documented as having been administered to elderly nursing home residents). Specifically in response to the congressional request, we included data regarding drugs prescribed for off-label conditions and/or in the presence of the condition specified by the FDA boxed warning. In response to CMS's concern, we changed the finding statement to separately address those atypical antipsychotic drug claims associated with off-label conditions and those associated with the condition specified in the FDA boxed warning. We still present the combined total in the text of the finding.

Lastly, we did not include Part D formulary requirements in the report because we do not believe this information is germane to the report's criteria and methodology.

The full text of CMS's comments can be found in Appendix G.

APPENDIX A

Food and Drug Administration-Approved Atypical Antipsychotic Drugs

Descriptions of each atypical antipsychotic drug listed below are drawn from the Food and Drug Administration's approved labels at the time of our review. The most common side effects listed are those that were considered to be reasonably associated with the use of the drug.

Aripiprazole (Abilify). Indicated for the treatment of schizophrenia and acute manic and mixed episodes associated with bipolar disorder. Side effects include, but are not limited to: increased chance of death in elderly persons; neuroleptic malignant syndrome; tardive dyskinesia; high blood sugar and diabetes; strokes; low blood pressure seen as dizziness, cardiac irregularities, and possibly fainting; seizures; increased body temperature; and difficulty swallowing. The most common side effects (incidence ≥10%) in adult patients in clinical trials were nausea, vomiting, constipation, headache, dizziness, akathisia, anxiety, insomnia, and restlessness.

Clozapine (Clozaril). Indicated for the treatment of severely ill schizophrenic patients who fail to respond adequately to standard drug treatment for schizophrenia and for reducing the risk of recurrent suicidal behavior in patients with schizophrenia or schizoaffective disorder who are judged to be at chronic risk for experiencing suicidal behavior. Side effects include, but are not limited to: increased chance of death in elderly persons, agranulocytosis, seizures, heart problems including myocarditis, lowering of blood pressure, neuroleptic malignant syndrome, tardive dyskinesia, high blood sugar and diabetes, fever, blood clots in the lung, increased blood sugar, and liver disease. The most common side effects (incidence ≥5%) in clinical trials were: central nervous system complaints, including drowsiness/sedation, dizziness/vertigo, headache, and tremor; autonomic nervous system complaints, including excessive salivation, sweating, dry mouth, and visual disturbances; cardiovascular findings, including tachycardia, hypotension, and syncope; gastrointestinal complaints, including constipation and nausea; and fever.

Olanzapine (Zyprexa). Indicated for the treatment of schizophrenia, acute mixed or manic episodes associated with bipolar I disorder, and agitation associated with schizophrenia and bipolar I mania. Side effects include, but are not limited to: increased chance of death in elderly persons, neuroleptic malignant syndrome, tardive dyskinesia, high blood sugar and diabetes, strokes, low blood pressure seen as dizziness and possibly fainting, cardiac irregularities, seizures, liver problems, increased body temperature, and difficulty swallowing. The most common side effects (incidence ≥5% and at least twice that for placebo) include: weight gain, dizziness, postural hypotension, constipation, personality disorder, akathisia, dry mouth, dyspepsia, increased appetite, somnolence, and tremor.

Olanzapine/Fluoxetine (Symbyax). Indicated for the treatment of depressive episodes associated with bipolar disorder. Side effects include, but are not limited to: suicidal thoughts or actions; increased chance of death in elderly persons; neuroleptic malignant syndrome; tardive dyskinesia; high blood sugar and diabetes; strokes; bleeding problems; sexual problems; mania; weakness, confusion, or trouble thinking caused by low salt levels in the blood; low blood pressure seen as dizziness and possibly fainting; cardiac irregularities; seizures; liver problems; increased body temperature; and difficulty swallowing. The most common side effects (incidence ≥5% and at least twice that for placebo) include: disturbance in attention, dry mouth, fatigue, hypersomnia, increased appetite, peripheral edema, sedation, somnolence, tremor, blurred vision, and weight gain.

Paliperidone (Invega). Indicated for the acute and maintenance treatment of schizophrenia. Side effects include, but are not limited to: increased chance of death and strokes in elderly patients with dementia; QT prolongation; neuroleptic malignant syndrome; tardive dyskinesia; high blood sugar and diabetes; dizziness and fainting caused by a drop in blood pressure; impaired judgment, thinking, or motor skills; overheating and dehydration; seizures; difficulty swallowing; suicidal thoughts or actions; persistent erection; fever; and bruising. The most common side effects (incidence ≥5% and at least twice that for placebo) include: extrapyramidal symptoms, tachycardia, akathisia, somnolence, dyspepsia, constipation, weight gain, and nasopharyngitis.

