

Department of Health and Human Services

**OFFICE OF
INSPECTOR GENERAL**

**SECOND-GENERATION
ANTIPSYCHOTIC DRUG USE
AMONG MEDICAID-ENROLLED
CHILDREN: QUALITY-OF-CARE
CONCERNS**



Daniel R. Levinson
Inspector General

March 2015
OEI-07-12-00320

EXECUTIVE SUMMARY: SECOND-GENERATION ANTIPSYCHOTIC DRUG USE AMONG MEDICAID-ENROLLED CHILDREN: QUALITY-OF-CARE CONCERNS

OEI-07-12-00320

WHY WE DID THIS STUDY

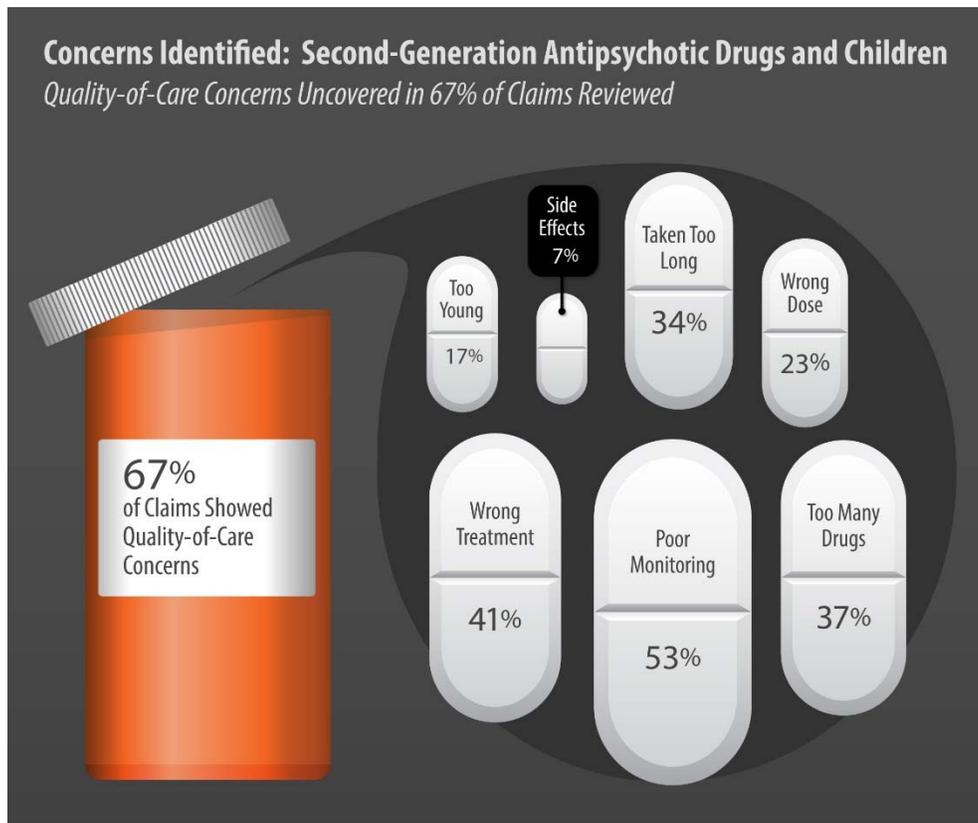
Second-generation antipsychotics (SGAs) are a class of drugs used to treat psychiatric disorders, such as schizophrenia, bipolar disorder, and psychotic depression. SGAs are widely used to treat children enrolled in Medicaid who have mental health conditions. However, SGAs can have serious side effects and little clinical research has been conducted on the safety of treating children with these drugs. Consequently, children’s treatment with SGAs needs careful management and monitoring. This evaluation examines the quality of care provided to children receiving SGAs that were paid for by Medicaid.

HOW WE DID THIS STUDY

We selected a sample of 687 claims for SGAs prescribed to children in California, Florida, Illinois, New York, and Texas. These States represented approximately 39 percent of total Medicaid payments for SGAs in 2011. Board-certified child and adolescent psychiatrists reviewed medical records related to the sampled claims using seven criteria related to quality-of-care concerns (see the chart below for the criteria). We established these criteria on the basis of information and guidelines issued by various Federal and State agencies and professional associations regarding the prescribing of psychotropic drugs to children.

WHAT WE FOUND

The graphic below illustrates the percentages of quality-of-care concerns identified in the medical records associated with claims for SGAs prescribed to children.



Medical reviewers identified multiple quality-of-care concerns for many claims.
Source: OIG analysis of Medicaid claims in five states, 2014.

In the five States, 8 percent of SGAs were prescribed for the limited number of medically accepted pediatric indications. There are only five SGAs with medically accepted pediatric indications. It is not uncommon for doctors to prescribe, or Medicaid to pay for, SGAs for children for indications that are not medically accepted. Medically accepted indications include both uses of drugs approved by the Food and Drug Administration (FDA) and uses supported by one or more of three drug compendia. It is difficult to conduct the clinical trials needed to obtain FDA approval or compendia support for pediatric uses of drugs.

Three of the eleven SGAs carry an FDA boxed warning regarding increased chances of suicidal thinking and behavior in pediatric patients. We found that over a third of SGAs were prescribed in the presence of conditions described in the FDA boxed warning. Physicians are not prohibited from prescribing a drug for a patient who has the condition(s) specified in the FDA boxed warning if the physician judges that the benefits may outweigh the risks.

WHAT WE RECOMMEND

To ensure the quality of the care provided to children receiving SGAs, we made three recommendations to the Centers for Medicare & Medicaid Services (CMS). First, we recommended that CMS work with State Medicaid programs to perform utilization reviews of SGAs prescribed to children. Second, we recommended that CMS work with State Medicaid programs to conduct periodic reviews of medical records associated with claims for SGAs prescribed to children. Third, we recommended that CMS work with States to consider other methods of enhanced oversight of SGAs prescribed to children, such as implementing peer review programs. CMS concurred with all three recommendations.

TABLE OF CONTENTS

Objectives	1
Background	1
Methodology	6
Findings.....	9
In the five States studied, quality-of-care concerns were identified in the medical records for 67 percent of claims for SGAs prescribed to children	9
In the five States studied, 8 percent of SGAs were prescribed for the limited number of medically accepted pediatric uses	12
Conclusion and Recommendations.....	15
Agency Comments and Office of Inspector General Response.....	16
Appendixes	17
A: FDA Boxed Warning Regarding Children on SGA Product Labeling.....	17
B: Sources of Guidance and Information on the Use of SGAs To Treat Children	18
C: Detailed Methodology.....	21
D: Descriptive Data on Population and Sampled Claims	26
E: Statistical Estimates and Confidence Intervals	29
F: Agency Comments.....	31
Acknowledgments.....	35

OBJECTIVES

To determine the extent to which claims for second-generation antipsychotics (SGAs) prescribed to children enrolled in Medicaid in five selected States:

1. presented quality-of-care concerns and
2. were prescribed for indications other than medically accepted indications and/or in the presence of conditions specified in the Food and Drug Administration (FDA) boxed warning.

BACKGROUND

FDA Approval of SGAs

FDA must approve drugs before companies can legally sell them in the United States.¹ If FDA determines that a drug's benefits for its intended use outweigh its known risks, then FDA approves the drug for sale.² At the time of our review, FDA had approved five SGAs for use by children in the treatment of schizophrenia, bipolar disorder, and irritability associated with autistic disorder.^{3,4} The five SGAs that FDA has approved for use by children are aripiprazole, olanzapine, paliperidone, quetiapine fumarate, and risperidone. Aripiprazole and risperidone are approved to treat all three of the diagnoses named above. Olanzapine and quetiapine fumarate are approved to treat schizophrenia and bipolar disorder. Paliperidone is approved to treat only schizophrenia. There are six additional SGAs with FDA-approved uses for adults.⁵

Off-label uses of FDA-approved drugs. After FDA approves a drug for a specific use, physicians are permitted to prescribe that drug for other uses. Prescribing drugs for nonapproved uses is often referred to as “off-label prescribing.” Off-label prescribing is not uncommon, especially for drugs prescribed to

¹ FDA approval of a drug is based on the results of testing for safety and efficacy by the company wishing to sell the drug. FDA, *Development and Approval Process (Drugs)*. Accessed at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm> on May 12, 2014.

² FDA, *Approved Drugs: Questions and Answers*. Accessed at <http://www.fda.gov/drugs/resourcesforyou/consumers/ucm054420.htm> on May 12, 2014.

³ Antipsychotic drugs are separated into two classes: first-generation (or conventional) and second-generation (or atypical). First-generation antipsychotic drugs were introduced in the 1950s; SGAs were introduced in the 1990s.

⁴ These five SGAs are approved by FDA for use by children under age 18. For purposes of this study, we defined “children” to include those 0–17 years old during the review period to conform to the FDA’s age ranges.

