

RETURN TO : Bruce J. Kinon, M.D.

Robert P Schmid 12/01/98 07:52 AM

To: Bruce Kinon/AM/LLY@Lilly
cc: Peter Clark/AP/LLY@Lilly, Jack E Jordan/AM/LLY@Lilly, Jeffrey T Ramsey/AM/LLY@Lilly, John R Richards/AM/LLY@Lilly
Subject: Re: Wishing/Goldstein articles


Bruce,

The statement that Peter outlined is the result of a discussion with Charles Beasley and the first attempt to establish what the scientific information is concerning diabetes/hyperglycemia. The strength of this position is in that this is that "people" (referring to the general population) who do gain weight may develop insulin resistance which may lead to hyperglycemia and diabetes. This is may also happen if it is a side effect of a drug regardless of the agent. The other stronghold is that this effect is already reflected in other labels including risperidone, clozapine and some typicals.

We'll follow up with Charles and the GSMT data. I would suggest we get a meeting to discuss this live with you and Charles to understand all aspects of the matter.

Rob

Bruce Kinon

 Bruce Kinon
12/01/98 12:42 AM

To: Peter Clark cc: Jack E Jordan, Jeffrey T Ramsey, John R Richards, Robert P Schmid

Dear Peter,

Thank you for advising me of the response to the hyperglycemia issue. I do have concerns regarding making any connections between olanzapine-induced weight gain and hyperglycemia. Therefore, in my opinion, I would not include your following statement:


"Patients who gain weight may develop insulin resistance which may lead to hyperglycemia and diabetes."

In addition, I would recommend that you obtain from Man Fung a summary of the GSMT post-marketing experience regarding olanzapine and weight gain.

Sincerely,

Bruce Kinon

Peter Clark

 Peter Clark
11/30/98 09:26 AM

To: Jack E Jordan, Bruce Kinon, John R Richards cc: Jeffrey T Ramsey, Robert P Schmid
Subject: Wishing/Goldstein articles

ZY 2133 1137

RETURN TO : Bruce J. Kinon, M.D.

Jack, Bruce and JR

Rob has asked me to summarize the points we would raise in response to the recent reports of hyperglycemia linked with Zyprexa use raised in the Wishing (published in the Society of Biological Psychiatry) and Goldstein (soon to be published in Psychosomatics journal) articles

The recent reports linking the use of olanzapine and the development of diabetes is an important issue. The conditions described in the papers are already described in the full prescribing information of Zyprexa (as it is with other antipsychotics). Although not a new issue, we do treat the issue with the upper most importance and in doing so, would like to state the following:

- Schizophrenia is an illness that results in patients having a higher incidence of diabetes than the normal population. Recent reports suggest the incidence may be as high as 24% (ACTION: Jeff Ramsey will get reference)
- Use of antipsychotics may result in weight gain (ACTION: Jeff Ramsey will get reference).
- Patients who gain weight may develop insulin resistance which may lead to hyperglycemia and diabetes.
- Conditions such as hyperglycemia, diabetes, diabetic ketoacidosis and hyperosmolar coma are all described in the Product Information's of other antipsychotics such as risperidone, clozapine and haloperidol

Specifically in response to the Wishing and Goldstein articles, the following points should be raised:

- The majority of the patients described in these publications have a family history of Diabetes. This would make them genetically predisposed to developing the illness
- Each of these patients was on multiple medications. Attributing an effect to any one drug would be difficult
- Patients in the Wishing study were on doses beyond the approved prescribing dose range
- One patient in the Goldstein article was not on olanzapine when they developed hyperglycemia

The following actions are underway:

1. Jeff Ramsey will get a literature search to see if other similar articles have appeared
2. Jeff Ramsey will discuss with MIS (Kevin Ferguson) to see if the medical letter can reflect these points
3. Jeff Ramsey will work with Charles Beasley to draft a "Letter to the Editor" of J. Biol. Psych. to state these points in reference to the Wishing article
4. Peter/Rob will draft summarize these points into a package for representatives

As more information comes to hand, we will let you know.
Peter

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