Quetiapine (Seroquel). Indicated for the treatment of schizophrenia and both depressive episodes associated with bipolar disorder and acute manic episodes associated with bipolar I disorder. Side effects include, but are not limited to: increased chance of death in elderly persons; neuroleptic malignant syndrome; tardive dyskinesia; high blood sugar and diabetes; low blood pressure seen as dizziness, cardiac irregularities, and possibly fainting; cataracts; seizures; low thyroid; elevated cholesterol or triglycerides; liver problems; persistent erection; increase or decrease in body temperature; and difficulty swallowing. The most common side effects (incidence ≥5% and at least twice that for placebo) in adults include: somnolence, dizziness, dry mouth, constipation, increase in alanine aminotransferase, weight gain, and dyspepsia.

Risperidone (Risperdal). Indicated for the treatment of schizophrenia and short-term treatment of acute manic or mixed episodes associated with bipolar I disorder. Side effects include but are not limited to: increased chance of death in elderly persons; neuroleptic malignant syndrome; tardive dyskinesia; high blood sugar and diabetes; strokes; low blood pressure seen as dizziness, cardiac irregularities, and possibly fainting; seizures; persistent erection; thrombotic thrombocytopenic purpura; increase or decrease in body temperature; and difficulty swallowing. The most common side effects (incidence ≥10%) include: somnolence, increase in appetite, fatigue, rhinitis, upper respiratory tract infection, vomiting, coughing, urinary incontinence, excessive saliva, constipation, fever, Parkinsonism, dystonia, abdominal pain, anxiety, nausea, dizziness, dry mouth, tremor, rash, akathisia, and dyspepsia.

Ziprasidone (Geodon). Indicated for the treatment of schizophrenia and acute agitation in people with schizophrenia. Side effects include, but are not limited to: dangerous problems with heart rhythm; increased chance of death in elderly persons; neuroleptic malignant syndrome; tardive dyskinesia; high blood sugar and diabetes; low blood pressure seen as dizziness, cardiac irregularities, and possibly fainting; seizures; persistent erection; increase or decrease in body temperature; and difficulty swallowing. The most common side effects (incidence ≥5% and at least twice that for placebo) include: somnolence, respiratory tract infection, extrapyramidal symptoms, dizziness, akathisia, abnormal vision, asthenia, and vomiting.

APPENDIX B

Example of the Food and Drug Administration Atypical Antipsychotic Drug Patient Information Sheet

Patient Information Sheet

[Generic drug name]
(marketed as [brand name])

This is a summary of the most important information about [drug name]. For details, talk to your healthcare professional.

What Is [drug name]?

- [Drug name] is in a class of medications called atypical antipsychotics. Antipsychotic medicines are used to treat symptoms of schizophrenia that may include hearing voices, seeing things, or sensing things that are not there, mistaken beliefs or unusual suspiciousness.
- [Drug name] is used to treat mixed or manic episodes in adults who have a condition called Bipolar I disorder. Bipolar disorder is a mental illness that causes extreme mood swings.

What Are The Risks?

The following are the risks and potential side effects of [drug name] therapy. However, this list is not complete.

- ***Increased chance of death in elderly persons.*** Elderly patients treated with atypical antipsychotics, such as [drug name], for dementia had a higher chance for death than patients who did not take the medicine. [Drug name] is not approved for dementia.
- ***A life-threatening nervous system problem called neuroleptic malignant syndrome (NMS).*** NMS can cause a high fever, stiff muscles, sweating, a fast or irregular heart beat, change in blood pressure, and confusion. NMS can affect your kidneys. NMS is a medical emergency. Call your healthcare professional right away if you experience these symptoms.
- ***A movement problem called tardive dyskinesia (TD).*** Call your healthcare professional right away if you get muscle movements that cannot be stopped.
- ***High blood sugar and diabetes.*** Patients with diabetes or who have a higher chance for diabetes should have their blood sugar checked often.
- ***Strokes*** have happened in older patients treated for mental illness from dementia. [Drug name] is not approved for this use.
- ***Other serious side effects*** with [drug name] may include low blood pressure seen as dizziness, increased heart beat and possibly fainting, seizures, increased body temperature; and difficulty swallowing.
- ***The most common side effects*** may include headache, weakness, nausea, vomiting, constipation, anxiety, problems sleeping, lightheadedness (dizziness), sleepiness, restlessness and rash.

What Should I Tell My Healthcare Professional?

Before you start taking [drug name], tell your healthcare professional if you:

- have or had heart problems
- have or had seizures
- have or had diabetes or increased blood sugar
- are trying to become pregnant, are already pregnant, or are breast-feeding
- drink alcohol

Are There Any Interactions With Drugs or Foods?

Because certain other medications can interact with [drug name] review all medications that you are taking with your healthcare professional, including those that you take without a prescription.

Your healthcare professional may have to adjust your dose or watch you more closely if you take the following:

- blood pressure medicines
- ketoconazole
- quinidine
- carbamazepine
- fluoxetine or paroxetine

Avoid drinking alcohol while taking [drug name].

Is There Anything Else I Need to Know?