⁵ The six additional SGAs with FDA-approved uses for adults are asenapine, clozapine, iloperidone, lurasidone, olanzapine/fluoxetine, and ziprasidone. FDA, *Atypical Antipsychotic Drugs Information*. Accessed at <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm094303.htm> on May 12, 2014.

children, as it is difficult to conduct the clinical trials needed for FDA approval of drugs for the pediatric population.⁶

FDA boxed warning. If drug manufacturers and/or FDA determine that a drug may have severe or life-threatening risks when used to treat patients with specific conditions, FDA requires that the product's labeling include a boxed warning describing those risks.⁷ However, physicians are not prohibited from prescribing a drug for a patient who has the condition(s) specified in the FDA boxed warning if the physician judges that the benefits may outweigh the risks.

As of June 2012, three SGAs—aripiprazole, olanzapine/fluoxetine, and quetiapine fumarate—carried an FDA boxed warning specific to children. The warning describes the increased chance of suicidal thinking and behavior in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders being treated with them. Two of these SGAs that carry the boxed warning—aripiprazole and quetiapine fumarate—are also among the five SGAs that have FDA-approved pediatric uses. See Appendix A for an example of the boxed warning for an SGA.

Medicaid Coverage of Outpatient Prescription Drugs

All State Medicaid programs cover outpatient prescription drugs.⁸ State Medicaid programs must pay for covered outpatient drugs prescribed for medically accepted indications and may pay for outpatient drugs not prescribed for medically accepted indications.

Medically accepted indications. The Act defines “medically accepted indications” as both the uses approved by FDA and those uses, including off-label uses, that are supported by one or more of three compendia.⁹ At the time of our review, only one SGA—risperidone—had any medically accepted indications for pediatric use beyond those approved by FDA.¹⁰ For the other SGAs, there were

⁶ FDA, *Drug Research and Children*. Accessed at <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143565.htm> on April 22, 2014. Institute of Medicine (US) Committee on Clinical Research Involving Children, Field and Berman, eds., *Ethical Conduct of Clinical Research Involving Children*, Washington, DC: National Academies Press, 2004; pp. 59 and 61. Accessed at <http://www.ncbi.nlm.nih.gov/books/NBK25557/pdf/TOC.pdf> on April 22, 2014.

⁷ FDA, *An FDA Guide to Drug Safety Terms*. Accessed at <http://www.fda.gov/forconsumers/consumerupdates/ucm107970.htm> on May 12, 2014.

⁸ Social Security Act (the Act) § 1905(a)(12); CMS, *Medicaid Prescription Drugs Program*. Accessed at <http://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Prescription-Drugs.html> on May 12, 2014.

⁹ Section 1927(g)(1)(B)(i)(I)–(III) of the Act. The three compendia are (1) the American Society of Health System Pharmacists, Inc.'s *American Hospital Formulary Service Drug Information*, (2) the *United States Pharmacopeia—Drug Information* (or its successor publications), and (3) *DrugDEX Information System*.

¹⁰ Medically accepted indications for risperidone include its FDA-approved uses as well as its use to treat (1) behavioral syndrome-mental retardation and (2) pervasive developmental disorder.

no medically accepted indications beyond the FDA-approved uses; the medically accepted indications and the FDA-approved uses are identical.

Limitations on Medicaid coverage of drugs. Section 1927 of the Act establishes the permissible limitations on and exclusions of Medicaid coverage of outpatient drugs.¹¹ Under section 1927, States can choose to limit or exclude coverage of outpatient drugs if the prescribed uses are not for medically accepted indications.¹²

However, State Medicaid programs may choose to cover outpatient drugs not prescribed for medically accepted indications. Table 1 shows which SGAs have FDA-approved pediatric uses, which SGAs have medically accepted pediatric indications other than the FDA-approved pediatric uses, and which SGAs carry the FDA boxed warning specific to children.

Table 1: FDA-Approved Pediatric Uses, Medically Accepted Pediatric Indications, and FDA Boxed Warnings on Second-Generation Antipsychotics

Drug Name	FDA-Approved Pediatric Use(s)	Medically Accepted Pediatric Indication(s) Other Than FDA-Approved Pediatric Use(s)	FDA Boxed Warning Specific to Children
aripiprazole	Yes	No	Yes
asenapine	No	No	No
clozapine	No	No	No
iloperidone	No	No	No
lurasidone	No	No	No
olanzapine	Yes	No	No
olanzapine/fluoxetine	No	No	Yes
paliperidone	Yes	No	No
quetiapine fumarate	Yes	No	Yes
risperidone	Yes	Yes	No
ziprasidone	No	No	No

Source: Office of Inspector General (OIG) analysis of compendia, 2014.

Four of the five States included in this evaluation—California, Florida, Illinois, and Texas—covered drugs not prescribed for medically accepted indications. These States used information regarding medically accepted indications in making case-by-case coverage decisions, such as decisions on requests for prior

¹¹ Section 1927(k)(2) of the Act defines “covered outpatient drugs” as drugs that are dispensed only upon prescription and that are approved for safety and effectiveness as prescription drugs under the Federal Food, Drug, and Cosmetic Act.

¹² Section 1927(d)(1)(B)(i) of the Act.

authorization.¹³ Of the five States reviewed, only New York limited coverage of drugs to those prescribed for medically accepted indications.

Sources of Guidance and Information on the Use of SGAs To Treat Children

There are no Federal Medicaid requirements regarding the appropriate prescribing of SGAs to children. However, a number of Federal and State agencies and professional associations have issued information and guidelines on the prescribing of such drugs to children.¹⁴ These guidelines and information include:

- **AACAP practice parameter**—The American Academy of Child and Adolescent Psychiatry’s (AACAP) practice parameter on the use of psychotropic medications to treat children identifies practices that may reduce the use of ineffective and inappropriate medications. These practices include developing monitoring plans, using adequate dosages and durations of treatment, and providing a clear rationale for the use of polypharmacy (the concurrent use of multiple drugs).¹⁵
- **HEDIS measures**—The National Committee for Quality Assurance (NCQA) publishes the Healthcare Effectiveness Data and Information Set (HEDIS), which is used to measure the performance of health plans.¹⁶ In July 2014, NCQA published new measures for HEDIS 2015 on the safe and judicious use of antipsychotics in children and adolescents. These measures assess the appropriate use and management of antipsychotic drugs in youth. Reporting on the new measures will begin in June 2015.
- **ACF information memorandum**—On April 11, 2012, the Administration for Children and Families (ACF) released an information memorandum entitled “Promoting the Safe, Appropriate, and Effective Use of Psychotropic Medication for Children in Foster Care.”¹⁷ This memorandum identifies three “outlier practices” that may indicate that issues other than clinical need are influencing the prescribing of SGAs:

¹³ States may require, as a condition of coverage or payment for a covered outpatient drug, that a drug be authorized before it is dispensed. This type of approval is known as prior authorization. Sections 1927(d)(1)(A) and (d)(5) of the Act.

¹⁴ The guidance discussed here covers all psychotropic drugs—a category that includes SGAs and several other types of drugs. Other classes of psychotropic drugs include attention deficit/hyperactivity disorder (ADHD) drugs, antianxiety drugs, antidepressants, first-generation antipsychotics, hypnotics, and mood stabilizers. This study focuses specifically on SGAs.

¹⁵ AACAP, “Practice Parameter on the Use of Psychotropic Medication in Children and Adolescents,” *J. Am. Acad. Child Adolesc. Psychiatry*, 2009; 48(9): 961–973.

¹⁶ State Medicaid programs may report voluntarily on the HEDIS measures.

¹⁷ ACF, *Promoting the Safe, Appropriate, and Effective Use of Psychotropic Medication for Children in Foster Care*, Log No. ACYF-CB-IM-12-03, April 11, 2012. Accessed at <http://www.acf.hhs.gov/sites/default/files/cb/im1203.pdf> on May 12, 2014.

prescribing too many concurrent drugs, prescribing dosages that are too high, and prescribing SGAs to children at too young an age.

- **Report and Resource Guide**—In 2010, a collaboration among 16 States, the Rutgers University Center for Education and Research on Mental Health Therapeutics (CERTs), and the Medicaid Medical Directors Learning Network (MMDLN) produced the *Antipsychotic Medication Use in Medicaid Children and Adolescents: Report and Resource Guide From a 16-State Study* (hereinafter referred to as the *Report and Resource Guide*).¹⁸ This guide contains information on utilization patterns and treatment practices that raise clinical concerns. Among the issues listed are polypharmacy, wrong dosages, and the prescribing of antipsychotic drugs to very young children.¹⁹
- **State utilization guidelines**—State agencies in Florida and Texas have each developed utilization guidelines that can help identify when further review of the treatment of children with SGAs is necessary. These States' guidelines address issues such as polypharmacy, inadequate indications for use of drugs, excessive dosage, and prescribing of drugs to very young children.

For detailed information on these sources of guidance, see Appendix B.

Related Studies

A 2011 Government Accountability Office (GAO) report found that in 2008, children in foster care in five selected States were prescribed psychotropic drugs, including antipsychotic drugs, at higher rates than children not in foster care.²⁰ The GAO report states that the higher rates of usage do not necessarily indicate inappropriate prescribing practices and notes that these higher rates could be due to the greater mental health needs of children in foster care and the challenges of coordinating their medical care. According to the GAO report, hundreds of children in the selected States had drug regimens consisting of five or more psychotropic drugs, although there is no medical evidence to support the concurrent use of this many drugs in children.

