

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

UNITED STATES OF AMERICA)	
<i>Ex Rel.</i> Linda Nicholson)	
)	Case No. 10 C 3361
Plaintiffs,)	
)	The Honorable Gary Feinerman
vs.)	
)	
)	Magistrate Judge Sidney I. Schenkier
Lilian Spigelman M.D., Hephzibah)	
Children’s Association, and Sears)	
Pharmacy,)	
)	
Defendants.)	

**MOTION BY RELATOR NICHOLSON FOR LEAVE TO FILE A HIGHLY
RELEVANT RECENT U.S. GOVERNMENT STATEMENT AND REPORT**

Counsel for Relator Nicholson lately (on May 11, 2011) became aware of a report by Daniel R. Levinson, Inspector General of the United States Department of Health and Human Services, entitled, *Medicare Atypical Antipsychotic Drug Claims For Elderly Nursing Home Residents*. (Attached as Exhibit 1.)

Among his recommendations at the end of the report, the Inspector General states, “Medicare will pay only for drugs that are used for medically accepted indications approved by the FDA or supported by the compendia.” (Page 19.) He suggests that the government should, “Explore alternate methods ... to promote compliance with Federal standards regarding unnecessary drug use in nursing homes.” (Page 20.) And

he cites a statistic that fully half of all claims for psychotropic drug prescriptions are not for medically accepted indications. (Appendix D, page 34.)

Relator's case is intended to discourage physicians (psychiatrists) from prescribing psychotropic medications to children not for medically accepted indications. The Inspector General's report concerns prescriptions of psychotropic medications to equally helpless individuals at the opposite end of the age spectrum. However, in both circumstances, psychotropic drugs not for medically accepted indications are paid for by government health care subsidy contrary to identical definitions in the law and clear Congressional intent.

Relator suggests that her litigation is a patently viable "alternative method" to effect compliance with Federal standards, which the HHS OIG's report now suggests will be critical for the future of our health care system. The report is therefore evidence striking directly against the purported reasonableness of the United States' motion to dismiss.

Due to the relevance of this report to the issue of the United States' motion to dismiss her case, Relator moves the Court for leave to file the report and the OIG's official statement about it, published on-line on May 9, 2011 (attached as exhibit 2) for the Court's consideration.

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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**

► E X E C U T I V E S U M M A R Y

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

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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.

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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.

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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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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

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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.

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(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

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.

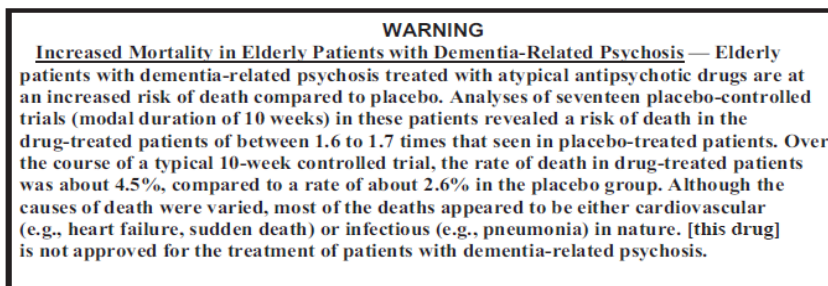
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FDA's Boxed Warning

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



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

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.

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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.

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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).

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- in the presence of adverse consequences²³ 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}

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).

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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.

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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 codes³⁵ 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.

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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 codes³⁷ 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 condition³⁹ 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).

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.

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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.

I N T R O D U C T I O N

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 undocumented⁴² 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.

I N T R O D U C T I O N

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.

► FINDINGS

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.

F I N D I N G S

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.

F I N D I N G S

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.

F I N D I N G S

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.

F I N D I N G S

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 unnecessary 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."

 R E C O M M E N D A T I O N S

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.

R E C O M M E N D A T I O N S

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

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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

R E C O M M E N D A T I O N S

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.

▶ A P P E N D I X 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 $\geq 10\%$) 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 $\geq 5\%$) 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.

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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 $\geq 5\%$ 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 $\geq 5\%$ 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 $\geq 5\%$ and at least twice that for placebo) include: extrapyramidal symptoms, tachycardia, akathisia, somnolence, dyspepsia, constipation, weight gain, and nasopharyngitis.

A P P E N D I X ~ A

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 $\geq 5\%$ 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 $\geq 10\%$) 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 $\geq 5\%$ and at least twice that for placebo) include: somnolence, respiratory tract infection, extrapyramidal symptoms, dizziness, akathisia, abnormal vision, asthenia, and vomiting.

▶ A P P E N D I X 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.

possibly fainting, seizures; increased body temperature; and difficulty swallowing

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.

- **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

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

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

▶ A P P E N D I X 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.

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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.

▶ A P P E N D I X 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;

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- 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.

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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.

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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.


 A P P E N D I X 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.


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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

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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.

