

Atypical Antipsychotics: Considerations for Medicaid Coverage

Richard C. Surles, PhD

Abstract

In every state across America, Medicaid programs are under serious budgetary pressure. The need to contain costs has led to various forms of restriction in the coverage for drug therapy, including psychiatric pharmacotherapy. Compared with conventional antipsychotic drugs, the atypical agents have higher acquisition costs but offer greater tolerability. Thus, the atypicals are widely accepted as first-line therapy for patients with schizophrenia, and they are also now being recognized for their efficacy in treating bipolar disorder. Nevertheless, the atypicals carry their own characteristic adverse effects, of which weight gain is among the most distressing, with the potential to interfere with compliance to treatment. Treatment compliance is crucial in terms of clinical outcome as well as cost containment, as inadequate compliance is clearly associated with a higher risk of relapse requiring costly rehospitalization. Therefore, antipsychotic therapy that is individually tailored to the patient's needs and thereby improves compliance may be more cost effective than restrictive drug coverage policies based only on acquisition costs. Conversely, individualization of pharmacotherapy is not feasible if some or all of the atypical antipsychotics are excluded from coverage.

(Am J Manag Care. 2005;11:S248-S253)

In 2003, at least 46 states made changes to reduce drug coverage for Medicaid patients. Medicaid expenditures for outpatient drugs had been expanding rapidly, although they still accounted for only 11% of total Medicaid expenditures in 2000.¹ A survey of state Medicaid policies on coverage of psychiatric drugs showed that all states follow one or more of the following restrictive policies: need for prior authorization, encouraging use of generic drugs, use of Preferred Drug Lists, fail-first policies, and

defined limits on coverage.¹ Although antipsychotic medications have traditionally been exempted from restrictions in use, new financial pressures are causing some states to reconsider these exemptions, sometimes creating the potential for negative consequences.

For example, when New Hampshire set a reimbursement limit of 3 prescriptions per month in 1990, drug use decreased in patients taking psychoactive drugs, but the accompanying increase in emergency care and hospitalization incurred costs that greatly exceeded the drug coverage savings.² Similarly, Tennessee abruptly shifted mental health services to multiple managed care providers in 1996, with detrimental effects on continuity of care, especially for patients at highest risk.³ Thus, restrictions can be counterproductive. Physicians must have the flexibility to tailor treatment to the needs of each patient, for each treatment failure resulting in relapse and rehospitalization is far more expensive than the savings represented by the difference in the cost between one drug and another. Each additional relapse increases the risk of creating a chronic state in which remission becomes more difficult to achieve.⁴

Medicaid Patients With Psychotic Disorders

When the Medicare Prescription Drug Improvement and Modernization Act of 2003 goes into effect on January 1, 2006, persons aged 65 as well as persons under 65 with disabilities that are eligible for both Medicare and Medicaid, known as "dual eligibles," will have access to prescription drugs either through new Medicare pre-

scription drug plans or through Medicaid Advantage Plans (health maintenance organizations [HMOs]). Under the new law, formulary managers are directed to be guided by data on the comparative effectiveness of different therapeutic options. However, reliable data are often lacking, as design and analysis problems in comparative trials may fail to reveal clinically important differences while focusing on differences that are of lesser clinical importance. For example, comparisons with placebo are routine in the registration trials submitted to obtain US Food and Drug Administration (FDA) approval of a new drug or a new indication for an existing drug, but such trials merely show that the agent works, not how well it works in comparison with other drugs used for the same purpose.⁵

Many trials involving atypical antipsychotics use haloperidol or another conventional antipsychotic as a comparator, and the data demonstrate what is already well known—that extrapyramidal symptoms (EPS) and elevations in prolactin are substantially less likely to occur with an atypical than with a conventional agent. From the smaller number of randomized controlled trials that compare atypical antipsychotics, no notable pattern of differential effectiveness has emerged in favor of or against any one agent of this class. Rather, the most consistent differences among the atypicals relate to safety and tolerability, with the risk of weight gain and metabolic disturbances highest with clozapine and olanzapine, moderate with risperidone and quetiapine, and low with ziprasidone and aripiprazole.⁶⁻⁸ Nevertheless, the full prescribing information for all of these atypicals includes recognition of a possible link to hyperglycemia and diabetes risk. Compared with weight gain, other adverse effects (AEs) are less common and less likely to interfere with treatment compliance, and they show a less consistent pattern of differential risk among the agents of this class.