- [Drug name] may impair judgment, thinking, or motor skills. You should be careful in operating machinery, including automobiles, until you know how [drug name] affects you.
- It is important to avoid overheating and dehydration lower while taking [drug name]. [Drug name] may make it harder to lower your body temperature.

[Drug name] FDA Approved 2002
Patient Information Sheet Revised 09/2006

Questions? Call Drug Information, 1-888-INFO-FDA (automated) or 301-827-4570
Druginfo@fda.hhs.gov

APPENDIX C

Survey and Certification and Examples of Nursing Home Noncompliance Related to Unnecessary Drugs

To determine a nursing home's compliance with the unnecessary drug requirement, the Centers for Medicare & Medicaid Services (CMS) completes a review for unnecessary drugs through the nursing home's survey and certification process. The objectives of this review are to determine whether (1) each resident is administered only those drug(s) that are clinically indicated in the dose and for the duration to meet the resident's assessed needs; (2) nonpharmacological approaches or alternatives are used when clinically indicated; and (3) gradual dose reduction is attempted, unless clinically contraindicated. This review should also determine whether the nursing home, in collaboration with a drug's prescriber, is monitoring the effectiveness of drug(s) by identifying the parameters for drug monitoring or drug combinations that could pose a risk of adverse consequences. The review should also determine whether the nursing home, in collaboration with a drug's prescriber, recognizes and evaluates the onset or worsening of signs or symptoms or a change in condition to determine whether these effects may be related to a drug regimen and follows up as necessary.

Examples of noncompliance related to unnecessary drugs in nursing homes drawn from CMS's *State Operations Manual* are listed below:[44]

Excessive Dose (Including Duplicate Therapy). Examples of noncompliance related to excessive dose include, but are not limited to: giving a total amount of any medication at one time or over a period of time that exceeds the amount recommended by the manufacturer's recommendations, clinical practice guidelines, evidence-based studies from medical/pharmacy journals, or standards of practice for a resident's age and condition without a documented clinically pertinent rationale; failure to consider periodically the continued necessity of the dose or the possibility of tapering a medication (i.e., gradually reducing the dose); and failure to provide and/or document a clinical rationale for using multiple medications from the same pharmacological class.

Excessive Duration. Examples of noncompliance related to excessive duration include, but are not limited to: (1) continuation beyond the manufacturer's recommended timeframes, the stop date or duration

[44] CMS, *State Operations Manual* (Internet-Only Manual), Pub. 100-07, Appendix PP: Guidance to Surveyors for Long Term Care Facilities, F329, § 483.25(l), Unnecessary Drugs.

indicated on the medication order, facility-established stop order policies, clinical practice guidelines, evidence-based studies from medical/pharmacy journals, or current standards of practice without documented clinical justification; and (2) continuation of a medication after the desired therapeutic goal has been achieved without evaluating whether the medication can offer any additional benefit.

Inadequate Monitoring. Examples of noncompliance related to inadequate monitoring include, but are not limited to: failure to monitor the responses to or effects of a drug and failure to respond when monitoring indicates a lack of progress toward the therapeutic goal or the emergence of an adverse consequence; failure to monitor a medication consistent with the current standard of practice or manufacturer's guidelines; and failure to carry out the monitoring that was ordered or failure to monitor for potential clinically significant adverse consequences.

Inadequate Indications for Use. Examples of noncompliance related to use of a medication without adequate indications include, but are not limited to: failure to document a clinical reason or demonstrate a clinically pertinent rationale, verbally or in writing, for using drug(s) for a specific resident; failure to provide a clear clinical rationale for continuing a drug that may be causing an adverse consequence; and initiation of an antipsychotic drug to manage distressed behavior without considering a possible underlying medical cause (e.g., urinary tract infection, congestive heart failure) or environmental or psychosocial stressor.

Adverse Consequences. Examples of noncompliance related to adverse consequences include, but are not limited to: failure to act (i.e., discontinue a drug, reduce the dose, or provide clinical justification for why the benefit outweighs the adverse consequences) upon a report of the risk for or presence of clinically significant adverse consequence(s).

Use of Antipsychotic Medications Without Gradual Dose Reduction and Behavioral Interventions Unless Clinically Contraindicated. Examples of noncompliance related to this requirement include, but are not limited to: failure to attempt gradual dose reduction in the absence of identified and documented clinical contraindications, prolonged or indefinite antipsychotic use without attempting gradual dose reduction, and failure to implement behavioral interventions to enable attempts to reduce or discontinue an antipsychotic medication.

APPENDIX D

Detailed Methodology

Data Sources

Identifying Atypical Antipsychotic Drug Claims. We obtained final action claims for Medicare Part D program Prescription Drug Event (PDE) and Part B program data. The PDE data are not the same as individual drug claim transactions; they are summary extracts that document the final adjudication of a dispensing event using the Centers for Medicare & Medicaid Services-defined standard fields. However, because these data contain claim-level information, we refer to the PDE and Part B records collectively as claims for the purposes of this study.

