

Alan Breier To: John C Lechleiter/AM/LLY@Lilly
07/08/03 04:13 PM cc:
Subject: 8 points - original draft

----- Forwarded by Alan Breier/AM/LLY on 07/08/2003 04:13 PM -----



Alan Breier To: Alan Breier/AM/LLY@Lilly, Barbara L Whitaker/AM/LLY@Lilly
06/06/2003 09:27 AM cc:
Subject: 8 points - original draft

----- Forwarded by Alan Breier/AM/LLY on 06/06/2003 09:15 AM -----



Michael E Bandick To: Alan Breier/AM/LLY@Lilly
06/04/2003 04:41 PM cc:
Subject: 8 points - original draft

Alan -
Did you request a copy of this? (or diagnose my auditory hallucination.....)
I don't have the slightly modified version you sent to Jack, but the changes were minimal.
MB

Michael E. Bandick
Director, Marketplace Strategy & Management
Zyprexa Product Team (DC 6324)
317 277 5396 Office
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 Redacted Cell

----- Forwarded by Michael E Bandick/AM/LLY on 06/04/2003 04:38 PM -----



Bonnie R Simons To: Michael E Bandick/AM/LLY@Lilly
NONLILLY cc:
06/04/2003 04:38 PM Subject:

Bonnie R. Simons
Administrative Assistant
Zyprexa Global Marketing Team
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----- Forwarded by Bonnie R Simons NONLILLY/AM/LLY on 06/04/2003 04:37 PM -----

Denice M Torres To: MARKETIN@Lilly
05/07/2003 01:30 PM cc: Enrique A Conterno/AM/LLY@Lilly, Thomas G
Wellner/EMA/LLY@Lilly, Alfonso G Zulueta/AM/LLY@Lilly
Subject:

Here is Alan's message... thought you would want it for a resource.
----- Forwarded by Denice M Torres/AM/LLY on 05/07/2003 01:27 PM -----



Alan Breier To: Denice M Torres/AM/LLY@Lilly
05/07/2003 12:02 PM cc: Alan Breier/AM/LLY@Lilly
Subject:

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----- Forwarded by Alan Breier/AM/LLY on 05/06/2003 10:47 AM -----



Alan Breier
05/06/2003 10:45 AM

To: Alan Breier/AM/LLY@Lilly
CC:
Subject:

Eight Key Questions About Zyprexa and Diabetes

In part because of the recent Wall Street Journal article, activities related to the Hirsch and Hirsch litigation and relentless focus from our competitors, the issue of hyperglycemia remains very much on the front burner. At times it may seem difficult to sort out the scientific facts from the noise and therefore I thought it would be timely to take a few minutes and answer 8 of the most pointed questions on this important issue:

1. Does Zyprexa cause diabetes? The most straight forward answer is we do not think so. Why do I not say Zyprexa definitively does not cause diabetes. In part because it is very difficult to prove a negative. When anyone develops diabetes in the general population it is often impossible to say definitively why they developed diabetes. We have been intensively investigating this issue for several years with clamp studies, animal studies, epidemiology studies and clinical trial studies and have found no direct link between diabetes and Zyprexa, or any other antipsychotic drug for that matter. This work includes demonstrating that Zyprexa does not affect insulin release from the pancreas and does not have a direct effect on insulin receptor sensitivity. Moreover, the numerous research groups around the world have also not found a direct causal link to diabetes. It is clear that this complicated area require more research and we intent to continue to be on the forefront of this scientific inquiry.

2. Why do I say no direct link as opposed to any link at all? We know and have well characterized that Zyprexa and all antipsychotics causes weight gain and weight gain is an established risk factor for diabetes. Thus in some patients the weight gain of Zyprexa could predispose them to diabetes, particularly if those patients have other risk factors for diabetes. However, and this is very important, most people who gain weight do not develop diabetes. Diabetes is an illness with multiple pathways leading to and contributing towards its development. Thus a patient who gains weight on Zyprexa or other antipsychotic drugs and mood stabilizers is probably like any one else who gains weight the general population. For the vast majority of individuals, their pancreases are healthy and the weight gain will not precipitate diabetes. For those in the minority whose pancreases are functioning suboptimally weight gain could push them over to diabetes - and that is weight gain caused by any means, over eating in the general population or weight gain produced by any antipsychotic, antidepressant or traditional mood stabilizer.

3. Okay, then how can I tell if a patient's pancreas is functioning suboptimally? The most efficient and practical way to get a handle on this is easy - just get a fasting glucose level. Parenthetically, a fasting glucose can be obtain for 40 cents.

4. If a schizophrenic or bipolar patient has an abnormal fasting glucose, should Zyprexa not be initiated? Absolutely not. First, remember the majority of Zyprexa patients gain no or only modest amounts of weight, approximately 10 pounds or less, Second, the approximately 20% of patients who gain very large amounts of weight on Zyprexa can be identified very early in treatment, with in the first few weeks, because of there rapid pattern of early weight gain and those patients are ripe for interventions. Third and most important, no matter what drug is chosen, including Abilify and Geodon, the same care in terms of monitoring these patients is needed. In fact it would be poor medical practice in my view to not carefully monitor all at risk patients equally irrespective of the psychotropic drug they

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are on. Lastly, having treated severely ill mental patients for over 15 years, I can not stress too much that the hardest and most clinically challenging part is successfully treating the schizophrenia and the bipolar not a specific side effect and therefore it is imperative to choose the best treatment for these severe mental conditions.

5. Since there is more weight gain with Zyprexa than most antipsychotic drugs and weight gain is a risk factor for diabetes, shouldn't there be more cases of diabetes associated with Zyprexa treatment? If it was only about weight gain and large enough numbers of patients were treated over several years, it would be reasonable to predict more cases of diabetes on Zyprexa than most other drugs. However, weight gain is only one of several risks factors and the impact of weight gain for those at risk patients generally takes several years to manifest itself. To support this point, the vast majority of epidemiology studies on this topic consistently demonstrated very little if no difference among the atypical antipsychotics even though they have quite varied weight gain profiles.

6. Is there information or data that we have on this issue that we are not sharing? I want to be very clear and emphatic on this point - the answer is a resounding no. All of the data we have collected has been shared or is in the process of being shared through publications and other appropriate scientific venues. It is my commitment that any future relevant information on this topic will be made available.

7. What is the worst possible outcome of this issue? The worst outcome would be the persistent perception that this is a good drug - bad drug issue. This is dangerous because patients will not be started on treatments that are most likely to help their core psychiatric illness and help them regain their lives, and other patients will not be given the appropriate monitoring for metabolic side effects because of the mistaken assumption they are on a so-called safe drug. Those patients are at greatest risk of developing serious even life threatening complications.

8. What are the best outcomes? The best outcomes are that all caregivers who are responsible for the care of the chronic mentally ill understand the facts about the alarmingly high rate of diabetes in their patients, to know the risk factors and how and when to monitor their patients. Since this is less about the drugs and more about the illness, any form of equitable class labeling, PR campaigns, white papers by professional groups like the ADA and more solid research that gets the facts out the better off our patients will be. We are in a great position to not only continue but to elevate our leadership in this vitally important area.

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