Even so, the main lesson is not that one atypical is better than another in terms of clinical outcome, but that they are not interchangeable. Therapy should be initiated, adjusted, and changed as needed, based on the patient's individual profile.

Administrative rules should not and cannot replace clinical judgment as to the optimal therapeutic regimen for each individual, since patient compliance to prescribed therapy depends on both effectiveness and tolerability. Similarly, in terms of cost effectiveness, drug acquisition costs cannot be the sole determinant of formulary policy and insurance coverage, for a poor clinical outcome is the most costly outcome.

Polypharmacy

A retrospective survey of over 31 000 Medicaid recipients diagnosed with schizophrenia revealed antipsychotic polypharmacy in 40% and long-term polypharmacy in 23%. Of particular interest, the prevalence of polypharmacy showed a statistically significant increase over the course of the study period, 1998-2000. Furthermore, polypharmacy was not limited to patients taking conventional antipsychotics, suggesting that prescribers may be using atypical agents at suboptimal dosages that do not provide adequate therapeutic effect, at which point they resort to add-on therapy rather than dosage escalation within the recommended range.⁹ A similar pattern of polypharmacy is also seen in psychiatric practices outside of the Medicaid system.¹⁰

What this indicates is that even in programs where protocols guide clinical practice, antipsychotic polypharmacy remains a substantial problem, incurring avoidable costs for unnecessary medication and the potential for additional avoidable costs associated with treatment of clinical problems brought on by drug-drug interactions. In addition, a complex dosing regimen associated with polypharmacy could have a negative impact on overall compliance to treatment, raising the specter of psychotic relapses requiring rehospitalization.

Policies and procedures that provide education and guidance to physicians are demonstrating that inappropriate polypharmacy can be reduced without restricting access.¹¹ Thus, significant opportunities exist for improving care while reducing unnecessary costs.

Compliance to Antipsychotic Therapy

A retrospective review of compliance among 4325 California Medicaid patients

receiving antipsychotic medications for schizophrenia revealed that poor compliance showed significant correlation with hospitalization and was more predictive of hospitalization than any other factor. When compliance was assessed in terms of gaps in medication coverage, the odds ratio for hospitalization was almost doubled with gaps of 1 to 10 days, almost tripled with gaps of 11 to 30 days, and almost quadrupled with gaps exceeding 30 days.¹² This study provides clear evidence that compliance is crucial to therapeutic success and cost containment; and compliance to antipsychotic pharmacotherapy is largely a function of tolerability.

Further evidence of the importance of proper compliance in schizophrenia treatment was obtained in a retrospective study of Medicaid claims data from San Diego County, California. Among these patients, 41% were compliant with antipsychotic medication, 24% were noncompliant, 16% were partially compliant, and 19% exceeded the claims expected for full compliance. As would be expected, the rates of psychiatric and medical hospitalization were lower for compliant patients (14% and 7%, respectively) than for patients in the other groups. Compared with partially or noncompliant patients, compliant patients had higher medication costs but significantly lower hospitalization costs. Patients with an unnecessary high number of prescriptions filled had the highest total costs of all 4 groups.¹³ Therefore, this study is especially interesting because it shows that compliance problems are still common, even in the era of atypical antipsychotics, and that the clinical and cost consequences of overfilling prescriptions exceed those of inadequate compliance to treatment.

Studies of the clinical and cost effectiveness of health services usually focus on quantifiable outcome measures. However, nonquantifiable factors are important to patients with mental disorders and could therefore affect compliance, clinical outcome, and the cost of treatment. In a study based on semistructured interviews with 51 adult Medicaid patients diagnosed with schizophrenia, several categories were identified as priorities for patients: getting some-

thing "extra" from the medical contact (anything not considered an integral part of the clinician's professional responsibility); finding common ground with the clinician (ie, values, ethnicity); knowing that the clinician is familiar with the particular details of one's problems; being known as a unique individual and not just another case; the sense of being able to talk openly; knowing that the clinician is available and willing to be flexible in setting up appointments; and having input into the treatment plan.¹⁴

The lesson for clinicians and insurers is that patient satisfaction with the quality of care often depends on factors other than the clinician's technical expertise, and satisfaction with care strongly influences continuity, compliance, clinical outcome, and overall cost.