¹⁸ CERTs and MMDLN are both funded by the Agency for Healthcare Research and Quality. The 16 States were Alabama, California, Colorado, Illinois, Indiana, Maine, Massachusetts, Missouri, New Hampshire, New York, Oklahoma, Oregon, Pennsylvania, Tennessee, Texas, and Washington. Of these, California, Illinois, New York, and Texas are among the five States included in this evaluation.

¹⁹ *Antipsychotic Medication Use in Medicaid Children and Adolescents: Report and Resource Guide From a 16-State Study*. MMDLN/Rutgers CERTs Publication No. 1, June 2010.

²⁰ The five States included in GAO's study were Florida, Massachusetts, Michigan, Oregon, and Texas. The children studied—both those in foster care and not in foster care—were enrolled in the Medicaid programs of the five States. GAO, *Foster Children: HHS Guidance Could Help States Improve Oversight of Psychotropic Prescriptions* (GAO-12-201), December 2011.

In 2011, OIG released a study on elderly nursing home residents' use of SGAs. This study determined that 14 percent of elderly nursing home residents had Medicare claims for SGAs.²¹ Eighty-three percent of Medicare claims for SGAs for elderly nursing home residents were associated with off-label conditions, and 88 percent were associated with the condition specified in the FDA boxed warning (i.e., dementia).

METHODOLOGY

State Selection

We purposively selected five States for inclusion in this evaluation: California, Florida, Illinois, New York, and Texas. These States were selected because they represented approximately 39 percent of total Medicaid payments for SGAs in 2011.²²

From these five States, we collected all fee-for-service Medicaid-paid claims for SGAs prescribed to children aged 0–17 years old between January 1 and June 30, 2011.²³ We also collected information from each State regarding which children were enrolled in foster care and information on the States' drug coverage policies.

To reduce the overall sample size, answer specific questions, and achieve precise estimates, we stratified the population into four groups based on foster care enrollment and payment amount. We selected a stratified random sample of 687 claims. For a presentation of the stratified sample and detailed methodological information, see Appendix C. For detailed descriptive information on the population of claims and the sampled claims, see Appendix D.

Development of Criteria for Medical Record Review. Because there are no Federal Medicaid requirements defining appropriate use of SGAs to treat children, we reviewed existing guidance and literature to identify criteria for determining whether quality-of-care concerns were present in children's treatment with SGAs. (Specifically, we reviewed all of the sources listed on pages 4 and 5 except for the HEDIS 2015 measures, which at the time had not yet been published.) We identified seven criteria related to quality of care in the treatment of children with SGAs; each criterion is supported by at least three of the sources

²¹ OIG, *Medicare Atypical Antipsychotic Drug Claims for Elderly Nursing Home Residents* (OEI-07-08-00150), May 2011.

²² The 39-percent figure is based on 2011 claims data from the Medicaid Statistical Information System (MSIS).

²³ The claims data collected included only fee-for-service claims. Initial discussions with Medicaid staff indicated that three of the five selected States had no managed-care coverage of SGAs for children during our review period. The other two States indicated that managed-care coverage of these drugs for children represented a very small percentage of paid claims for drugs in the review period.

of guidance previously described. Table 2 describes each of the seven quality-of-care criteria we identified and shows which of the sources of guidance and information that we reviewed address the issue.²⁴

Table 2: Descriptions of and Support for Medical Record Review Criteria and Corresponding Quality-of-Care Concerns

Criterion	Source				
	AACAP Practice Parameter	ACF Memo	<i>Report and Resource Guide</i>	Florida Utilization Guidelines	Texas Utilization Guidelines
Dosage (wrong dose)	X	X	X	X	X
Duration (taken too long)	X	X		X	
Indications for use (wrong treatment)	X		X	X	X
Monitoring (poor monitoring)	X	X	X		X
Polypharmacy (too many drugs)	X	X	X	X	X
Patient age (too young)		X	X	X	X
Side effects	X	X	X	X	X

Source: OIG analysis of guidance documents, 2014.

Review of Medical Records and Claims Data

The psychiatrists who performed the medical reviews were board-certified child and adolescent psychiatrists with extensive experience and expertise in treating children with mental health conditions. To ensure a consistent interpretation of the seven criteria, we provided the contracted psychiatrists with the same sources of guidance and information that we used to develop the criteria. The contracted psychiatrists determined whether quality-of-care concerns existed in each child’s SGA treatment, assessing each of the seven criteria using their clinical experience and judgment. They also identified the diagnosis/diagnoses or indication(s) that the SGAs were prescribed to treat. OIG staff used this diagnosis information, as well the children’s ages, to determine whether the drugs were prescribed for medically accepted indications.

We received records for 485 of the 687 sampled claims for an overall weighted response rate of 75 percent. The remaining 202 claims were undocumented or insufficiently documented, or the providers could not be located to request the records. Specifically, we could not locate or contact the providers or facilities that had custody of the medical records for 170 sampled claims. Although we

²⁴ Because the new HEDIS measures regarding the use of antipsychotic drugs by children had not been published at the time of our review, we could not include them in the sources of guidance we used to develop the medical record review criteria.

were able to contact the providers, we did not receive any medical records for 7 sampled claims, and we received insufficient medical records for an additional 25 claims. See Appendix C for details on the response rates and a nonresponse analysis.

Limitations

It is possible that the children in our sample received SGAs that were not paid for by Medicaid; therefore, these children's use of SGAs may be underestimated. Additionally, the psychiatrists' reviews were based solely on the medical record documentation received; some of the quality-of-care concerns identified could be the result of poor documentation rather than poor quality of care.

Standards

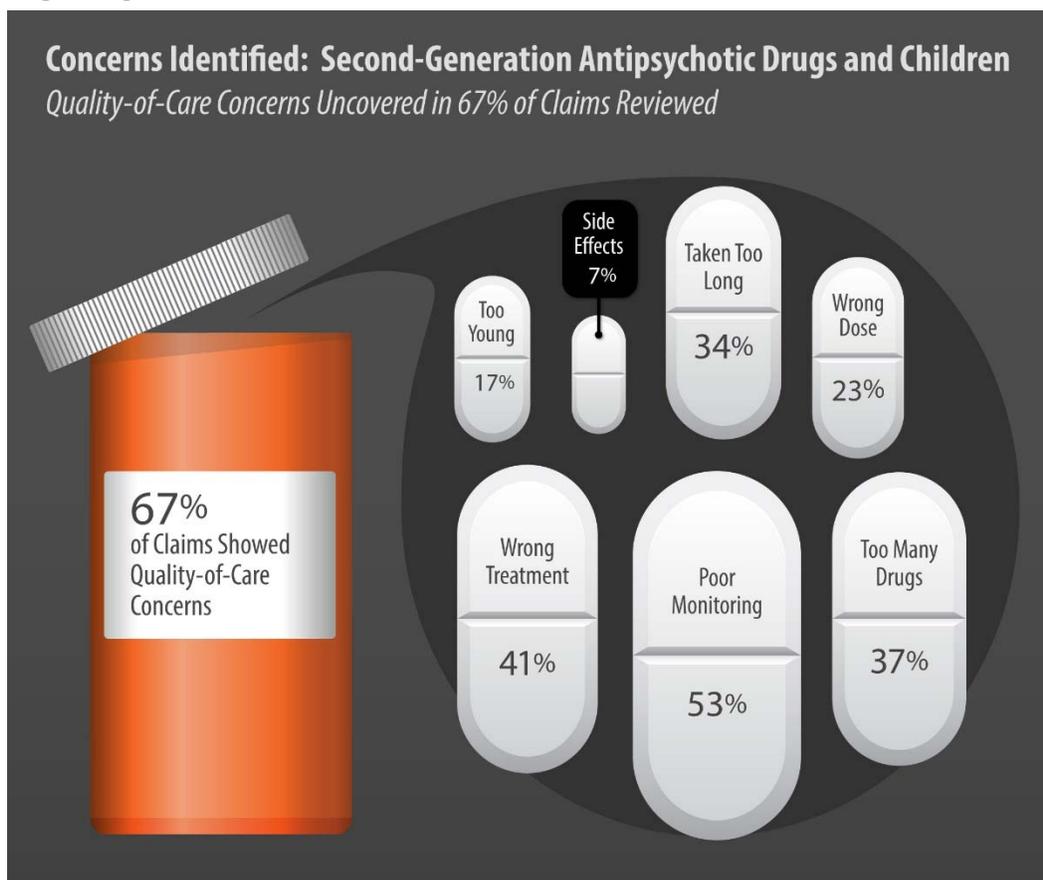
This study was conducted in accordance with the *Quality Standards for Inspection and Evaluation* issued by the Council of the Inspectors General on Integrity and Efficiency.

