

What can you tell me about the Koller article that appeared in Pharmacotherapy?

- Drs. Koller and Doraiswamy are calling attention to the very important issue of co-morbidity of diabetes in patients with serious mental illness. Diabetes occurs at a higher rate in people with schizophrenia and bipolar disorder than in the general population, so it is not surprising that patients may develop diabetes during treatment for their psychiatric disorder.
- Dr. Koller's group has previously presented data on comorbid diabetes and its complications in a paper on clozapine (Koller, 2001) and a poster on risperidone (Koller, 2002)
- In the risperidone abstract, the authors conclude there are similar reports of hyperglycemia with risperidone, olanzapine, clozapine and quetiapine and suggests, "antipsychotic use may unmask or precipitate diabetes in psychotic patients". However, they also report that no conclusions on causality or relative risk between agents can be drawn without further studies.
- Collectively, these data demonstrate that patients taking any antipsychotic should be appropriately monitored for risk factors for diabetes.

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What can you tell me about the recent article by Koro that appeared in the British Medical Journal?

- This Bristol Meyers Squibb sponsored article does not provide new information to help answer questions about diabetes in patients taking antipsychotics.
- The article is incorrect in its statement about the existence of case reports for only Zyprexa. There are case reports of diabetes and hyperglycemia for many other newer and older generation antipsychotics, including risperidone.
- Among the many study limitations, the authors state the study lacked direct information on the severity of schizophrenia, race, social class or weight gain, which may impact development of diabetes. The inability to account for these variables makes it difficult to conclude the role medications may have played. However, this study is consistent with other studies that would indicate that people with mental illness have an increased risk for the development of diabetes.
- To put the study into context, the actual number of cases of new onset diabetes observed in patients on Zyprexa was seven out of 970 – less than 1 per cent. This is similar to the number of cases found during clinical trials with Zyprexa and noted in the SmPC.
- Lilly is committed to educating physicians about the link between diabetes and severe mental illness and appropriate monitoring of patients on antipsychotics, including Zyprexa, based on risk factors such family history, ethnicity, age and obesity.

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What can you tell me about Zyprexa and increased lipid levels?

- Abnormalities in cholesterol and triglyceride levels are very common in the general population, occurring in as high as 50 percent of the U.S. population.
- Clinical trial and spontaneous adverse event reports of elevated triglycerides in patients taking Zyprexa are rare.
- For many patients, increases in lipids can be managed through dietary interventions, medication and behavior modifications such as exercising and refraining from smoking

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I've heard that Zyprexa can lead to ketoacidosis. Is this true?

•DKA is an infrequent complication of diabetes mellitus. Cases of DKA have been reported in association with Zyprexa treatment, as well as with other atypical antipsychotics. However, these reports are very rare, reported in less than 0.01 percent of patients treated with Zyprexa and a direct causal relationship has not been established.

•Fortunately, DKA is potentially preventable if diabetes is identified and properly controlled. Lilly is committed to educating physicians about the link between diabetes and severe mental illness and appropriate monitoring of patients on antipsychotics, including Zyprexa, based on risk factors such family history, ethnicity, age and obesity.

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What is the association between Zyprexa and the development of diabetes?

- Diabetes occurs at a higher rate in people with schizophrenia and bipolar disorder than in the general population, so it is not surprising that patients may develop diabetes during treatment for their psychiatric disorder.
- In head-to-head trials and epidemiological studies, the reported differences, if any, between commonly prescribed antipsychotic medications is very small when compared to the absolute risk of developing diabetes that is associated with having a severe psychiatric illness. *These studies have not demonstrated a direct causal relationship between any antipsychotic agent and the development of diabetes.*
- Because the differences between commonly prescribed agents – if any – appears to be relatively small, and the patient population is at higher risk, all patients should be monitored appropriately and the primary focus should be on treating the underlying schizophrenia or bipolar disorder.

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Label Changes

***I heard you recently had a change to your label in Europe.
What can you tell me about that?***

- Over a year ago, Lilly revised its EU label to include language with respect to appropriate clinical monitoring of patients with diabetes. This is part of good clinical practice.

Is it true that Zyprexa will have a label change regarding diabetes in the US?

The FDA has not requested a label change with regards to diabetes.

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What can you tell me about the Zyprexa label change in Japan?

- The Package Insert (PI) in Japan has been modified with regard to patients with diabetes.
- We believe the MHLW's decision was an overreaction given the body of global scientific evidence supporting Zyprexa's overall safety profile and the clinical facts of the cases in Japan .
- We are not in agreement with the MHLW's decision because the changes might result in Zyprexa being inappropriately withheld from thousands of patients with diabetes and schizophrenia in Japan.
- Lilly is committed to educating physicians about the link between diabetes and severe mental illness and appropriate monitoring of patients on antipsychotics, including Zyprexa, based on risk factors such family history, ethnicity, age and obesity.

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