Additionally, the Food and Drug Administration (FDA) identifies a drug product by using a National Drug Code (NDC), which is a unique, universal three-segment numerical product identifier for human drugs. NDCs are listed directly in PDE data and crosswalked through Healthcare Common Procedure Coding System (HCPCS) codes in Part B data. At the time of our review, 909 NDC and 11 HCPCS codes were associated with the 8 atypical antipsychotic drugs. We calculated dollar amounts for claims by adding the ingredient cost, dispensing fee, and sales tax for Part D claims and using the allowed payment amount for Part B claims.

Identifying Elderly Nursing Home Residents With Atypical Antipsychotic Drug Claims. We analyzed Medicare Part A inpatient and skilled nursing facility claims data to determine whether a beneficiary's nursing home stay was interrupted by an admission to a different medical facility (i.e., hospital) during our 6-month review period. If these data indicated that a resident was not in the nursing home as identified through the Minimum Data Set (MDS) data at the time of a drug claim, we excluded that beneficiary from our universe of elderly nursing home residents.

Identifying Elderly Nursing Home Residents' Diagnoses for Stratification. For purposes of this report, we identified diagnoses of interest (bipolar disorder, schizophrenia, and dementia) using the following indicators:

- ten fields for International Statistical Classification of Diseases and Related Health Problems (ICD-9) codes listed in Part A home health, hospice, inpatient, and skilled nursing facility claims and Part B outpatient claims;
- two fields for ICD-9 codes in Medicare Part B physician data;

- five fields for ICD-9 codes in MDS data; and
- one specific data field in MDS data for each of the following: dementia, Alzheimer's disease, schizophrenia, and manic depression (i.e., bipolar disorder).

Requesting Medical Records. Documentation requested from nursing homes for each sampled elderly nursing home resident included:

- the first mental health or medical evaluation upon admission to the facility if the beneficiary was already receiving the drug at the time of admission, or
- the hospital discharge summary or evaluation if the drug was first administered during a hospital stay, or
- the evaluation immediately preceding the initiation of the drug if the drug was initiated at the facility.

Additional information requested included documentation for the 6 months prior to and after the date of the sampled claim: pharmacy review documents/drug utilization review forms; daily Medication Administration Records; resident care plans; history and physical notes; physician orders, progress notes, evaluations, and consults; nurses' progress notes; behavior monitoring notes/logs; social services records/notes; and MDS/Resident Assessment Protocol assessments.

A medical record was considered complete and forwarded to medical reviewers if (1) the nursing home provided the resident's date of admission to the facility and information regarding when the drug associated with the sampled claim was first administered to the resident and (2) all requested documents were received or the reason(s) for any missing requested documents were provided.

Identifying Medically Accepted Indications for Use of Atypical Antipsychotic Drugs. We identified the medically accepted indications from each of the three statutorily named compendia for the use of the eight atypical antipsychotic drugs included in our review.[45] If an indication was noted in

[45] At the time of our review, the three statutorily named compendia were: (1) the *American Hospital Formulary Service Drug Information*, (2) the *United States Pharmacopeia-Drug Information* (or its successor publications), and (3) *the DrugDEX Information System*. Prior to our review period, the *American Medical Association Drug Evaluations* was included in the list of statutorily named compendia but was incorporated into the *United States Pharmacopeia-Drug Information* in 1994 and discontinued in 1996.

any of the three compendia for a drug, we included that indication on that drug's list of accepted indications.[46] Medically accepted indications identified from each compendium included both FDA-approved and off-label uses.

Data Analysis

Identifying Claimed Drugs That Met Medicare Reimbursement Criteria. We used the diagnosis determined by medical reviewers for each resident to determine whether the claimed drug met Medicare reimbursement criteria. We matched the resident's diagnosis to the list of medically accepted indications for the claimed drug that each resident received. If the resident's diagnosis was not found on the claimed drug's list of medically accepted indications, then the claimed drug did not meet Medicare reimbursement criteria. We determined claims for drugs to be erroneously paid if they were undocumented or did not meet Medicare reimbursement criteria.

Sampling Frame and Strata.
We stratified claims based on whether the data indicated that the claimed drug was used off-label and/or in the presence of the condition specified in the boxed warning (see Table D-1).

Table D-1: Original Sampling Frame and Number of Claims in Each Stratum

Stratum	Stratum Definition (Diagnoses)	Claims (Population)	Claims (Sample)
1	FDA-approved condition* and no dementia	149,301	175
2	FDA-approved condition and dementia	510,725	175
3	No FDA-approved condition and no dementia	77,795	175
4	No FDA-approved condition and dementia	941,053	175
Total**		**1,678,874**	**700**

Source: Office of Inspector General (OIG) analysis of 2008 MDS and Medicare Part A, Part B, and Part D claims data.
*For the purposes of this report, an FDA-approved condition is a medical indication for which FDA had approved the use of a drug at the time of our review period.
**The population figures are based on diagnosis data in the Medicare Part A and Part B claims and MDS system.

