

**Standby Statement: Approved**

**STB ID: 00-**

**Date: October 16, 2000**

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**Issue: Zyprexa and Hyperglycemia**

**Background Info for User: Recently there has been increased interest in the association between mental illness and hyperglycemia. Some case reports have suggested that some atypical antipsychotics may induce clinically significant alterations in glucose metabolism. A majority of these case reports—15-20—have implicated Zyprexa.**

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**Statement Containing Key Messages:**

**Recent studies have reported an increase in the incidence and prevalence of diabetes in the general population in the United States. A survey conducted by the Centers for Disease Control and Prevention (CDC) in collaboration with state agencies, showed the prevalence of diabetes increased from 4.9 percent in 1990 to 6.5 percent in 1998—a rise of 33 percent. Increases were seen in men and women, all ages, all ethnic groups, all education levels and in nearly all states.**

**The incidence of hyperglycemia and/or diabetes is even higher in patients with schizophrenia than in the general population. In fact, the prevalence of diabetes is two to four times greater in these patients and the risk increases with age.**

**Lilly conducted an analysis of data from clinical trials to determine how often abnormally high glucose readings occur during treatment with Zyprexa, comparative drugs or placebo. Among the 7,030 patients in the trials, almost 10 percent had high glucose and/or history of hyperglycemia or diabetes before randomization to Zyprexa or a comparator.**

**The large data analysis we performed does not support an elevated risk of treatment-emergent hyperglycemia in comparison to other typical and atypical antipsychotics and to placebo.**

**While we're very reassured that this analysis does not suggest that Zyprexa is associated with hyperglycemia more than other treatments, we're concerned that data shows patients with mental illness may have a**

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high potential for developing hyperglycemia or diabetes. Further work is needed to clarify this issue and specifically whether and how psychotropic drugs contribute to it.

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### Questions and Answers

**Q1. Is there any data which supports that Zyprexa does not cause hyperglycemia?**

**A1. Lilly conducted a comprehensive analysis of the 7,030 Zyprexa patients from our clinical trial database to determine the potential relationship between Zyprexa and hyperglycemia. Rates of glucose elevation were 3.1 percent versus 2.5 percent for Zyprexa and placebo, respectively. The data base analysis further confirmed that the emergence of hyperglycemia does not appear to increase over time.**

**Q2. Aren't there case reports which support that Zyprexa causes hyperglycemia?**

**A2. A case report of hyperglycemia occurring during treatment with a particular drug cannot confirm that the drug caused the glucose abnormality. Placebo comparison allows us to better determine if the drug truly increases the risk of hyperglycemia. A retrospective analysis of our clinical trials evaluated Zyprexa patients as well as patients taking other antipsychotics or placebo.**

**Q3. How does Zyprexa compare with other antipsychotics with regard to hyperglycemia?**

**A3. Based on a retrospective review of clinical trial data, risk for treatment-emergent hyperglycemia was similar on Zyprexa, haloperidol and risperidone. The risk was higher on clozapine. Estimated rates of hyperglycemia for Zyprexa versus haloperidol were 7.3 percent versus 11.2 percent. In comparing Zyprexa with**

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risperidone, the estimated rates were 2.7 percent versus 7 percent. Comparing Zyprexa with clozapine, the rates were 3.0 percent versus 9.4 percent, the one comparison pointing to a relative difference between drugs.

**Q4. Patients can gain weight while on Zyprexa. Can't weight gain cause onset of hyperglycemia and/or diabetes?**

**A4. There's been no definitive association between weight gain with Zyprexa and hyperglycemia. While obesity is a risk factor for hyperglycemia and diabetes, in our analysis, weight gain was not significantly associated with glucose elevation.**

**Q5. Aren't you seeing onset of hyperglycemia independent of weight gain?**

**A5. The large data analysis we performed does not confirm elevated risk of hyperglycemia/diabetes emerging on Zyprexa relative to placebo or other antipsychotic drugs. However, it appears to confirm that hyperglycemia is an important comorbid condition for patients with mental illness, and that it deserves close clinical attention.**

**Q6. Can people who are already diabetic be treated with Zyprexa?**

**A6. Zyprexa is not currently contraindicated for diabetic patients. Further work is needed to clarify this issue, specifically whether and how psychotropic drugs contribute to it. Lilly is currently performing trials to relationship between Zyprexa and hyperglycemia.**

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