

# Metabolic Testing With Antipsychotics Still Lags

BY SHERRY BOSCHERT

Clinicians reduced prescriptions for one second-generation antipsychotic medication associated with metabolic problems after the Food and Drug Administration required warnings in 2003 about increased risk for diabetes and hyperlipidemia with that class of drugs, a new study shows.

Clinicians did not increase metabolic testing, however, despite recommendations issued at that time by the American Diabetes Association (ADA) and the American Psychiatric Association (APA) to test glucose and lipid levels in all patients who start a second-generation antipsychotic, a large controlled study found.

The study looked at 109,451 Medicaid recipients who started second-generation antipsychotic medications, and a control cohort of 203,527 patients who began taking albuterol but did not receive a second-generation antipsychotic.

Before the FDA warnings and the ADA/APA recommendations, 27% of patients who started a second-generation antipsychotic underwent baseline serum glucose testing, compared with 26% of control patients. Clinicians got baseline lipid tests in 10% of patients starting a second-generation antipsychotic and 11% of controls.

The only statistically significant change in testing rates during or after issuance of the warnings and guidelines was a clinically insignificant 2% increase in baseline lipid testing in patients starting a second-generation antipsychotic, Elaine H. Morrato, Dr.P.H., and her associates reported (*Arch. Gen. Psychiatry* 2010;67:17-24).

Previous studies have shown that the warnings produced no clinically meaningful change in glucose and lipid monitoring in commercially insured patients. The current retrospective cohort study is the first to find a similar pattern in a Medicaid population, reported Dr. Morrato of the University of Colorado, Denver.

The FDA compelled drug manufacturers to change labels for second-generation antipsychotics starting in December 2003 and to mail "Dear healthcare professional" letters to neuropsychiatric health care providers through August 2004 to warn of increased risk for hyperglycemia and diabetes with use of second-generation antipsychotics and to recommend monitoring of glucose levels in patients with diabetes, risk factors for diabetes, or hyperglycemia.

Concurrently, ADA and APA consensus statements described the metabolic risks of second-generation antipsychotics and provided a monitoring protocol that included baseline tests of glucose levels and lipid profiles.

The current study used data from patients in California, Missouri, and Oregon during a prewarning period (January 2002 through November 2003), a warning period during which the letters were mailed and the ADA/APA recommendations came out (December 2003

## VITALS

**Major Finding:** Food and Drug Administration warnings and consensus recommendations have not increased testing for glucose levels and lipid profiles in Medicaid patients who are starting second-generation antipsychotics.

**Data Source:** Retrospective, population-based case-control study of data on 312,978 patients receiving Medicaid in three states.

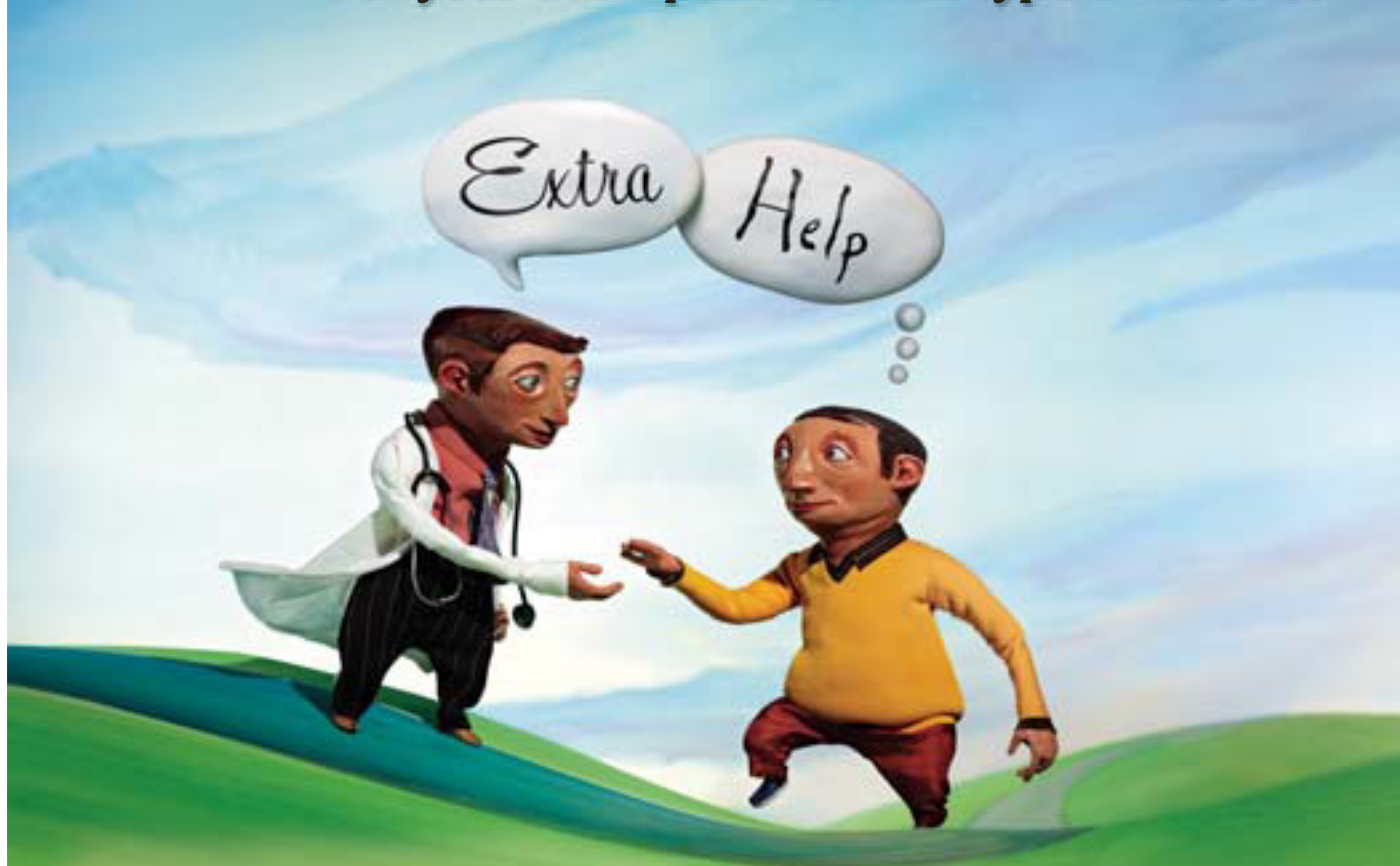
**Disclosures:** The study was funded by Pfizer, which makes ziprasidone. The investigator has received research funds from Eli Lilly and Co., maker of olanzapine. Several other investigators have received funding from or been consultants to those and other companies that make second-generation antipsychotics.