FINDINGS

In the five States studied, quality-of-care concerns were identified in the medical records for 67 percent of claims for SGAs prescribed to children

Quality-of-care concerns were identified in the medical records associated with 67 percent of claims for SGAs prescribed to children; two or more quality-of-care concerns were identified in the medical records for 49 percent of claims. Chart 1 below illustrates the percentages of claims for which concerns related to each medical record review criterion were identified in medical records; see Table D-5 in Appendix D for estimated totals and percentages of claims with each quality-of-care concern. See Appendix E for all estimates and 95-percent confidence intervals for projections.

Chart 1: Percentages of Medicaid Claims With Quality-of-Care Concerns Regarding Children's Use of SGAs in 2011



Medical reviewers identified multiple quality-of-care concerns for many claims.

Source: OIG analysis of Medicaid claims in five States, 2014.

Medical reviewers identified many specific concerns related to each of the seven criteria for the medical record review. Below are four case studies that illustrate some of the quality-of-care concerns that medical reviewers identified regarding each criterion.

Case Study 1 – a 10-year-old child diagnosed with ADHD

Monitoring—The medical record lacked documentation of monitoring for side effects, including a lack of recognition of or monitoring for akathisia.²⁵

Indications for use (wrong treatment)—This child’s ADHD was clearly documented as being treated with a stimulant medication, but there was no documented reason for the child’s treatment with the SGA.

Polypharmacy (too many drugs)—This child was prescribed three psychotropic drugs during the review period, one of which was an SGA.

Duration (taken too long)—The medical reviewer stated: “The [SGA] should have been tapered down and possibly discontinued completely.”

Dosage (wrong dose)—This child presented symptoms that appeared to worsen with the prescribed course of treatment with the SGA. When the dosage of the SGA was increased, the child’s symptoms worsened. The pattern of increasing dosage and worsening symptoms was repeated several times throughout the review period.

Side effects—The medical reviewer stated: “It is very possible the [SGA] caused the side effect of akathisia, and increasing the dosage caused the patient to get worse instead of better.”

Case Study 2 – a 4-year-old child diagnosed with ADHD and a mood disorder

Monitoring—There was no evidence in the child’s medical records of any monitoring while the child was taking the sampled SGA.

Indications for use (wrong treatment)—This child was placed in the custody of child protective services at 4 weeks old and had a history of abuse and neglect and severe psychosocial issues, such as aggression, anxiety, and mood swings. The reviewer stated that individual, family, and behavior therapy should have been attempted before initiating treatment with drugs. However, there was no evidence in the child’s medical record indicating that such therapies were attempted.

Polypharmacy (too many drugs)—This child was prescribed four psychotropic drugs during the review period, of which two were SGAs.

²⁵ Akathisia is “a pathologic condition characterized by restlessness and agitation, such as an inability to sit still,” and is a common side effect of many SGAs. *Mosby’s Medical Dictionary*, 7th Ed. Mosby-Elsevier, 2006.

Dosage (wrong dose)—The reviewer noted that there is no appropriate dosage of the prescribed SGA for this child’s conditions.

Age (too young)—The reviewer stated that treatment with SGAs was not appropriate for a 4-year-old.

Case Study 3 – a 16-year-old child diagnosed with bipolar disorder

Monitoring—This child experienced significant weight gain while taking the SGA, but there was no evidence in the child’s record of monitoring of blood sugar, cholesterol, or other hormone levels in response to the weight gain.

Indications for use (wrong treatment)—The reviewer stated that the diagnosis which the SGA was prescribed to treat was poorly documented, saying, “Multiple antipsychotic agents were used with vague documentation of hallucinations [as the only explanation].”

Polypharmacy (too many drugs)—This child was prescribed a total of six psychotropic drugs during the review period, of which three were SGAs.

Duration (taken too long)—The SGA was prescribed to this child in response to a report of hallucinations. However, the medical reviewer stated: “When all medications were discontinued... hallucinations were not reported nor was the patient reporting suicidal ideation [i.e., suicidal thinking].” The SGA should have been discontinued as soon as it became apparent that its side effects were outweighing any treatment benefit.

Side effects—This child experienced paranoia, hostility, unstable mood, hallucinations, and suicidal thoughts. This child also experienced significant side effects potentially resulting from the prescribed drugs, including a 22-pound weight gain, insomnia, and edema (swelling) of hands and feet.

Case Study 4 – a 16-year-old child diagnosed with bipolar disorder and ADHD

Monitoring—Although the child’s medical record indicated that laboratory testing was performed, there were no notes in the record of the results of that testing. The medical record also lacked any evidence of monitoring of the child’s height, weight, or vital signs.

Polypharmacy (too many drugs)—This child was prescribed a total of six psychotropic drugs during the review period, of which two were SGAs. The medical reviewer noted that although the regimen of six psychotropic drugs might have been beneficial in treating the child’s diagnoses, the medical record lacked documentation to support why any of the drugs were chosen to treat the child and the symptoms these drugs were targeting.

Dosage (wrong dose)—This child was prescribed double the maximum recommended dosage of the SGA to treat bipolar disorder.

Lack of monitoring was the most commonly identified quality-of-care issue

In the five States we reviewed, quality-of-care concerns regarding lack of monitoring were identified in the medical records for 53 percent of claims for SGAs prescribed to children. Reviewers were concerned about a lack of monitoring for many physiological and behavioral changes. They especially noted that the following were not being regularly performed: measuring of height, weight, vital signs, and blood pressure; measuring of abnormal involuntary movements; laboratory testing (e.g., tests of liver function, measures of blood glucose levels, measures of lipid levels); and electrocardiograms. In all four case studies described above, reviewers identified a lack of monitoring, including a failure to recognize or manage side effects, such as akathisia, significant weight gain, insomnia, and edema.

In the five States studied, 8 percent of SGAs were prescribed for the limited number of medically accepted pediatric indications

Eight percent of claims for SGAs were for drugs prescribed for the limited number of medically accepted pediatric indications. As noted in the background, there are only five SGAs with medically accepted pediatric indications; most of those indications are limited to specific age ranges for each drug. Furthermore, physicians are not prohibited from prescribing SGAs for indications that are not medically accepted. See Table 3 for a list of medically accepted pediatric indications of SGAs.

Among the 92 percent of claims that were not prescribed for medically accepted pediatric indications, common diagnoses that SGAs were prescribed to treat were bipolar disorder (20 percent), mood disorders (13 percent), and autism spectrum disorders (8 percent).²⁶

²⁶ Although there are medically accepted indications for certain drugs to treat bipolar disorder and autistic disorder, the children who were prescribed these drugs for nonmedically accepted indications were (1) not in the age range specified and/or (2) were not diagnosed with the symptoms specified. For example, a child diagnosed with bipolar disorder may not have had mania or mixed episodes; a child diagnosed with autistic disorder may not have had irritability.

Table 3: Medically Accepted Pediatric Indications for SGAs

SGA	Medically Accepted Pediatric Indication(s) ¹	Age Range
aripiprazole	Schizophrenia	13–17 years
	Mania or mixed episodes associated with bipolar I disorder ²	10–17 years
	Irritability associated with autistic disorder	6–17 years
olanzapine	Schizophrenia	13–17 years
	Mania or mixed episodes associated with bipolar I disorder	13–17 years
paliperidone	Schizophrenia	12–17 years
quetiapine fumarate	Schizophrenia	13–17 years
	Mania associated with bipolar I disorder	10–17 years
risperidone	Schizophrenia	13–17 years
	Mania or mixed episodes associated with bipolar I disorder	10–17 years
	Irritability associated with autistic disorder	5–16 years
	Behavioral syndrome-mental retardation	-- ³
	Pervasive developmental disorder	-- ³

¹Medically accepted indications include both the uses approved by FDA and those uses, including off-label uses, supported by one or more of the compendia.

²Bipolar disorder is a brain disorder that causes unusual shifts in mood, energy, activity levels, and the ability to perform daily tasks. There are two primary forms of bipolar disorder: bipolar I disorder and bipolar II disorder. Each of these two types of bipolar disorder have distinct and separate symptoms.

³The FDA-approved uses for risperidone have specific age ranges; the compendia-supported indications do not have specific age ranges, but are simply noted as "pediatric use."

Source: OIG analysis of compendia information, 2014.

New York had a coverage policy stating that its Medicaid program would pay only for SGAs prescribed for medically accepted indications. However, at least 3,366 claims totaling \$773,607 were paid in violation of this policy.²⁷ New York State Medicaid staff told us that because of the lack of diagnosis information on drug claims, this coverage policy is difficult to enforce without conducting a medical record review.

Over a third of SGAs were prescribed for conditions described in the FDA boxed warning

For drugs that may have severe or life-threatening risks when used to treat patients with specific conditions, FDA may require that the product’s labeling

²⁷ To determine whether a drug is prescribed for a medically accepted pediatric indication, we must know the diagnosis it was prescribed to treat. However, diagnosis information is not included in drug claims data; it is available only from medical records. To identify claims that did not meet New York’s coverage policy, we identified all the claims in New York’s population data that were for the five SGAs that have no medically accepted pediatric indications: aripiprazole, paliperidone, risperidone, quetiapine fumarate, and olanzapine. There could be additional claims in the population data that were not prescribed for medically accepted pediatric indications and thus violate New York’s coverage policy but that we cannot identify without diagnosis information and/or medical review.

include a boxed warning describing those risks. Three of the SGAs included in this evaluation carried an FDA boxed warning describing the increased chance of suicidal thinking and behavior in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders being treated with these SGAs. However, physicians are not prohibited from prescribing a drug for a patient who has the condition(s) specified in the FDA boxed warning if the physician judges that the benefits may outweigh the risks.