Differences Between Atypical Antipsychotics

Atypicals are not interchangeable, especially in terms of safety and tolerability. The fact that these agents have unique clinical profiles means that prescribers have a wide range of options in devising an individualized regimen that will produce the best clinical outcome in each patient, balancing effectiveness and tolerability without having to resort prematurely to polypharmacy.

Clinical evidence confirms that differences in pharmacologic profile translate into differences in clinical outcome. A retrospective survey of Michigan Medicaid claims of almost 1200 patients treated with olanzapine, risperidone, or haloperidol for schizophrenia revealed significant differences in treatment compliance (better with olanzapine than with risperidone, better with risperidone than with haloperidol) but not in total costs (the higher acquisition cost for olanzapine was offset by lower inpatient costs).¹⁵ This study implies that just as atypicals in general offer greater tolerability than conventional agents, certain atypicals tend to be more tolerable than others in different patients, which allows for the possibility of further improvement in compliance and more cost reduction through carefully individualized treatment plans.

The critical point is that there is no way to predict which patients will always re-

spond to a specific medication. Even in cases where a positive clinical response is recognized, AEs may increase medical risks to the point that other agents must be considered. For example, in a randomized study of 191 patients with schizophrenia and other psychoses, weight gain and hypertriglyceridemia were significantly more prominent in patients treated with olanzapine than in those treated with ziprasidone.¹⁶ Thus, although the atypicals are generally safer and better tolerated than conventional antipsychotics, their use does not relieve the clinician from the responsibility to maintain continuous assessment of medical risks as well as clinical effectiveness.

Cost Effectiveness of Atypical Antipsychotics

Medicaid programs must function as fiscally responsible agents of the nation's insurance program for people with low income or disabilities. Each state Medicaid program will continue to review benefit design and appropriate use.

Although atypical antipsychotics have been the class of drugs most often excluded from restrictions, questions concerning the relatively high cost of acquisition (in comparison with conventional antipsychotics) and optimal individualized utilization are increasing. In order to justify open access to these agents, states need verifiable data to support the hypothesis that the right antipsychotic given at the right dose has a positive clinical impact and is associated with a reduced need for more expensive types of mental health and medical care.

Reviews of published studies have found that the use of atypical antipsychotics in place of conventional agents is either cost-neutral or cost-saving, as the higher acquisition costs for these agents are completely offset by reductions in the need for emergency care and hospitalization.¹⁷ Because of the long-term nature of schizophrenia, it may be more realistic to think of outpatient treatment as a fixed baseline cost, and assess the effectiveness of treatment in terms of reduced need for emergency care or hospitalization for acute exacerbations.¹⁸

Data from published studies of switching from conventional to atypical antipsychotics were analyzed to estimate the impact of costs. For patients treated with conventional agents, the annual cost averaged approximately \$29 000, and patients experienced an average of 80 days of moderate-to-severe psychotic symptoms and over 90 days of treatment-related EPS. Over a 3-year period following a switch to atypicals, costs decreased by as much as 19%, symptom days by as much as 33%, and EPS days up to 50%.¹⁹

These findings are consistent with another study showing that for patients treated with conventional antipsychotics for schizophrenia, annual per-patient costs ranged from \$16 000 to \$57 000, depending on the severity of the condition, and that costs may be lower with atypicals because of better compliance.²⁰

Comorbid diseases that may develop or worsen in part from the AEs of some of the atypical antipsychotics, such as heart disease and diabetes, can also increase the costs of a patient on an atypical antipsychotic. Diabetes, for example, cost the healthcare system \$132 billion in 2002 and estimated costs for heart disease in 2005 will be about \$393.5 billion.^{21,22} These costs added on to the treatment for schizophrenia can substantially increase the total medical costs for a patient with schizophrenia.

These considerations of safety, tolerability, and the possibility of comorbid diseases strongly influence overall treatment costs in patients with schizophrenia. The acquisition costs of the atypical antipsychotics vary (although they are generally higher than the costs of conventional agents); ziprasidone and risperidone have the lowest acquisition costs, olanzapine the highest. However, the greatest determinant of overall cost is effectiveness, because of the very high cost of rehospitalization for relapses and acute exacerbations. Effectiveness depends largely on compliance, which in turn depends on tolerability. Therefore, effectiveness requires a team effort: the physician's selection of the most appropriate medication and dosage regimen to achieve maximum therapeutic benefit with minimal risk for

the individual patient, and the patient's decision to remain in treatment.

