

To: CN=Michael E Bandick/OU=AM/O=LLY@Lilly; CN=Melanie A Bruno/OU=AM/O=LLY@Lilly;
CN=Anthony M Fiola/OU=AM/O=LLY@Lilly; CN=Jared G Kerr/OU=AM/O=LLY@Lilly; CN=Mark D
Millikan/OU=AM/O=LLY@Lilly; CN=Matthew R Pike/OU=AM/O=LLY@Lilly
Date: 09/03/2002 04:16:06 PM
From: CN=Patrizia Cavazzoni/OU=AM/O=LLY
Subject: Re: request from Israel MOH re Australia label change

All

This is similar to the request we had from Israel MOH re NZ label change request. While I agree that the Australia label change is not of such nature to warrant proactive communications other Regulatory agencies, I would support sharing information with Israel MOH if they have asked specifically about Australia label change.

Jared

As per my VM. Would you kindly follow-up with Leora about this, and confirm if this is a specific request from Israel MOH re Australia. If so, could we ensure that Leora has all the facts, as I imagine she would be handling this type of response either by phone, or with a very brief (one page) written communication. If she would prefer written communication, I would suggest that, given current workload and priorities, Leora DRAFT the letter on the basis of the facts provided to her, with subsequent review by CRT

Thank you for taking the lead on this

Patrizia

Matthew R Pike

09/03/2002 12:50 PM To: Melanie A Bruno/AM/LLY@Lilly, Patrizia Cavazzoni/AM/LLY@Lilly
cc: Michael E Bandick/AM/LLY@Lilly, Anthony M Fiola/AM/LLY@Lilly
Subject: Re: Issues Management / Australian Label Update & Positive News Article

Request to share info with Israeli MOH. I am not clear about what we may have already communicated. I realize not every label change is newsworthy, however it appears the MOH has requested this info. Please advise.

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Matt Pike, R.Ph.
Issues Management Manager
Zyprexa Global Marketing
317-651-3990

----- Forwarded by Matthew R Pike/AM/LLY on 09/03/2002 12:47 PM -----

Anthony M Fiola

09/03/2002 08:55 AM

To: Matthew R Pike/AM/LLY@Lilly
cc:
Subject: Re: Issues Management / Australian Label Update & Positive News Article

Matt,

Any thoughts on this one??? I would imagine that what's been shared about the Australian label is public knowledge and therefore would be alright to share but the truth is I'm not sure??

What do you think?

Tony Fiola
Global Marketing Associate
Zyprexa Product Team
(317) 276-9417

----- Forwarded by Anthony M Fiola/AM/LLY on 09/03/2002 08:54 AM -----

Leora Garten

09/01/2002 01:43 AM

To: Anthony M Fiola/AM/LLY@Lilly
cc: Sheherazad Aftabroushad/EMA/LLY@Lilly
Subject: Re: Issues Management / Australian Label Update & Positive News Article

Hello Anthony,

Israel MOH has asked me about the situation in Australia so now that it is finalized I would like to ask for your permission to share the approved

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change with our MOH, Pls let me know if OK,

Thanks
Leora Garten
Regulatory and Health Outcomes Manager
Eli Lilly Israel, 7 Shenkar St. Gav-Yam Center 2
POB 2160, Herzliya Pituach 46120 ISRAEL

PLEASE NOTE NEW OFFICE AND DIRECT PHONE NUMBERS

Office: *972-9-9606234
Direct Tel: *972-9-9606215
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redacted

Harley Goldstone

01-09-02 08:25

To: Leora Garten/EMA/LLY@Lilly, Chana Lotan/EMA/LLY@Lilly, Doron Shalit/EMA/LLY@Lilly
cc:
Subject: Issues Management / Australian Label Update & Positive News Article

FYI. I hope we wont need this but if our MoH asks questions regarding possible label changes this could be a favourabele response.

ATB

Harley

----- Forwarded by Harley Goldstone/EMA/LLY on 09/01/2002 07:28 -----

Anthony M Fiola

08/28/2002 15:43

To: PM_ONLY
cc: Katherine A Armington/AM/LLY@Lilly, Michael E Bandick/AM/LLY@Lilly, Peter Beardsall/EMA/LLY@Lilly, Frances Beves/EMA/LLY@Lilly, Allan Dryden/AP/LLY@Lilly, Eric Edgell/AM/LLY@Lilly, Peter Grossmann/EMA/LLY@Lilly, Lars Hagen Jensen/EMA/LLY@Lilly, Florence Leroux/AM/LLY@Lilly, Mickael Lothgren/EMA/LLY@Lilly, Jacques Mosseri/EMA/LLY@Lilly, Vincenzo Navarra/EMA/LLY@Lilly, Matthew R Pike/AM/LLY@Lilly, Roland Powell/EMA/LLY@Lilly, John C Saunders/EMA/LLY@Lilly, Robert Schnitzler/EMA/LLY@Lilly, Cameron Stokes/AM/LLY@Lilly
Subject: Issues Management / Australian Label Update & Positive News Article

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Zyprexa MDL 1596: Confidential-Subject to Protective Order

Australian Regulatory Board Accepts Lilly's Language Purposal with Respect to Glucose

Today, Lilly Australia received word that the Australian Regulatory Board (TGA) has accepted the changes Lilly suggested to the Zyprexa PI regarding glucose dysregulation. A special congratulations to **Kylie Murray, Patrizia Cavazzoni** and everyone else involved in these negotiations that have been ongoing since last March!