Thirty-seven percent of claims for SGAs were prescribed for conditions described in the FDA boxed warning—i.e., for major depressive disorders and other psychiatric disorders. The language of the warning—particularly the phrase “other psychiatric disorders”—is broad and could apply to almost any child with a mental health condition. All children taking the three SGAs that carry this warning, regardless of their exact diagnoses or conditions, should be appropriately monitored for suicidal thoughts and other side effects.

CONCLUSION AND RECOMMENDATIONS

SGAs are widely used to treat children enrolled in Medicaid who have mental health conditions. However, SGAs have been previously found to cause serious side effects and little clinical research has been conducted on the treatment of children with these drugs. Quality-of-care concerns were identified in the medical records for 67 percent of claims for SGAs prescribed to children. Lack of monitoring was the most commonly identified quality-of-care issue, being identified in just over half of the claims for SGAs.

The high percentage of claims for which our reviewers identified quality-of-care concerns indicates that more needs to be done to ensure the quality of care provided to children receiving SGAs paid for by Medicaid. To ensure the quality of the care provided to these children, we recommend that CMS work with State Medicaid programs to:

Perform utilization reviews of SGAs prescribed to children

Utilization reviews could specifically focus on the children's age, the duration of their treatment with SGAs, and their overall drug regimens. The previously described guidance and information on using SGAs to treat children—such as the utilization guidelines developed by the Florida and Texas Medicaid programs—may be of use to CMS and to other State Medicaid programs in developing guidelines for such utilization reviews. The medical review criteria that OIG developed for this evaluation may also be helpful in developing such guidelines.

Conduct periodic reviews of medical records associated with claims for SGAs prescribed to children

Periodic reviews of medical records could ensure that (1) there are clear rationales for prescribing the SGAs, (2) children are being properly monitored, and (3) children's dosages are properly adjusted.

Consider other methods of enhanced oversight of SGAs prescribed to children

Some of the other methods of enhanced oversight that CMS and State Medicaid programs could consider include:

- implementing peer review programs through which prescribers encourage one another to improve quality of care and
- undertaking voluntary reporting of the HEDIS measures regarding children's use of antipsychotic drugs or adopting the HEDIS measures in State oversight of SGAs.

In addition to making these recommendations, we have forwarded to CMS the information on the undocumented claims identified in our sample, so that it may take appropriate action.

AGENCY COMMENTS AND OFFICE OF INSPECTOR GENERAL RESPONSE

CMS concurred with all three of our recommendations.

In responding to our first recommendation, CMS stated that it would work with States through the Medicaid Drug Utilization Review Program to monitor children's use of antipsychotic drugs and provide feedback to States regarding any quality-of-care concerns identified using the criteria we established.

In responding to our second recommendation, CMS stated that it would encourage States with managed care programs to request that their External Quality Review Organizations conduct periodic reviews of medical records of children treated with SGAs. We suggest that CMS also consider methods of periodically reviewing medical records of children who receive SGAs paid through fee-for-service arrangements.

In response to our third recommendation, CMS plans to take a number of actions. In general, CMS will:

- share our report to spur conversation about how to promote safe treatment of children with SGAs,
- promote best practices in appropriate oversight of treatment of children with mental or behavioral health issues,
- use measures regarding the safe and judicious treatment of children and adolescents with antipsychotics, and
- engage with other Federal agencies to improve access to screening and treatment for children with substance use or mental health disorders.

We support CMS's effort to ensure quality of care in children's treatment with SGAs and its commitment to engaging with Federal partners and other stakeholder organizations. For the full text of CMS's comments, see Appendix F.

APPENDIX A

FDA Boxed Warning Regarding Children on SGA Product Labeling

Three SGAs carry an FDA boxed warning regarding suicidality when used by children, adolescents, and young adults who have major depressive disorders or other psychiatric disorders. In recent years, FDA has approved these three SGAs to treat depression; therefore, the boxed warning has been applied to these SGAs and refers to their use as antidepressants. The text of the warning, which is shown in Figure A-1, is the same for all three SGAs.²⁸

Figure A-1: SGA Boxed Warning Regarding Children

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of [drug name] or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. [Drug name] is not approved for use in pediatric patients with depression [see WARNINGS AND PRECAUTIONS (5.2)].

²⁸ The name of the drug has been elided from the warning.

APPENDIX B

Sources of Guidance and Information on the Use of SGAs To Treat Children

To develop the criteria for the medical record review in this evaluation, we reviewed the following documents issued by Federal and State agencies and by professional psychiatric associations.²⁹

1. **AACAP practice parameter.** AACAP’s practice parameter identifies practices that may reduce the use of ineffective and inappropriate medications. These practices include conducting complete psychiatric and medical evaluations, developing treatment and monitoring plans, educating patients and their families about treatment and obtaining consent for treatment, using adequate dosages and durations of treatment, assessing responses to treatment, and providing a clear rationale for the use of polypharmacy.
2. **ACF information memorandum.** On April 11, 2012, ACF released an information memorandum titled “Promoting the Safe, Appropriate, and Effective Use of Psychotropic Medication for Children in Foster Care.”³⁰ This memorandum identifies three “outlier practices” that may indicate that issues other than clinical need are influencing the prescribing of SGAs, including:
 - ***Polypharmacy.*** ACF identifies the following patterns as being of issue: use of three or more concurrent drugs, two or more concurrent drugs in the same class for more than 30 days, and use of multiple concurrent drugs before testing the effectiveness of a single drug.
 - ***Dosages of drugs that are too high.*** ACF notes that because so few SGAs have received FDA approval for pediatric populations, there are no recommended dosages for children for most SGAs. They note that the lack of this information reinforces the need for effective monitoring of children receiving SGAs for off-label uses.
 - ***Children being prescribed SGAs at too young an age.*** ACF notes the dramatic rise in the use of SGAs among very young children and concludes that because this population may be especially vulnerable to adverse effects, careful management and oversight are necessary.

²⁹ The guidance discussed here covers all psychotropic drugs—a category that includes SGAs and several other types of drugs. Other classes of psychotropic drugs include ADHD drugs, antianxiety drugs, antidepressants, first-generation antipsychotics, hypnotics, and mood stabilizers. This study focuses specifically on SGAs.

³⁰ ACF, *Promoting the Safe, Appropriate, and Effective Use of Psychotropic Medication for Children in Foster Care*, Log No. ACYF-CB-IM-12-03, April 11, 2012. Accessed at <http://www.acf.hhs.gov/sites/default/files/cb/im1203.pdf> on May 12, 2014.

3. **Report and Resource Guide.** The Rutgers University CERTs, the MMDLN, and 16 States collaborated in 2010 to produce a publication for State Medicaid programs and other stakeholders concerned with care of children and youth. This publication is entitled *Antipsychotic Medication Use in Medicaid Children and Adolescents: Report and Resource Guide From a 16-State Study*.³¹ It contains background on issues about the use of antipsychotic drugs by children, data from the 16 States reflecting use of antipsychotic drugs by children, and information on how the 16 States are managing the use of antipsychotic drugs.³² Among the issues listed are polypharmacy, dosages, and the prescribing of antipsychotic drugs to very young children.
4. **State utilization guidelines.** State agencies in Florida and Texas have each developed utilization guidelines that can help identify when further review of the prescribing of SGAs to children is necessary. Florida and Texas' guidelines address concerns such as polypharmacy (the concurrent use of multiple drugs), inadequate indications for use of drugs, excessive dosage, prescribing of drugs to very young children, and prescribing by a primary care provider who has not received previous specialty training.³³

NCQA publishes the HEDIS, a set of measures used to assess the performance of health plans.³⁴ In July 2014, NCQA adopted the new measures for HEDIS 2015 regarding the safe and judicious use of antipsychotics in children and adolescents; reporting on the new HEDIS measures will begin in June 2015.

We did not use the HEDIS measures in developing our medical record review criteria because the measures had not yet been adopted. We include information on the measures here to provide additional context to our

³¹ CERTs and MMDLN are both funded by the Agency for Healthcare Research and Quality. The 16 States were Alabama, California, Colorado, Illinois, Indiana, Massachusetts, Maine, Missouri, New Hampshire, New York, Oregon, Oklahoma, Pennsylvania, Tennessee, Texas, and Washington. Of these, California, Illinois, New York, and Texas are among the five States we included in this evaluation.

³² *Antipsychotic Medication Use in Medicaid Children and Adolescents: Report and Resource Guide From a 16-State Study*. MMDLN/Rutgers CERTs Publication No. 1, June 2010.