Atypical Antipsychotics in Bipolar Disorder

The issues that apply to Medicaid coverage for the use of atypical antipsychotics in patients with schizophrenia now also apply to their use in patients with bipolar disorder. All of the atypicals are FDA approved for treatment of acute mania in bipolar disorder.

Bipolar disorder incurs heavy clinical and financial costs, with hospitalization accounting for a large portion of direct medical costs.²³ Thus, just as in patients with schizophrenia, measures that reduce the need for hospitalization and shift the burden to less costly outpatient services should result in cost savings in patients with bipolar disorders. As has been stated, there are important correlations between drug tolerability and treatment satisfaction, between treatment satisfaction and compliance, and between compliance and reduced need for hospitalization. Thus, the atypical antipsychotics, offering greater tolerability than the conventional agents, represent a positive approach to reducing costs without compromising outcomes.

In a database survey of health service utilization and costs for insured patients with bipolar disorder, cyclothymia, or schizoaffective disorder (compared with general medical outpatients, patients with depression, and patients with diabetes), total mean costs for 1 year of general medical care did not differ dramatically among the groups (from \$1386 in general medical outpatients to \$3034 in patients with diabetes), but the mean cost for mental health and substance abuse services (inpatient and outpatient medical care plus psychotropic medications) was 6- to 32-fold higher in the patients with bipolar disorder (\$1566) than in any of the comparator groups (\$259 in patients with depression, \$76 in general medical outpatients, and \$49 in patients with diabetes). The survey also showed that a small proportion of patients accounted for a disproportionate share of these added costs. Therefore, easing or eliminating restrictions on mental health coverage would only have a small effect on overall costs.²⁴

More recent research confirms the higher costs associated with bipolar disorder compared with major depressive disorder. A survey of almost 3500 patients with bipolar disorder revealed that the mean total annual cost was almost \$9900, roughly three fourths for medical care and medication, and the rest for loss of work time. These costs are significantly higher than those incurred for patients with major depressive disorder, because patients with bipolar disorder are at significantly higher risk for substance abuse, suicide, and injury.²⁵ From the same sample, it was clear that many patients received no treatment or inappropriate treatment. The mainstay of treatment was mood stabilizers, but patients who also received concomitant therapy with atypical antipsychotics showed an average annual savings of almost \$4800 per patient compared with mood stabilizer monotherapy, as the increase in drug costs was less than the amount saved in reduced medical costs and work-loss costs.²⁶ Therefore, there are opportunities for new and innovative interventions that would educate physicians on the potential benefits of adding atypical antipsychotics to certain bipolar patients' treatment regimens.

Conclusions

Budgetary pressures in Medicaid programs could result in restrictive drug coverage policies that ultimately cost the patient and society far more than the amounts saved. The single most important consideration for patients with psychotic disorders is that costly hospitalization can be avoided by improved compliance with antipsychotic pharmacotherapy, that compliance improves with tolerability, and that tolerability requires that therapy be individualized according to the patient's needs and the unique clinical profile of each of the atypical antipsychotics.

The risk of relapse in patients receiving antipsychotic pharmacotherapy is more a function of noncompliance than of the intrinsic limitations of the drugs prescribed. Financial pressures on private insurers, Medicaid, HMOs, and, starting in 2006, Medicare are driving new questions about the effectiveness and appropriate use of the atypical antipsychotics. A strong case can be

made that restricting physician and patient choice and proper access to these agents will not only reduce the quality of life for persons with severe mental illness but in the long run increase the cost to government and private insurance plans.

The greater number of adverse events associated with the older conventional agents and the prospect of treatment failure and relapses can require far more expensive emergency and inpatient care.