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Agency Comments

	DEPARTMENT OF HEALTH & HUMAN SERVICES	Centers for Medicare & Medicaid Services
		<i>Administrator</i> Washington, DC 20201
DATE:	MAR 1 1 2011	
TO:	Daniel R. Levinson Inspector General	
FROM:	Donald M. Berwick, MD /S/ Administrator	
SUBJECT:	Office of Inspector General (OIG) Draft Report: "Medicare Atypical Antipsychotic Drug Claims for Elderly Nursing Home Residents," (OEI-07-08-00150)	
<p>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:</p> <ul style="list-style-type: none">• 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. <p>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</p>		

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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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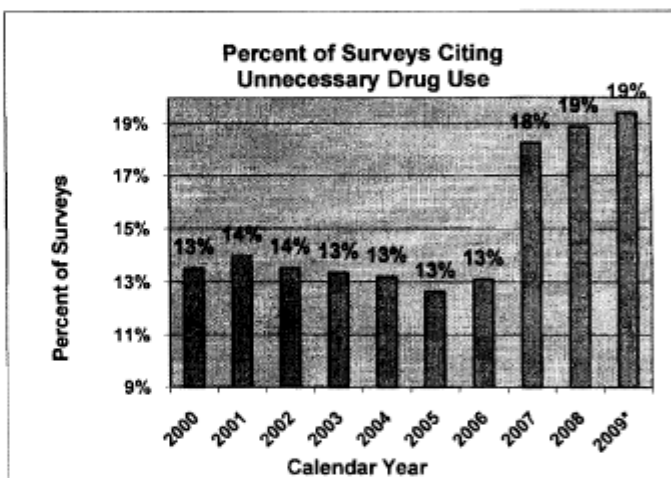
OIG Recommendation

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.

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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(I) 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.

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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.



A C K N O W L E D G M E N T S

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 Taitzman.

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Overmedication of Nursing Home Patients Troubling

May 9, 2011

By Daniel R. Levinson, Inspector General, Department of Health and Human Services

With 46 million beneficiaries, any issue facing Medicare is a cause for concern.

A [government report](#) this week has documented a problem regarding the use of antipsychotic drugs in nursing homes. Too many of these institutions fail to comply with federal regulations designed to prevent overmedication, giving nursing home patients antipsychotic drugs in ways that violate federal standards for unnecessary drug use.

The report also found that these powerful, at times dangerous drugs were often prescribed for uses that are not approved by the Food and Drug Administration and do not qualify as medically accepted for Medicare coverage. Potentially most alarming, 88 percent of the time these drugs were prescribed for elderly patients with dementia, a population the FDA has warned faces an increased risk of death from this class of drugs.

Despite the fact that it is potentially lethal to prescribe antipsychotics to patients with dementia, there's ample evidence that some drug companies aggressively marketed their products towards such populations, putting profits before safety.

Government, taxpayers, nursing home residents, as well as their families and caregivers should be outraged - and seek solutions.

The Department of Health and Human Services initiated the report when a member of Congress questioned how many nursing home residents received a class of antipsychotic drugs introduced in the 1990s, among them risperidone and olanzapine. These drugs, known as "atypical" or "second generation" antipsychotics, replaced (at much higher cost) antipsychotic drugs introduced in the 1950s and 1960s to treat schizophrenia.

The FDA approves these and other drugs based on scientific proof of safety and effectiveness for specific uses. The agency also reviews scientific evidence to determine what warnings a drug must carry.

For atypical antipsychotics, the FDA imposes its strongest safety warning, often called a "black box warning," emphasizing an increased risk of death when used in elderly people with dementia. Physicians can use their medical judgment to prescribe drugs for uses unapproved by the FDA, including to patients for whom the boxed warning applies. Ideally, however, physicians who prescribe in such ways first determine that the benefits outweigh the risks.

The report also found:

- About 14 percent of nursing home residents, or nearly 305,000, had Medicare claims for these antipsychotic drugs.
- A little more than half of the antipsychotic drug claims for which Medicare paid should not have been covered because the claimed drugs were not used for medically accepted indications or not documented as provided to patients.
- For one in five residents, nursing homes dispensed these drugs in a way that violated the government's standards for their use. For example, the prescribed dose was too high or residents were on medication for too long.

Obviously, millions of taxpayer dollars are misspent if the Medicare program is paying for thousands of nursing home residents to get these drugs in violation of program requirements.

And although most physicians and nursing homes dispense antipsychotic drugs with the best interests of patients in mind, it is of great concern that so many nursing home residents are prescribed these drugs in the first place. The report didn't explore this issue, but a series of lawsuits and settlements that DHHS helped bring about suggest that many pharmaceutical companies have improperly promoted these drugs to doctors and nursing homes for many years.

For example, Eli Lilly pled guilty to criminal charges associated with illegally marketing its drug Zyprexa (olanzapine), including to doctors that treat elderly nursing home patients. Several other pharmaceutical companies -- Bristol-Meyers Squibb, Astra Zeneca and Pfizer -- settled government allegations that they improperly promoted their antipsychotic drugs for unapproved uses. Federal prosecution is pending against Johnson & Johnson for allegedly paying millions of dollars in kickbacks to induce Omnicare, the nation's largest long-term care pharmacy, to recommend the use of Risperdal in treating nursing home patients, many of whom

had dementia.

The drug companies have paid billions to resolve these civil and criminal liabilities under federal health and safety laws. But money can't make up for years of corporate campaigns that market drugs with questionable benefits and potentially deadly side effects for vulnerable, elderly patients.

To solve this problem, everyone has a role to play.

Doctors should base prescribing decisions on their best medical judgments, weighing scientific evidence and an especially careful analysis when they are prescribing drugs for off-label use.

Nursing homes and pharmacies that serve the elderly should base drug-dispensing decisions on the best interest of the patient, not on improper influence of drug companies.

Family members of nursing home residents must ask questions about medications that their loved ones take, learning the reasons for their use, proper dosages and possible side effects.

Government must uphold patient safety standards established for nursing homes and combat off-label promotion of these powerful and potentially lethal drugs.

And drug companies should follow laws designed to protect patients and not promote drugs for unapproved uses -- or pay kickbacks to doctors and institutions to influence their prescribing.

As the huge Baby Boom generation ages, 10,000 Americans a day for the next 18 years will become newly eligible for Medicare. The future is challenging enough; we must not leave unaddressed the current, urgent problem of antipsychotic drug use among nursing home patients.

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