[46] We used the versions of the compendia published closest to our review period. We used the 2007 versions of *American Hospital Formulary Service Drug Information* and *United States Pharmacopeia-Drug Information*. We used the 2008 version of *DrugDEX*; see the Limitations section of this report for more information.

Medical reviewers determined that elderly nursing home residents' diagnoses in the medical record were sometimes different from the diagnoses in the data sources we used for sample stratification (see Table D-2).

Table D-2: Sampling Frame With the Number of Claims in Each Diagnosis Group After Medical Reviewers Determined Diagnoses

Stratum	FDA-Approved Condition and No Dementia	FDA-Approved Condition and Dementia	No FDA-Approved Condition and No Dementia	No FDA-Approved Condition and Dementia	Claims (Medical Review)
1	54	19	50	27	150
2	6	49	5	90	150
3	2	1	76	71	150
4	0	3	4	143	150
Total	**62**	**72**	**135**	**331**	**600**

Source: OIG medical review analysis of nursing home records, 2009.

Determining Relationship of Diagnosis Groups to Error Rates. Our analysis identified differences in rates of payment error among the four diagnosis groups (see Table D-2 above). Because FDA-approved conditions are medically accepted indications, claims for atypical antipsychotic drugs prescribed to elderly nursing home residents diagnosed with such conditions were not considered errors. For the claimed drugs that were determined to be used off-label, 62 percent did not have medically accepted indications and were therefore in error.

Our analysis also identified differences in rates of compliance with CMS standards regarding unnecessary drugs among the diagnosis groups. The 34 percent of claims for drugs prescribed for residents who were not diagnosed with dementia were significantly more likely to comply with CMS criteria regarding unnecessary drugs than the 21 percent of claims for drugs prescribed for residents who were diagnosed with dementia (i.e., the condition specified in the FDA boxed warning).[47]

[47] All references to error rates are statistically significant at the 95-percent confidence level.

APPENDIX E

Nonresponse Analysis

We examined the potential for effects of nonresponse bias on key statistics. We analyzed how nonresponse of the 100 sampled claims for which medical review was not conducted may have affected our estimates used in this report.

For the purposes of this analysis, we considered all records that were not reviewed as nonrespondents. A total of 100 sampled claims did not receive medical review because 1 nursing home was under investigation, 39 provided the requested documentation after 150 records had already been received for the corresponding stratum, 21 did not provide sufficient records for review, 3 indicated that the beneficiary was not a resident at the time of the sampled claim, and 36 did not respond to our record request.

We compared reviewed claims to nonreviewed claims according to the following six variables: type of nursing home ownership, whether the nursing home was part of a chain, the nursing home's total number of beds, beneficiary age, beneficiary gender, and beneficiary race. We determined whether reviewed and nonreviewed claims differed statistically at the 95-percent confidence level on these variables and found only two statistically significant differences. Claims for residents in for-profit nursing homes were less likely to have been reviewed (83.1 percent) compared with not-for-profit (92.8 percent) and government (90.1 percent) nursing homes. Also, claims for residents in nursing homes that were part of a chain were less likely to have been reviewed (81.8 percent) compared with all other claims (90.0 percent).

Because claims for residents in for-profit nursing homes and in chain nursing homes were underrepresented in our sample, we investigated whether this might bias our results. To do this, we first classified the reviewed claims into six categories corresponding to the ownership and chain variables. Then we assigned the average of reviewed values to nonreviewed claims within the same ownership and chain categories. Finally, we determined whether estimates based on both reviewed actual values and nonreviewed imputed values differed significantly from the estimates based only on the reviewed values. Based on this analysis, we found no statistical evidence that our results were biased because of nonresponse.

