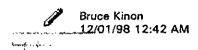
RETURN TO: Bruce J. Kinon, M.D.



To:

Peter Clark/AP/LLY@Lilly

cc:

Jack E Jordan/AM/LLY@Lilly, Jeffrey T Ramsey/AM/LLY@Lilly, John R Richards/AM/LLY@Lilly,

Robert P Schmid/AM/LLY@Lilly

Subject: Re: Wishing/Goldstein articles 📸

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:

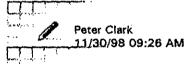
"Patients who gain weight may develop insulin resistance which may lead to hyperglycemia and diabetes."

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

Sincerely,

Bruce Kinon

Peter Clark



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

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 Psychosomitics 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

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

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 clanzapine 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