The changes are as follows:

Under Precautions:

There is an increased prevalence of diabetes in patients with schizophrenia. As with some other antipsychotics, exacerbation of preexisting diabetes has been reported very rarely. Hyperglycemia, diabetic coma and diabetic ketoacidosis have been reported in very rare cases, sometimes in patients with no reported history of hyperglycemia (see ADVERSE REACTIONS). Appropriate clinical monitoring is advisable in diabetic patients.

Changes have also been made to the Adverse reaction section as follows:

Adverse events identified from clinical trials

In clinical trials with olanzapine in over 5000 patients with baseline non-fasting glucose levels 7.8 mmol/L, the incidence of non-fasting plasma glucose levels 11mmol/L (suggestive of diabetes) was 1.0%, compared to 0.9% with placebo. The incidence of non-fasting plasma glucose levels 8.9mmol/L but <11mmol/L (suggestive of hyperglycemia) was 2.0%, compared to 1.6% with placebo;

Adverse events identified from spontaneous post marketing surveillance

Metabolic - Very rare (< 0.01%): exacerbation of preexisting diabetes

Fox News columnist attacks studies critical of Zyprexa!!

The following column appeared Friday the 23rd on FoxNews.com and JunkScience.com. The author is a critic of so-called "junk science" -- poorly designed or biased studies reported on in the media that are usually competitively or politically motivated. The column hits right at the heart of the limitations of the studies that our competitors have been using to criticize Zyprexa.

The ZPT suggests that affiliates work aggressively to leverage this article through out their marketing mix. The link to the actual web site follows, as well.

<http://www.foxnews.com/story/0,2933,61084,00.html>

Stop Scaring the Mentally Ill

Friday, August 23, 2002

By Steven Milloy

Schizophrenics may be the latest victims of the junk science mob. There seems to be a move afoot to link the leading medication for treating schizophrenia with diabetes.

Zyprexa (olanzapine) is one of a new class of so-called "atypical antipsychotics" that treat not only the "negative" symptoms of schizophrenia (low motivation and diminished motivations) but the "positive" symptoms (delusions and hallucinations) as well.

Zyprexa is the first atypical antipsychotic to show long-term effectiveness in patients with schizophrenia and has been prescribed to nine million people worldwide.

This success seems to have made the medication a target.

A new study published in the Aug. 3 *British Medical Journal* concluded that Zyprexa "is associated with a clinically important and significant increased risk of diabetes." The researchers reported about a three-to-five-fold increase in diabetes among Zyprexa users compared to non-users of antipsychotics.

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Unfortunately for the researchers' conclusion, though, there were only nine cases of diabetes among the 970 study subjects who used Zyprexa. No doubt this is why the margin of error for the study results was three times larger than the size of the reported increase in risk.

The study was also limited by the researchers' failure to consider key risk factors for diabetes, including race and weight gain, as possibly being responsible for the observed cases of diabetes among study subjects.

There are some other studies that purport to show a causal link between atypical antipsychotics and diabetes, but these studies report similarly weak statistical results based on data of unknown-to-suspect reliability.

USA Today trumpeted one of these studies with the headline "Anti-psychotic drug linked to diabetes" -- even though the study data was not collected in a scientific manner and the authors acknowledged their finding did not prove a cause-and-effect relationship.

Finally, all study results to date are hopelessly confounded by the recognized phenomenon of increased incidence of diabetes among people with schizophrenia. This isn't really unexpected. Schizophrenics tend to suffer from multiple health complications and tend to lead relatively unhealthier and sedentary lifestyles.

So why the rash conclusion? There seems to be some skullduggery occurring.

Bristol Myers Squibb is the source of funding for the *British Medical Journal* study and is awaiting FDA approval of its own antipsychotic drug (aripiprazole) later this year.

BMS obviously doesn't want to scare physicians and patents away from antipsychotics altogether. But a little temporary fearmongering might raise enough questions about Zyprexa to give BMS' Johnny-come-lately drug a fighting chance when it's finally approved.

Oh, and did I mention that one of the study's researchers was a BMS employee?

This situation smacks of the 1995 scare involving Pfizer's calcium channel blockers, a type of blood pressure medication. Researchers released pre-publication study results at a medical conference reporting that CCBs were statistically associated with increased risk of heart attack. Ensuing media reports caused a number of CCB users to stop taking their medication. Two people were reported to have died as a result.

The study turned out to be so flawed, though, that the researchers were forced to apologize to their colleagues. Evidence later turned up linking the scare with a rival pharmaceutical company that manufactured a competitor to CCBs.

Such cutthroat competition is not unusual for the pharmaceutical industry. **But patients scared away from their medication pay the price.**

Antipsychotic treatments like Zyprexa help people with schizophrenia function day-to-day. Schizophrenia is a condition that must be treated and the new atypical antipsychotic drugs so far are the most effective with fewest side effects.

There are 9 million Zyprexa users worldwide. Clinical research into the atypical antipsychotics-diabetes question is ongoing. Until the results are in, it should take more than poor quality statistics before schizophrenics and their doctors are scared off a beneficial medication.

*Steven Milloy is the publisher of JunkScience.com, an adjunct scholar at the Cato Institute and the author of *Junk Science Judo: Self-defense Against Health Scares and Scams* (Cato Institute, 2001).*

Kind Regards,

Tony Fiola
Global Marketing Associate
Zyprexa Product Team
(317) 276-9417

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