APPENDIX F

Point Estimates and Confidence Intervals for Selected Statistics

Description	Sample Size (n)	Point Estimate	95-Percent Confidence Interval
Percentage of claims for drugs used for off-label conditions and/or in the presence of the condition specified in the FDA boxed warning (net)	600	95.3	94.0–96.5
Total claims for drugs used for off-label conditions and/or in the presence of the condition specified in the FDA boxed warning (net)	600	1,372,823	1,354,910–1,390,736
Percentage of claims for drugs used for off-label conditions	600	83.1	80.3–85.9
Claims for drugs used for off-label conditions	600	1,197,442	1,157,389–1,237,495
Percentage of claims for drugs used in the presence of the condition specified in the FDA boxed warning	600	87.7	85.6–89.8
Claims for drugs used in the presence of the condition specified in the FDA boxed warning	600	1,263,641	1,233,783–1,293,500
Total claims for drugs used for off-label conditions and/or in the presence of the condition specified in the FDA boxed warning (gross)	600	2,461,083	2,409,185–2,512,981
Total claims for drugs used for off-label conditions and/or in the presence of the condition specified in the FDA boxed warning (overlapping)	600	1,088,260	1,043,144–1,133,377
Percentage of claims for drugs used for off-label conditions and/or in the presence of the condition specified in the FDA boxed warning (overlapping)	600	75.5	72.4–78.6
Percentage of claims for drugs used neither for off-label conditions nor in the presence of the condition specified in the FDA boxed warning (net)	600	4.7	3.5–6.0
Total claims for drugs neither off-label nor in the presence of the condition specified in the FDA boxed warning (net)	600	68,277	50,364–86,190
Total claims for which records were reviewed	700	1,441,100	1,379,118–1,492,003
Total claims for which records were not reviewed	700	237,774	186,871–299,756
Percentage of claims for elderly nursing home residents who exhibited symptoms that presented one or more of the following: a danger to themselves or others, inconsolable or persistent distress, a significant decline in functioning, and/or substantial difficulty in receiving needed care	535	88.6	85.3–91.9
Number of claims for elderly nursing home residents who exhibited symptoms that presented the conditions listed above	535	1,216,823	1,171,381–1,262,265
Total errors: percentage (net)	600	50.4	45.5–55.3
Total errors: dollar amount (net)	600	$116,479,018	$100,800,390–$132,157,646
Total errors: claims (net)	600	726,782	655,956–797,608
Number of claims for undocumented drugs	600	3,807	0–9,668
Percentage of claims for undocumented drugs	600	0.3	0.0–0.7
Dollar amount for claims for undocumented drugs	600	$559,333	$0–$1,318,866
Number of claims for drugs without medically accepted indication	600	722,975	652,242–793,706
Percentage of claims for drugs without medically accepted indication	600	50.2	45.3–55.1
Dollar amount for claims for drugs without medically accepted indication	600	$115,919,685	$100,243,543–$131,595,827

continued on next page

Description	Sample Size (n)	Point Estimate	95-Percent Confidence Interval
Percentage of claims for drugs that did not comply with CMS* standards regarding unnecessary drug use in nursing homes (net)	600	22.1	17.8–26.3
Total claims for drugs that did not comply with CMS standards regarding unnecessary drug use in nursing homes (net)	600	317,971	257,214–378,729
Dollar amount for claims for drugs that did not comply with CMS standards regarding unnecessary drug use in nursing homes (net)	600	$63,194,984	$48,933,121–$77,456,846
Percentage of claims for drugs determined to be unnecessary for more than one reason	149	42.4	31.7–53.3
Number of claims for drugs taken in excessive dose	600	150,106	107,499–192,713
Percentage of claims for drugs taken in excessive dose	600	10.4	7.4–13.4
Dollar amount for claims for drugs taken in excessive dose	600	$36,050,851	$24,142,398–$47,959,303
Number of claims for drugs taken for excessive duration	600	135,199	91,706–178,692
Percentage of claims for drugs taken for excessive duration	600	9.4	6.4–12.4
Dollar amount for claims for drugs taken in excessive duration	600	$29,369,213	$17,510,089–$41,228,337
Number of claims for drugs taken without adequate indications for use	600	115,818	75,136–156,500
Percentage of claims for drugs taken without adequate indications for use	600	8.0	5.2–10.8
Dollar amount for claims for drugs taken without adequate indications for use	600	$21,396,226	$13,220,119–29,572,334
Number of claims for drugs taken without adequate monitoring	600	110,949	69,948–151,950
Percentage of claims for drugs taken without adequate monitoring	600	7.7	4.8–10.5
Dollar amount for claims for drugs taken without adequate monitoring	600	$18,150,616	$10,772,976–$25,528,257
Number of claims for drugs taken in the presence of adverse consequences	600	67,923	36,021–99,824
Percentage of claims for drugs taken in the presence of adverse consequences	600	4.7	2.5–6.9
Dollar amount for claims for drugs taken in the presence of adverse consequences	600	$11,479,869	$6,088,283–$16,871,455
Total claims for drugs that did not comply with CMS's standards regarding unnecessary drug use in nursing homes (gross)	600	579,994	437,574–722,414
Percentage of claims for drugs that did not comply with CMS's standards regarding unnecessary drug use in nursing homes (gross)	600	40.2	30.4–50.1
Dollar amount for claims for drugs that did not comply with CMS's standards regarding unnecessary drug use in nursing homes (gross)	600	$116,446,775	$84,276,682–$148,616,869
Total claims for drugs that did not comply with CMS's standards regarding unnecessary drug use in nursing homes (overlapping)	600	262,023	161,822–362,163
Percentage of claims for drugs that did not comply with CMS's standards regarding unnecessary drug use in nursing homes (overlapping)	600	18.2	11.2–25.1
Dollar amount for claims for drugs that did not comply with CMS's standards regarding unnecessary drug use in nursing homes (overlapping)	600	$53,251,792	$32,241,106–$74,262,477

Source: Office of Inspector General medical review analysis of nursing home records, 2009.
*CMS is the Centers for Medicare & Medicaid Services, and FDA is the Food and Drug Administration.