³³ University of South Florida, *Bipolar I Acute or Mixed Mania—6–17 Years*. Accessed at <http://medicaidmentalhealth.org/ViewGuideline.cfm?GuidelineID=32> on June 6, 2014. University of South Florida, *Principles of Practice Regarding the Use of Psychotropic Medication under Age 6*. Accessed at <http://medicaidmentalhealth.org/ViewGuideline.cfm?GuidelineID=32> on May 23, 2014. Texas Department of Family and Protective Services, *Psychotropic Medication Utilization Parameters for Foster Children*, December 2010. Accessed at <http://www.dfps.state.tx.us/documents/about/pdf/txfostercareparameters-december2010.pdf> on May 12, 2014. Health Information Designs, *Texas Prior Authorization Program—Clinical Edit Criteria: Antipsychotics*. Accessed at <https://paxpress.txpa.hidinc.com/antipsychotics.pdf> on May 6, 2014.

³⁴ State Medicaid programs also report on the HEDIS measures, but their HEDIS reporting is voluntary.

recommendations. The HEDIS measures regarding the safe and judicious use of antipsychotics in children and adolescents are:

- use of higher-than-recommended doses of antipsychotics in children and adolescents,
- use of multiple concurrent antipsychotics in children and adolescents,
- use of first-line psychosocial care for children and adolescents on antipsychotics,
- followup visits for children and adolescents on antipsychotics,
- metabolic screenings for children and adolescents newly on antipsychotics, and
- metabolic monitoring for children and adolescents on antipsychotics.

APPENDIX C

Detailed Methodology

We stratified the sample by foster care enrollment, with the intention of determining whether there were differences in quality of care between children enrolled in foster care and those not enrolled in foster care. However, we were unable to test for such differences because of the low response rate among the providers associated with the claims in the foster care stratum, as described in the section on response rates below. We also stratified the sample by payment amount, in order to enhance the precision of our statistical estimates. Table C-1 provides details on the population and sample sizes by strata.

Table C-1: Population, Strata, and Sample Size

Stratum	Claims in Population	Claims in Sample
Claims for children who were in foster care on the service date of the claim	49,058	147
Claims for children who were not in foster care on the service date of the claim and for which the paid amount was less than or equal to \$187	173,596	92
Claims for children who were not in foster care on the service date of the claim and for which the paid amount was greater than \$187 but did not exceed \$557	99,419	267
Claims for children who were not in foster care on the service date of the claim and for which the paid amount was greater than \$557	28,460	181
Total	350,533	687

Source: OIG analysis of 2011 MMIS claims data from five States, 2014.

Identification of FDA-Approved Uses and Medically Accepted Indications

To identify FDA-approved uses and medically accepted pediatric indications for the 11 SGAs, we obtained copies of the compendium publications that would have been the most recent available during our review period.³⁵ Specifically, we obtained the 2011 version of the *American Hospital Formulary Service Drug Information* and the June 2011 *DrugPoints*.³⁶

Collection of Medical Records

We developed a letter for our medical review contractor's use in requesting medical records from the prescribing providers identified on the sampled claims.

³⁵ FDA-approved uses are included in the definition of medically accepted indications and therefore are listed among the medically accepted indications in the compendia.

³⁶ The Act lists three compendia: (1) *American Hospital Formulary Service Drug Information*, (2) the *United States Pharmacopeia—Drug Information* (or its successor publications), and (3) *DrugDEX Information System*. However, we obtained copies of only the first and third of these. The second compendium listed in the Act, the *United States Pharmacopeia—Drug Information*, is no longer published. Its successor publication is *DrugPoints*, which contains information derived from *DrugDEX*—the third compendium.

For each of these providers, the contractor sent a letter requesting the medical records associated with the sampled claim(s). If a provider did not respond to this initial letter, the contractor sent up to two followup letters at predetermined time intervals. For providers that did not respond to the initial letter or two followup letters, the contractor followed up by telephone. We considered any provider that had not submitted the requested records after being contacted at least five times (three letters and two telephone calls) to be a nonresponder.

Response Rates

Table C-2 shows how the response rate for the 485 claims for which we received medical records were distributed among the 4 strata. Response rates varied by stratum.

Table C-2: Response Rates by Stratum

<u>Stratum</u>	<u>Response Rate</u>
Claims for children who were in foster care on the service date of the claim	62%
Claims for children who were not in foster care on the service date of the claim and for which the paid amount was less than or equal to \$187	80%
Claims for children who were not in foster care on the service date of the claim and for which the paid amount was greater than \$187 but did not exceed \$557	73%
Claims for children who were not in foster care on the service date of the claim and for which the paid amount was greater than \$557	69%

Source: OIG analysis of sampled claims and medical records received, 2014.

Nonresponse Analysis

Our findings are based on estimates made solely from medical records collected for the associated sampled claims. We did not statistically adjust our results on the basis of any assumptions about nonrespondent claims.

We performed a nonresponse analysis to determine the representation of subpopulations in respondent claims and to determine the extent of the potential nonresponse bias. We compared whether the respondents and nonrespondents differed with regard to two variables that are available for the entire population and that may be associated with response: (1) foster care enrollment and (2) State of residence. We looked to see whether the response rates were significantly different at the 95-percent confidence level. We estimated the proportion of respondent and nonrespondent claims within these variables and performed Rao-Scott chi-square tests of significance.

We found significant differences in response rates for these two variables. Records for children in foster care were less likely to have been submitted (62 percent) compared with those for children not enrolled in foster care (77 percent). Further, records for children residing in California were less likely to have been submitted (65 percent) compared to those for children residing in the

other four States (79 percent). Therefore, claims for children in foster care and claims from California are underrepresented among the respondent claims.

Potential Effects of Nonresponse on Estimates. To explore the effects that the nonrespondent claims could have had on our results, we imputed and estimated the following:

- the percentage of claims that would have had at least 1 quality-of-care concern if *none* of the 202 nonrespondent claims had had any quality-of-care concerns and
- the percentage of claims that would have been for drugs prescribed for medically accepted uses if *all* of the 202 nonrespondent claims had been for drugs prescribed for medically accepted uses.

If *none* of the 202 nonrespondent claims had had any quality-of-care concerns, the percentage of all claims with at least 1 quality-of-care concern would still have been at least 50 percent. If *all* of the 202 nonrespondent claims had been prescribed for medically accepted uses, the percentage of all claims for drugs prescribed for medically accepted uses would have been approximately 31 percent. See Table C-3 for 95-percent confidence intervals for these new estimates based on the assumptions of errors in the nonrespondent claims.

Table C-3: Potential Effects of Nonresponse on Main Findings

Estimate Description	Sample Size	Point Estimate	95-Percent Confidence Interval
Percentage of claims that would have had at least 1 quality-of-care issue if <i>none</i> of the 202 claims for which we did not receive responses had had any quality-of-care concerns	687	50.2%	44.7%–55.6%
Percentage of claims that would have been for drugs prescribed for medically accepted uses if <i>all</i> of the 202 claims for which we did not receive responses had been for drugs prescribed for medically accepted uses	687	31.5%	26.7%–36.7%

Source: OIG analysis of sampled claims and medical records received, 2014.

Review of Medical Records

Pretest of Medical Review Instrument. To test and refine the medical review instrument, we pretested it with six randomly sampled claims from the MMIS claims data from the selected States. For the pretest, we requested medical records from the prescribing providers for the six sampled claims and asked the medical reviewers to complete the medical review instrument. We then used the reviewers’ feedback to improve the medical review instrument.

Determination of Medically Accepted Indications and Conditions Described in the FDA Boxed Warning. Using (1) the diagnosis and behavior information that the reviewers compiled from the medical records, (2) the age of each child with a

sampled claim, and (3) the compendia information, we determined whether each claimed SGA was prescribed:

- for medically accepted indications and/or
- in the presence of conditions specified in the FDA boxed warning.

Development of Medical Record Review Criteria. Appendix B describes the documents we reviewed to determine medical record review criteria for whether children’s treatment with SGAs posed one or more quality-of-care concerns. The criteria we identified include:

- **Dosage**—All five documents support the idea that dosage needs to be appropriate. Specifically, they say that children’s treatment should start with the lowest effective dose; the dose should be adjusted and targeted; and the dosage should not exceed any recommended dosage guidelines, such as those for the FDA-approved uses.
- **Duration of use**—Three of the five documents support the idea that treatment with SGAs should be of appropriate duration. Specifically, they say that a dose reduction should be planned after several months of treatment, that the treatment plan should include a plan for discontinuing the drug, and that medication trials should be of adequate duration to assess the effects of the drug.
- **Indications for use**—Four of the five documents support the idea that the prescribed drug should be consistent with the child’s diagnosis. The documents also say that there should be thorough and complete evaluations of all aspects of a child’s condition and situation—including a complete medical history and a psychiatric evaluation—and that the target symptoms and diagnosis for each drug that a child is prescribed should be clearly documented. In most instances, psychosocial interventions should be tried before starting treatment with drugs.
- **Monitoring**—Four of the five documents support the idea that a monitoring plan should be developed before the child starts taking an SGA. The documents say that ongoing monitoring requires assessment of the child’s clinical response to the drug; regular observation of physiological changes, such as in height, weight, vital signs, or changes in the results of bloodwork; and observation of any side effects experienced by the patient, such as involuntary movements, insomnia, and other physical and mental effects. The documents also say that that lack of clinical drug trials and evidence-based data for pediatric uses of SGAs reinforces the need for close monitoring of children taking these drugs.
- **Polypharmacy**—All five documents support the idea that treatment with a single drug should be tried before treatment with multiple drugs. They

say that there needs to be a clearly documented rationale regarding the need for each drug when a child is treated with multiple drugs.