through August 2004), and a postwarning period (September 2004 through December 2005).

Prescriptions for clozapine were excluded from the study because of the drug's unique requirement for neutropenia-related testing.

Although the warnings and recommendations did not increase rates of metabolic testing in patients starting second-generation antipsychotics, clinicians

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### Indication and Important Limitations of Use

ONGLYZA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

ONGLYZA should not be used for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

ONGLYZA has not been studied in combination with insulin.

### Important Safety Information

• **Use with Medications Known to Cause Hypoglycemia:** Insulin secretagogues, such as sulfonylureas, cause hypoglycemia. Therefore, a lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia when used in combination with ONGLYZA

• **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with ONGLYZA or any other antidiabetic drug

**Most common adverse reactions** (regardless of investigator assessment of causality) reported in ≥5% of patients treated with ONGLYZA and more commonly than in patients treated with control were upper respiratory tract infection (7.7%, 7.6%), headache (7.5%, 5.2%), nasopharyngitis (6.9%, 4.0%) and urinary tract infection (6.8%, 6.1%). When used as add-on combination therapy with a thiazolidinedione, the incidence of peripheral edema for ONGLYZA 2.5 mg, 5 mg, and placebo was 3.1%, 8.1% and 4.3%, respectively.

did reduce their use of olanzapine, which would be consistent with intent to reduce metabolic risk, the investigators noted.

Before the FDA warnings, olanzapine use was already declining by 5% per year, compared with other second-generation antipsychotics; during the warning period, olanzapine use declined by 20% per year.

Use of a second-generation antipsychotic with lower metabolic risk—aripiprazole—increased significantly during the warning period but not the post-warning period, a change that might have been attributable more to Califor-

nia's elimination of the need for prior authorization for aripiprazole prescriptions during that time than to concerns about diabetes and hyperglycemia, Dr. Morrato and her associates suggested. The warnings by the FDA and the ADA/APA recommendations did not affect the use of patients receiving second-generation antipsychotics and monitoring for meta-

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People with serious mental illness are 1.5-2 times more likely to develop dyslipidemia, hypertension, obesity, and type 2 diabetes, compared with the general population. More effort is needed to increase screening for diabetes and dyslipidemia in patients receiving second-generation antipsychotics and monitoring for meta-

bolic side effects of these drugs, the authors suggested.

In some previous studies, 60%-80% of psychiatrists reported that they do regularly monitor glucose and lipid levels in patients taking second-generation antipsychotics, and two-thirds of community mental health centers reported having protocols or procedures to screen patients for diabetes and dyslipidemia.

More research is needed to understand the discrepancy between these reports and the low rates of screening found in the current study. ■

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**Drug Interactions:** Because ketoconazole, a strong CYP3A4/5 inhibitor, increased saxagliptin exposure, the dose of ONGLYZA should be limited to 2.5 mg when coadministered with a strong CYP3A4/5 inhibitor (e.g., atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin).

**Patients with Renal Impairment:** The dose of ONGLYZA is 2.5 mg once daily for patients with moderate or severe renal impairment, or with end-stage renal disease requiring hemodialysis (creatinine clearance [CrCl] ≤50 mL/min). ONGLYZA should be administered following hemodialysis. ONGLYZA has not been studied in patients undergoing peritoneal dialysis. Assessment of renal function is recommended prior to initiation of ONGLYZA and periodically thereafter.

**Pregnant and Nursing Women:** There are no adequate and well-controlled studies in pregnant women. ONGLYZA, like other antidiabetic medications, should be used during pregnancy only if clearly needed. It is not known whether saxagliptin is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when ONGLYZA is administered to a nursing woman.

**Pediatric Patients:** Safety and effectiveness of ONGLYZA in pediatric patients have not been established.

\*metformin, glyburide, or thiazolidinedione (pioglitazone or rosiglitazone)

<sup>†</sup>"Patients" means covered lives as calculated by Fingertip Formulary® as of 10/09.

**Please read the adjacent Brief Summary of the Product Information.**

For more information about ONGLYZA visit [www.onglyza.com](http://www.onglyza.com).

Reference: 1. Fingertip Formulary® data as of October 25, 2009. Data on File, October 2009.

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