APPENDIX G

Agency Comments

DEPARTMENT OF HEALTH & HUMAN SERVICES

Centers for Medicare & Medicaid Services

Administrator
Washington, DC 20201

DATE: MAR 1 1 2011

TO: Daniel R. Levinson
Inspector General

FROM: Donald M. Berwick, MD
Administrator

SUBJECT: Office of Inspector General (OIG) Draft Report: "Medicare Atypical Antipsychotic Drug Claims for Elderly Nursing Home Residents," (OEI-07-08-00150)

Thank you for the opportunity to review and comment on the subject draft report "Medicare Atypical Antipsychotic Drug Claims for Elderly Nursing Home Residents." The OIG study examined claims for the period January 1 through June 30, 2007. Specifically, the study determined the extent to which:

- Nursing home residents aged 65 and older had Medicare claims for atypical antipsychotic drugs;
- Medicare claims for atypical antipsychotic drugs for nursing home residents aged 65 and older were associated with conditions off-label and/or specified in the Food and Drug Administration's (FDA) boxed warning;
- Claimed atypical antipsychotic drugs for nursing home residents aged 65 and older complied with Medicare reimbursement criteria; and
- Claimed atypical antipsychotic drugs were provided in accordance with Center for Medicare & Medicaid Services (CMS) standards regarding unnecessary drug use in nursing homes.

The concern over whether atypical antipsychotics and other drugs are being appropriately prescribed to elderly nursing home residents is one we share with the OIG and Congress. In particular, we are very concerned about the nature of the contractual arrangements involving long-term care (LTC) facilities, LTC pharmacies, LTC consultant pharmacists, and pharmaceutical manufacturers and/or distributors, and the incentives such arrangements provide for inappropriate prescribing practices that may adversely affect the health and safety of LTC residents. Based on the November 2009 Omnicare settlement, the OIG identified these contractual relationships as the cause of the inducement to over-utilize antipsychotics in nursing

homes, and we strongly believe this should be referenced in this report. We are very concerned that if an official OIG report ignores the causative behavior of the LTC pharmacies, and instead suggests that the problem is limited to a Medicare Part D claims payment issue, the issuance of this report may be used as a defense of the practice, and may seriously interfere with any future efforts of OIG, Department of Justice, and CMS to correct the fundamental problem.

Below is CMS response to the OIG recommendations and additional general comments:

General Comments on OIG Findings

The CMS has additional comments with regard to other study findings. The OIG found that 95 percent of Medicare claims associated with atypical antipsychotic drugs used off-label and /or against the FDA black-box warning. Although a member of Congress requested that the OIG evaluate the extent to which elderly nursing home residents receive atypical antipsychotic drugs, the off-label uses that are cited in the compendia are still considered by law to be medically accepted indications. We believe that reporting these uses together with uses against the boxed warning incorrectly overstates inappropriate use.

The CMS requests that Part D formulary policies relating to antipsychotic medications be included in the final report. With few exceptions (such as brand/generic substitution), all antipsychotics must be on all Part D formularies. Further, Part D sponsors may not impose step therapy or prior authorization requirements for beneficiaries who are taking the drug. Part D sponsors are required to perform retrospective drug utilization reviews and are able to identify non-medically accepted uses through this mechanism.

OIG Recommendation

CMS facilitate access to information necessary to ensure accurate coverage and reimbursement determinations.

CMS Response

We do not concur with OIG's recommendation. Currently, diagnosis information is not a required data element on pharmacy billing transactions nor is it generally included on prescriptions. As such, this information is not readily available to dispensing pharmacists.

The industry has not developed a standardized process to collect diagnosis related information as part of the prescription drug claim. Until such time as state boards of pharmacy require that this information be included on prescriptions, and the industry agrees upon an industry standard for reporting diagnosis-related information as part of the claim, CMS will not add any new data fields to the prescription drug event (PDE) elements until such data is useful and can be used to determine if Part D reimbursement was appropriate.

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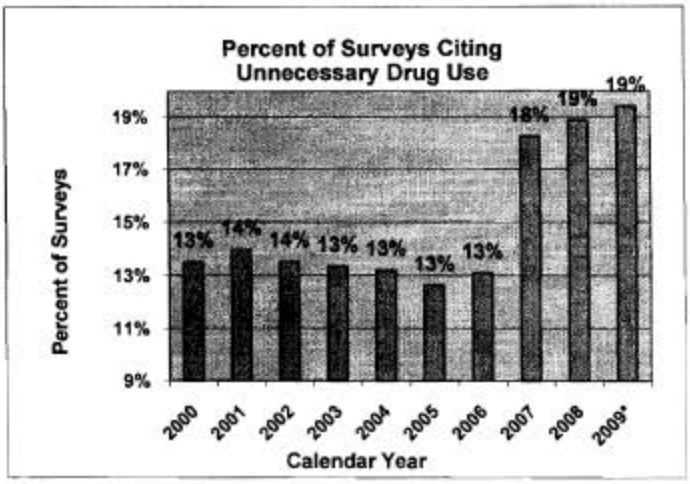
OIG Recommendation

CMS assess whether survey and certification processes offer adequate safeguards against unnecessary antipsychotic drug use in nursing homes.