- **Side effects**—All five documents support the idea that the use of SGAs can have side effects. Some sources outlined specific measures to monitor side effects, such as taking baseline and ongoing measures for height, weight, blood pressure, and body mass index, as well as measuring baseline and ongoing blood glucose and lipid levels.
- **Patient age**—Four of the five documents support the idea that the treatment of young children with SGAs should be rare and carefully managed. Two of these four documents defined “young children” as those under 4 years of age, another defined them as those under 6 years of age, and the remaining document did not define an age.

To ensure a consistent interpretation of the seven criteria, we provided the contracted psychiatrists with the same sources of guidance and information that we reviewed to develop the criteria. The psychiatrists reviewed the medical records for each sampled claim for an SGA and determined whether there were quality-of-care concerns about the child’s treatment with the SGA with regard to the seven criteria. Using their clinical experience and judgment, the psychiatrists described any concerns they identified about the children’s treatment with regard to any of the seven criteria.

Determination of Violations of State Coverage Policies

New York is the only State included in this evaluation that had a coverage policy based on the compendia. New York’s policy limits Medicaid coverage to drugs prescribed for medically accepted indications. To determine the extent of compliance with this policy, we identified all New York claims in the population data that were for the five SGAs for which there were no pediatric medically accepted indications.

APPENDIX D

Descriptive Data on Population and Sampled Claims

Tables D-1 through D-3 present descriptive information on the population of claims, including the number of claims per State, each State's foster-care enrollment, and the SGAs prescribed. Table D-4 presents information on the types and specialties of the prescribing providers in the sample of claims. Table D-5 presents estimates of the percentages and total numbers of claims in the five States for which reviewers identified quality-of-care concerns.

Table D-1: Number of Claims and Children in Population by State of Residence

State	Number of Children With Claims for SGAs	Number of Claims for SGAs in Population
California	23,344	104,598
Florida	7,016	26,990
Illinois	15,704	74,329
New York	15,919	67,429
Texas	22,671	77,187
Total:	84,654	350,533

Source: OIG analysis of population claims data from five State MSIS systems, 2014.

Table D-2: Number of Children Enrolled in Foster Care With Claims in Population by State of Residence

State	Number of Children With Claims While Not in Foster Care	Number of Children With Claims While in Foster Care	Number of Children With Claims Both While in Foster Care and While Not in Foster Care
California	18,856	4,110	378
Florida	6,673	281	62
Illinois	13,960	1,635	109
New York	13,463	2,456	0
Texas	22,274	192	205
Total:	75,226 (89%)	8,674 (10%)	754 (1%)

Source: OIG analysis of population claims data from five State MSIS systems, 2014.

The table below provides information regarding the total number and percentage of claims in the population for each of the 11 SGAs. Three SGAs—risperidone, quetiapine fumarate, and aripiprazole—represented nearly all claims in the population. This high representation is not unexpected. These three SGAs were among the first SGAs to be approved by FDA. Additionally, these drugs are three of the five SGAs that have been approved by FDA for specific pediatric indications. Furthermore, the FDA-approved indications for two of these drugs—quetiapine fumarate and aripiprazole—have been expanded to include the treatment of depression associated with bipolar disorder and major depressive disorder. These factors likely contributed to the wider use of these three drugs over other SGAs.

Table D-3: Claims in the Population by SGA

Drug	Total Claims	Percentage of Claims
risperidone*	164,636	47.0%
quetiapine fumarate*	91,830	26.2%
aripiprazole	49,360	14.1%
ziprasidone	21,924	6.3%
olanzapine	17,832	5.1%
paliperidone	1,650	0.5%
clozapine	1,482	0.4%
asenapine	1,296	0.4%
olanzapine/fluoxetine	330	0.1%
iloperidone	179	0.1%
lurasidone	14	0.0%
Total:	350,533	100.0%

*Includes an additional formulation, such as extended release, of the drug.

Source: OIG analysis of population claims data from five State MSIS systems, 2014.

Table D-4: Prescribing Provider Type for Sampled Claims

Provider Type/Specialty	Number in Sample	Percentage of Sample
Psychiatrist	494	71.9%
Nonpsychiatrist MD	129	18.8%
Non-MD*	43	6.3%
Unknown	21	3.0%
Total:	687	100.0%

*Examples of non-MD prescribing provider types included nurse practitioners, physician assistants, prescribing psychologists, and social workers.

Source: OIG analysis of sampled-claims data from five State MSIS systems and provider type and specialty information from the National Provider Identifier Registry, 2014.

Table D-5: Estimated Percentages of and Total Claims for SGAs with Quality-of-Care Concerns for the Five States Reviewed

Medical Record Review Criteria	Percentages of Claims With Concern (n=485)*	Number of Claims With Concern
Monitoring	52.8%	138,679
Indications for use	40.6%	106,674
Polypharmacy	37.3%	97,986
Duration of treatment	34.1%	89,542
Dosage	22.5%	59,123
Patient age	16.7%	43,924
Side effects	6.8%	17,773

*Percentages do not total 100% because medical reviewers identified multiple quality-of-care concerns for many claims.

Source: OIG analysis of Medicaid claims data from five States and medical record reviews, 2014.

APPENDIX E

Statistical Estimates and Confidence Intervals

Table E-1: Sample Sizes, Point Estimates, and Confidence Intervals

Estimate Description	Sample Size	Point Estimate	95-Percent Confidence Interval
Quality-of-Care Concerns (Percentages of Claims)			
Percentage of SGA claims with at least one quality-of-care concern	485	67.0%	60.6%–72.9%
Percentage of SGA claims with multiple quality-of-care concerns	485	49.0%	42.5%–55.5%
Percentage of SGA claims with quality-of-care concerns related to monitoring	485	52.8%	46.3%–59.3%
Percentage of SGA claims with quality-of-care concerns related to indications for use	485	40.6%	34.5%–47.1%
Percentage of SGA claims with quality-of-care concerns related to polypharmacy	485	37.3%	31.3%–43.8%
Percentage of SGA claims with quality-of-care concerns related to duration of treatment	485	34.1%	28.2%–41.0%
Percentage of SGA claims with quality-of-care concerns related to dosage	485	22.5%	18.0%–27.8%
Percentage of SGA claims with quality-of-care concerns related to patient age	485	16.7%	13.0%–21.3%
Percentage of SGA claims with quality-of-care concerns related to side effects	485	6.8%	4.2%–11.0%
Medically Accepted Indications and Boxed Warning			
Percentage of claims for SGAs prescribed for medically accepted indications	485	8.5%	5.2%–13.6%
Percentage of claims for SGAs not prescribed for medically accepted indications	485	91.5%	86.4%–94.8%
Percentage of claims for SGAs prescribed in the presence of conditions listed in the FDA boxed warning	485	37.4%	32.3%–43.0%
Percentage of claims for SGAs that (1) were not prescribed for medically accepted uses and (2) were prescribed to treat bipolar disorder	459	20.1%	15.4%–25.9%
Percentage of claims for SGAs that (1) were not prescribed for medically accepted uses and (2) were prescribed to treat mood disorders	459	13.0%	9.2%–17.9%
Percentage of claims for SGAs that (1) were not prescribed for medically accepted uses and (2) were prescribed to treat autism spectrum disorders	459	8.4%	5.6%–12.5%

continued on the next page

Table E-1: Sample Sizes, Point Estimates, and Confidence Intervals (Continued)

Quality-of-Care Concerns (Numbers of Claims)			
Number of SGA claims with quality-of-care concerns related to monitoring	485	138,679	119,568–157,790
Number of SGA claims with quality-of-care concerns related to indications for use	485	106,674	88,875–124,474
Number of SGA claims with quality-of-care concerns related to polypharmacy	485	97,986	80,469–115,502
Number of SGA claims with quality-of-care concerns related to duration of treatment	485	89,542	72,442–106,642
Number of SGA claims with quality-of-care concerns related to dosage	485	59,123	46,057–72,189
Number of SGA claims with quality-of-care concerns related to patient age	485	43,924	32,944–54,905
Number of SGA claims with quality-of-care concerns related to side effects	485	17,773	9,111–26,434

Source: OIG analysis of claims data and medical records, 2014.

