75-5

Printed by Lisa Vierhile

Bonnie A Meloche
10/04/2001 01:50 PM

To: Lisa A Vierhile/AM/LLY@Lilly
cc: Venn Mutambirwa/AM/LLY@Lilly
Subject: Re: Proposed safety revisions to the ZYPREXA Product Monograph - Glucose Monitoring

Notifiable Change submissions have a 90-day default review time, therefore we would expect approval by DEC 21-2001. This request would come as a clarification request any time between now and DEC 21st. We would have 15 calendar days to respond. The response has to be there on the 15th day.

I figured this would generate a lot of discussion. I thought that I might try to act as proactively as possible. We have not received the request yet and I am not certain how to proceed. Would you suggest emailing the product team, PhV and legal about the ADR Newsletter issued on atypical antipsychotics and the implications this may have on the ZYPREXA labelling in Canada? If so, <and this may seem like a stupid question but....> there are so many ZYPREXA product teams exactly who should I direct the email to?

Bonnie A. Meloche
Regulatory Affairs
Eli Lilly Canada Inc.
Tel: 416-699-7460
Fax: 416-699-7352
email: meloche_bonnie_a@lilly.com
Lisa A Vierhile

Lisa A Vierhile
10/04/2001 02:36 PM

To: Bonnie A Meloche/AM/LLY@Lilly
cc: Venn Mutambirwa/AM/LLY@Lilly
Subject: Re: Proposed safety revisions to the ZYPREXA Product Monograph - Glucose Monitoring

Bonnie,

A request such as this is outside of the information contained in the CDS and would need to be evaluated by the product team, pharmacovigilance, and legal. If the product team and PhV are in alignment as to whether or not we should challenge the inclusion of such text then we could move forward without going to GPLC (we would report it via the Quarterly Report), however, if there is disagreement between the groups, GPLC must be involved.

When do you anticipate receiving such a request? How much time do you anticipate we would have to respond? My guess is a request such as this will generate a lot of discussion. Please let me know your thoughts. Thanks.

Lisa

Bonnie A Meloche

Bonnie A Meloche
10/04/2001 01:09 PM

To: Lisa A Vierhile/AM/LLY@Lilly
cc: Venn Mutambirwa/AM/LLY@Lilly
Subject: Proposed safety revisions to the ZYPREXA Product Monograph - Glucose Monitoring

Lisa,

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Printed by Lisa Vierhile

I know you must be extremely busy with [redacted]. Unfortunately, I must bother you.

Below you will find a TPD ADR Newsletter on atypical antipsychotics. As you know we have also just filed a Notifiable Change to update safety information related to olanzapine. We feel it is very likely they will ask for a statement to be added to the PM similar to the following statement in light of this ADR Newsletter:

"Patients may require glucose monitoring upon initiation and titration of antipsychotic medications, and regular monitoring thereafter."

Can you tell me what issues GOLD et al may have if this is requested by TPD? (if any)

Thanks, Bonnie

Bonnie A. Meloche
Regulatory Affairs
Eli Lilly Canada Inc.
Tel: 416-699-7460
Fax: 416-699-7352
email: meloche_bonnie_a@lilly.com
----- Forwarded by Bonnie A Meloche/AM/LLY on 10/04/2001 02:09 PM -----

Carlo Di Fonzo
10/04/2001 08:32 AM

To: Bonnie A Meloche/AM/LLY@Lilly
cc: Ruth Dickson/AM/LLY@Lilly, Barry Jones/AM/LLY@Lilly, Venn Mutambirwa/AM/LLY@Lilly, Joel Raskin/AM/LLY@Lilly, Joerg Rustige/AM/LLY@Lilly
Subject: Re: Proposed safety revisions to the ZYPREXA Product Monograph - Glucose Monitoring

Bonnie:
I have had another look at the issued TPD ADR Newsletter article on "Atypical Antipsychotics:Impaired Glucose Metabolism". The concluding statement says: "Patients may require glucose monitoring upon initiation and titration of antipsychotic medications, and regular monitoring thereafter."

[redacted]
ADR Newsletter Volume 11 Number 4 - October 200

As part of the Notifiable Change to update the safety information in the Zyprexa PM, I know we added increased glucose levels under Adverse Reactions.
However, did we add any information regarding glucose monitoring? We should anticipate that TPD may require this to be added. Therefore, should check with Global Regulatory - GOLD on their position re. this issue.
Carlo.

Carlo J. Di Fonzo
Regulatory Affairs & Quality Compliance
Eli Lilly Canada
Tel: 416-693-3520
----- Forwarded by Carlo Di Fonzo/AM/LLY on 10/04/2001 08:22 AM -----

Carlo Di Fonzo

To: Joerg Rustige/AM/LLY@Lilly
cc: Ruth Dickson/AM/LLY@Lilly, Ruth Dickson/AM/LLY@Lilly, Barry

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09/28/2001 05:16 PM

Jones/AM/LLY@Lilly, Barry Jones/AM/LLY@Lilly, Bonnie A Meloche/AM/LLY@Lilly, Bonnie A Meloche/AM/LLY@Lilly, Venn Mutambirwa/AM/LLY@Lilly, Venn Mutambirwa/AM/LLY@Lilly, Joel Raskin/AM/LLY@Lilly

Subject: Re: Proposed safety revisions to the ZYPREXA Product Monograph

Joerg: I think we have it covered in the proposed revisions to the Product Monograph.

Under the Adverse Reactions section (page 38 of the revised PM), Venn has added "random glucose" increases (160 to 200 mg/dL "suggestive of potential hyperglycemia" and greater than 200 mg/dL "suggestive of potential diabetes") to the adverse drug reactions table.

Carlo.

Carlo J. Di Fonzo
Regulatory Affairs & Quality Compliance
Eli Lilly Canada
Tel: 416-693-3520
Joerg Rustige

Joerg Rustige
09/28/2001 03:24 PM

To: Carlo Di Fonzo/AM/LLY@Lilly
cc:
Subject: Re: Proposed safety revisions to the ZYPREXA Product Monograph

Carlo -

one of my concerns is the rapid rising glucose level in rare cases .

The autopsy report I sent earlier shows that this is not always accompanied with Ketoacidosis.

Did we capture this in the notifiable change?

Joerg
----- Forwarded by Joerg Rustige/AM/LLY on 09/28/2001 03:28 PM -----

Joerg Rustige
09/28/2001 02:40 PM

To: Venn Mutambirwa/AM/LLY@Lilly
cc:
Subject: Re: Proposed safety revisions to the ZYPREXA Product Monograph

Venn - a lot of work. Congratulation.

I have one question though:
without wanting to read the whole document:
do we have a warning somewhere relating to rising glucose levels
or the possibility of rising glucose levels after taking the drug?

Joerg

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