CMS Response

We concur and have already assessed the survey & certification process and made improvements.

We have assessed survey & certification processes and in late 2006 implemented substantial improvements to the CMS onsite surveys, as described below. One result was a substantial increase in the number of deficiencies cited for unnecessary drug use. As shown in the following graph, the percent of onsite surveys in which the facility was cited for unnecessary drug use increased from 13 percent in 2003-2006 to 18 percent in 2007 and 19 percent in 2008-2009. We noted that the level of deficiencies identified through onsite surveys did not decrease after the reforms were implemented in late 2006, despite the added scrutiny and enforcement that CMS put in place. We therefore concluded that the survey process is pushing against very strong counter-forces, such as financial counter-forces, that require other actions to address the financial incentives for unnecessary drug use.



In September 2006, CMS released S&C Memorandum 06-29 which provided much more information regarding the Issuance of Revised Surveyor Guidance for Unnecessary Medications (F329) and the entire Pharmacy Services section at §483.60. We combined current regulatory language into three tags (F425, F428, and F431) in Appendix PP of the State Operations Manual, as well as medication related revisions in Appendix P Task 5 and Sub-Tasks 5A, 5C, and 5E. The memo identified not only the changes to the guidelines and survey process, but also included information regarding training surveyors regarding these changes.

The CMS entirely revised interpretive guidelines for F329 (Unnecessary Medications), including clarifications of several aspects of medication management and a new medication table that includes medications that are problematic to the nursing home population. We provided an Investigative Protocol that also covers both Medication and Medication Regimen Review issues and severity guidance for F329. This guidance was developed with experts in the area of medications and with survey agency, nursing home advocates and nursing home provider input.

For Pharmacy Services at §483.60, we combined regulatory guidance Tags F425-431 into three tags, F425 Pharmacy Services, F428 Drug Regimen Review, and F431 Labeling and Storage of Drugs and Biologicals. The guidance addresses the provision of pharmaceutical services for the entire distribution system, from ordering and acquisition to administration and disposal of medications to assure a safe system for each resident. In addition, we provided severity guidance for each of these F Tags. The guidance is available on the CMS Website - http://cms.gov/manuals/Downloads/som107ap_pp_guidelines_ltcf.pdf at CFR 483.25(l) F329 – Unnecessary Drugs and CFR 483.60, F425 – F431 Pharmacy Services.

Training materials on these revisions were provided through various methods:

- Power point training materials;
- Two, two-day train-the-trainer sessions in Baltimore in November 2006; and
- A satellite presentation on F329 on December 15, 2006.

We believe that the surveyor guidelines and protocols provide effective direction for surveyors in determining the presence of an unnecessary medication, but that other efforts are needed in combination with onsite surveys to achieve the progress desired to also address the financial incentives for unnecessary drug use.

OIG Recommendation

CMS explore alternative methods beyond survey and certification processes to promote compliance with established Federal standards regarding unnecessary drug use in nursing homes.

CMS Response

CMS concurs with this recommendation, but do not believe the examples provided in the report are practicable (excluding provider education). The report recommendations suggest CMS adopt (1) provider education and incentive programs, (2) strategies to prevent Medicare payments, and (3) requirements for nursing homes to reimburse for claims not meeting CMS standards. Although CMS can identify opportunities to improve provider education in this area, the remaining recommendations (incentive programs, prevention of payment, and nursing home reimbursement) are beyond our statutory authority. CMS is, however, continuing to explore alternative strategies within our statutory authority that more directly address the financial incentives in contractual arrangements among pharmaceutical manufacturers, LTC pharmacies, facilities and consultant pharmacists that are responsible for the increased and unnecessary use of atypical antipsychotics by patients in nursing homes.

OIG Recommendation

CMS should take appropriate action regarding the claims associated with erroneous payments identified in the OIG's sample.

CMS Response

CMS concurs and will consider what appropriate actions need to be taken when the claims data are received from the OIG.

Thank you for the opportunity to review and comment on the draft report.

ACKNOWLEDGMENTS

This report was prepared under the direction of Brian T. Pattison, Regional Inspector General for Evaluation and Inspections in the Kansas City regional office, and Deborah K. Walden, Deputy Regional Inspector General.

Amber Meurs served as the project leader for this study. Other principal Office of Evaluation and Inspections staff from the Kansas City regional office who contributed to the report include Julie Dusold and Rae Hutchison; central office staff who contributed include Robert Gibbons, Sandy Khoury, and Julie Taitsman.

Office of Inspector General

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