APPENDIX F

Agency Comments



DEPARTMENT OF HEALTH & HUMAN SERVICES

Centers for Medicare & Medicaid Services

Administrator
Washington, DC 20201

JAN 16 2015

DATE:

TO: Daniel R. Levinson
Inspector General

FROM: Marilyn Tavenner */S/*
Administrator

SUBJECT: Second-Generation Antipsychotic Drug Use Among Medicaid-Enrolled Children: Quality of Care Concerns OEI-07-12-00320

The Centers for Medicare & Medicaid Services (CMS) appreciates the opportunity to review and comment on the above subject draft report. This study provides CMS with important new information to further our efforts to improve the quality of care provided to children with mental, developmental, and/or behavioral health problems. CMS is committed to working with states, other federal partners, and providers to address the significant quality of care issues identified in the report.

As the draft report notes, during the period of January through June 30, 2011, the OIG examined medical records from a stratified random sample of 687 Medicaid fee-for-service paid claims to determine the extent to which second-generation antipsychotics (SGAs) prescribed to children enrolled in Medicaid in five selected states¹: 1) presented at least one quality of care issue; and 2) were prescribed for medically accepted indications and/or prescribed despite the Food and Drug Administration (FDA) boxed warning.

The OIG found that the medical records for 67 percent of claims for SGAs prescribed to children presented at least one quality of care issue in the five states reviewed. Lack of monitoring was the most commonly identified quality of care issue; 53 percent of claims for SGAs prescribed to children lacked documentation of monitoring in the five States reviewed. Furthermore, only 8 percent of SGAs were prescribed for medically accepted pediatric uses in the five states reviewed; over one-third of SGAs were prescribed for conditions described in the FDA black-box warning.

CMS has been working over the past two years with its many partners, including the Medicaid Medical Directors Network (MMDN), as well as other federal agencies such as the Administration for Children and Families (ACF) and the Substance Abuse and Mental Health Services Administration (SAMHSA), to strengthen oversight and monitoring of psychotropic medications use among children. Examples of these efforts include:

¹ California, Florida, Illinois, New York, and Texas

- Issuing guidance in a 2013 State Medicaid Director letter² concerning the safe, appropriate and effective use of these medications among children;
- Organizing a two day state summit in August 2012, “*Because Minds Matter: Collaborating to Strengthen Psychotropic Medication Management for Children and Youth in Foster Care*,” that brought together child welfare, mental health and Medicaid leaders from across the country to address the issue;
- Releasing a CMS Informational Bulletin in August 2012 that encouraged states to use “drug utilization review” to address the use of psychotropic medications in vulnerable populations and provided states with additional tools to promote the appropriate use and enhanced oversight of psychotropic medications for children in foster care;³
- Promoting patient safety and best practices by surveying states annually and publishing exemplary findings of drug utilization review practices and prior authorization criteria on www.medicaid.gov for all states to review;⁴
- Posting on [Medicaid.gov](http://www.medicaid.gov) the FFY 2013 Medicaid Drug Utilization Review State Comparison/Summary Annual Report, which describes state practices in monitoring use of psychotropic medications among children. The summary shows that: 41 states have programs in place to monitor the use of psychotropic medications in children; 37 states monitor all children (not just those children in foster care); and 41 states have restrictions or special programs in place to monitor/control the use of stimulants.⁵

OIG Recommendation

The OIG recommends that CMS work with State Medicaid programs to perform utilization reviews of SGAs prescribed to children.

CMS Response

The CMS concurs with the OIG’s recommendation. CMS plans to take the following additional actions:

- Work with states through its Medicaid Drug Utilization Review (DUR) Program to monitor use of antipsychotic medication by children and provide feedback to states if any of the criteria for quality of care concerns (e.g., around dosage, duration, indications for use, polypharmacy use, patient age, side effects) are identified.
- Collaborate with the American Academy of Child and Adolescent Psychiatry (AACAP) and the MMDNs to identify and share utilization review guidelines that can help identify practices that signal when more intense review of prescribing of SGAs to children is necessary.

² <http://www.medicaid.gov/Federal-Policy-Guidance/Downloads/SMD-13-07-11.pdf>

³ <http://www.medicaid.gov/Federal-Policy-Guidance/downloads/CIB-08-24-12.pdf>

⁴ <http://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Drug-Utilization-Review.html>

⁵ <http://www.medicaid.gov/medicaid-chip-program-information/by-topics/benefits/prescription-drugs/downloads/dur-survey-comparison-report-2013.pdf>

OIG Recommendation

The OIG recommends that CMS work with State Medicaid programs to conduct periodic reviews of medical records related to SGAs prescribed to children.

CMS Response

CMS concurs with the OIG’s recommendation. CMS plans to take the following action step:

Encourage states that contract with managed care plans (42 states as of the date of this memo) to request that their External Quality Review Organizations (EQROs) conduct periodic reviews of SGA medical records using the methodology outlined in the EQRO protocols for a focused study of a health care service. EQRO activities are financed with an enhanced matching rate. This function is within the scope of EQRO responsibilities, and encouraging these activities is consistent with CMS statutory authority.

OIG Recommendation

The OIG recommends that CMS work with states to consider other methods of enhanced oversight of SGAs prescribed to children.

CMS Response

CMS concurs with the OIG’s recommendation. CMS plans to take the following action steps:

- Convene a 2015 Medicaid Quality Technical Advisory Group (QTAG) meeting with states to discuss the findings of the OIG report and discuss how best to more effectively promote the safe use of antipsychotics among children;
- Work with the Medicaid Pharmacy Administrators and the American Drug Utilization Review Society to share with state Medicaid pharmacy staff best practices from drug utilization reviews and related clinical information to promote appropriate oversight for quality of care for children with mental or behavioral health issues;
- Convene a meeting of regional office Early and Periodic, Screening, Diagnostic and Treatment contacts to share the OIG report findings and seek their input on how to engage in enhanced oversight of SGAs prescribed to children;
- Submit for consideration to National Quality Forum Measure Applications Partnership’s Medicaid Child Task Force the three new HEDIS measures on psychotropic use for potential inclusion in the Medicaid/CHIP Child Core Set of measures; and,
- Engage with Federal partners, including ACF and SAMHSA, to improve access to screening and treatment for children and youth exposed to trauma, or with substance use or mental health disorders.

We would also note that the President’s Fiscal Year 2015 Budget proposes a five-year joint ACF and CMS competitive demonstration project to encourage states to implement evidence-based psychosocial interventions targeting children in the foster care system as an alternative to the

Page 4 – Daniel R. Levinson

prescribing of psychotropic medications, reflecting the priority that the Federal government places on promoting the appropriate care to children with behavioral health needs.

CMS thanks the OIG for the work done on this issue; we recognize that CMS can do more to ensure the quality of the care provided to children with behavioral health needs. During the next year, we plan to enhance our collaboration with states, other federal partners, and providers on this matter.

ACKNOWLEDGMENTS

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

Michala Walker served as the team leader for this study. Other Office of Evaluation and Inspections staff from the Kansas City regional office who conducted the study include Michael Barrett and Rae Hutchison. Central office staff who provided support include Eddie Baker, Berivan Demir Neubert, Althea Hosein, Kevin Manley, Christine Moritz, Jessica Swanstrom, and Julie Taitsman, M.D.

Office of Inspector General

<http://oig.hhs.gov>

The mission of the Office of Inspector General (OIG), as mandated by Public Law 95-452, as amended, is to protect the integrity of the Department of Health and Human Services (HHS) programs, as well as the health and welfare of beneficiaries served by those programs. This statutory mission is carried out through a nationwide network of audits, investigations, and inspections conducted by the following operating components:

Office of Audit Services

The Office of Audit Services (OAS) provides auditing services for HHS, either by conducting audits with its own audit resources or by overseeing audit work done by others. Audits examine the performance of HHS programs and/or its grantees and contractors in carrying out their respective responsibilities and are intended to provide independent assessments of HHS programs and operations. These assessments help reduce waste, abuse, and mismanagement and promote economy and efficiency throughout HHS.

Office of Evaluation and Inspections

The Office of Evaluation and Inspections (OEI) conducts national evaluations to provide HHS, Congress, and the public with timely, useful, and reliable information on significant issues. These evaluations focus on preventing fraud, waste, or abuse and promoting economy, efficiency, and effectiveness of departmental programs. To promote impact, OEI reports also present practical recommendations for improving program operations.

Office of Investigations

The Office of Investigations (OI) conducts criminal, civil, and administrative investigations of fraud and misconduct related to HHS programs, operations, and beneficiaries. With investigators working in all 50 States and the District of Columbia, OI utilizes its resources by actively coordinating with the Department of Justice and other Federal, State, and local law enforcement authorities. The investigative efforts of OI often lead to criminal convictions, administrative sanctions, and/or civil monetary penalties.

Office of Counsel to the Inspector General

The Office of Counsel to the Inspector General (OCIG) provides general legal services to OIG, rendering advice and opinions on HHS programs and operations and providing all legal support for OIG's internal operations. OCIG represents OIG in all civil and administrative fraud and abuse cases involving HHS programs, including False Claims Act, program exclusion, and civil monetary penalty cases. In connection with these cases, OCIG also negotiates and monitors corporate integrity agreements. OCIG renders advisory opinions, issues compliance program guidance, publishes fraud alerts, and provides other guidance to the health care industry concerning the anti-kickback statute and other OIG enforcement authorities.