REFERENCES

- Koyanagi C, Forquer S, Alfano E.** Medicaid policies to contain psychiatric drug costs. *Health Aff (Millwood)*. 2005;24:536-544.
- Soumerai S.** Unintended outcomes of Medicaid drug cost-containment policies on the chronic mentally ill. *J Clin Psychiatry*. 2003;64(suppl 17):19-22.
- Ray WA, Daugherty JR, Meador KG.** Effect of a mental health "carve-out" program on the continuity of antipsychotic therapy. *N Engl J Med*. 2003;348:1885-1894.
- Muller N.** Mechanisms of relapse prevention in schizophrenia. *Pharmacopsychiatry*. 2004;37(suppl 2):S141-S147.
- Teutsch SM, Berger ML, Weinstein MC.** Comparative effectiveness: asking the right questions, choosing the right method. *Health Aff (Millwood)*. 2005;24:128-132.
- Nasrallah H.** A review of the effect of atypical antipsychotics on weight. *Psychoneuroendocrinology*. 2003;28(suppl 1):83-96.
- Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care*. 2004;27:596-601.
- Travis MJ, Burns T, Dursun S, et al.** Aripiprazole in schizophrenia: consensus guidelines. *Int J Clin Pract*. 2005;59:485-495.
- Ganguly R, Kotzan JA, Miller IS, et al.** Prevalence, trends, and factors associated with antipsychotic polypharmacy among Medicaid-eligible schizophrenia patients, 1998-2000. *J Clin Psychiatry*. 2004;65:1377-1388.
- West JC, Wilk JE, Olfson M, et al.** Patterns and quality of treatment for patients with schizophrenia in routine psychiatric practice. *Psychiatr Serv*. 2005;56:283-291.
- Parks J, Surlis R.** Using best practices to manage psychiatric medications under Medicaid. *Psychiatr Serv*. 2004;55:1227-1229.
- Weiden PJ, Kozma C, Grogg A, et al.** Partial compliance and risk of rehospitalization among California Medicaid patients with schizophrenia. *Psychiatr Serv*. 2004;55:886-891.
- Gilmer TP, Dolder CR, Lacro JP, et al.** Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. *Am J Psychiatry*. 2004;161:692-699.
- Ware NC, Tugenberg T, Dickey B.** Practitioner relationships and quality of care for low-income persons with serious mental illness. *Psychiatr Serv*. 2004;55:555-559.
- Gibson PJ, Damler R, Jackson EA, et al.** The impact of olanzapine, risperidone, or haloperidol on the cost of schizophrenia care in a Medicaid population. *Value Health*. 2004;7:22-35.
- Brown RR, Estoup MW.** Comparison of the metabolic effects observed in patients treated with ziprasidone versus olanzapine. *Int Clin Psychopharmacol*. 2005;20:105-112.
- Hamann J, Leucht S, Kissling W.** Are the second-generation antipsychotics cost-effective? A critical review on the background of different health systems. *Pharmacopsychiatry*. 2003;36:18-26.
- Tunis SL, Ascher-Svanum H, Stensland M, et al.** Assessing the value of antipsychotics for treating schizophrenia: the importance of evaluating and interpreting the clinical significance of individualized service costs. *Pharmacoeconomics*. 2004;22:1-8.
- Mauskopf J, Muroff M, Gibson PJ, et al.** Estimating the costs and benefits of new drug therapies: atypical antipsychotic drugs for schizophrenia. *Schizophr Bull*. 2002;28:619-635.
- Mauskopf JA, David K, Grainger DL, et al.** Annual health outcomes and treatment costs for schizophrenia populations. *J Clin Psychiatry*. 1999;60(suppl 19):14-19.
- American Diabetes Association.** Economic costs of diabetes in the US in 2002. *Diabetes Care*. 2003;26:917-932.
- American Heart Association.** Heart Disease and Stroke Statistics—2005 Update. Dallas, TX: American Heart Association, 2005.
- Kleinman L, Lowin A, Flood E, et al.** Costs of bipolar disorder. *Pharmacoeconomics*. 2003;21:601-622.
- Simon GE, Unutzer J.** Health care utilization and costs among patients treated for bipolar disorder in an insured population. *Psychiatr Serv*. 1999;50:1303-1308.
- Parece A, Wu E, Birnbaum H, et al.** Comorbidities and costs associated with bipolar disorder (abstract). American Public Health Association 132nd Annual Meeting, November 6-10, 2004, Washington, DC.
- Wu E, Birnbaum H, Greenberg P, et al.** Drug treatment patterns and associated costs in bipolar disorder (abstract). American Public Health Association 132nd Annual Meeting, November 6-10, 2004, Washington, DC.