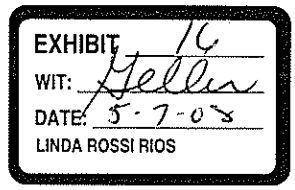
Id : i.m.1d84fa6d4639f89d2a0c24c368cc6f5f
CN : SQ1ED00428635
Date : Tuesday, October 31, 2000 8:00:00 AM GMT
From : Giddins, Russell E
To : Geller, Wayne
Subject : FW: Seroquel and Diabetes
Custodians : Geller, Wayne



From:
Giddins, Russell E

Sent:
Tuesday, October 31, 2000 3:41 PM

To:
Geller, Wayne

Subject:
FW: Seroquel and Diabetes

FYI

From:
Brecher Martin M

Sent:
26 October 2000 14:35

CONFIDENTIAL

To:

Giddins Russell RE

Cc:

Jones Martin AM - PHMS

Subject:

RE: Seroquel and Diabetes

Russell,

We should include our monotherapy weight data in our response to the Dutch College. This allows clear differentiation from olanzapine.

Martin

From:

Giddins Russell RE

Sent:

Wednesday, October 25, 2000 1:52 PM

To:

Brecher Martin M; Geller Wayne

Cc:

Lindstrom Diane DD; O'Brien Shawn SP; Czupryna Michael MJ; Duffy Paul PA - SAFA; Dev Vikram VJ; De Vriese Geert; Dartee Wim WP; Vree Jeroen; Witch Emma E; Grant Tom T - WWRA

Subject:

FW: Seroquel and Diabetes

Dear All,

The Dutch Agency have been informed that the document provided on diabetes was sent to them in error and that we shall provide them with new data. We have therefore managed to pull back from the position of "offering" a label change and so have avoided undermining the core datasheet.

We now have time to thoroughly consider our position on this issue, and proceed as suggested by Wayne's action plan (see below). The data package can then be transmitted to the Agency.

Please note that this issue is unlikely to go away and it is likely to encompass the other antipsycotics. If we are hoping to maintain a differential in this respect to Zyprexa, I suggest that, in addition to establishing our stance with regard to Seroquel, we should also examine the profiles of the competition so that if there is an opportunity to differentiate ourselves, we should try to do so.

Best regards,

Russell

From:

Vree, Jeroen

Sent:

25 October 2000 11:04

To:

Giddins, Russell RE

Subject:

RE: Seroquel and Diabetes

Importance:

High

Dear Russell,

In view of the below and after consultation with my DSO, I decided to contact the MEB Pharmacovigilance Head of Department Arthur Meiners directly. He gratefully acknowledged the use of the document provided by us. I have explained the fact that he had received the wrong document for the intended use. I also explained the internal process for which the doc was intended without much detail. Arthur told me that a new document and new data will be reviewed if submitted, but that it would not change his view very much.

After being asked Arthur told me that this is an initiative to target the whole atypical group, so also our competitors. If the Department can find internal agreement on this issue (you only saw the draft assessment report, it isn't final), the MAHs of the whole group would be asked to include this identical information. We therefore have little chance to escape. In any case he found the effect, if any, to be very minor, but to ensure correct information and guidance to doctors just in case, he has chosen very general and superficial wording. We are welcome to submit new data and an explanatory letter and this will be reviewed, but as I said, the chances of being left out are small. Please check whether we have NO cases at all, that's our only chance. It is also good to know that submission of our document did not do any harm; we would presumably have ended up with a request to include information whether or not we submitted a response.

I hope this may clear the air.

Kind regards,

Jeroen

Drs. J.B. Vree

Registration Officer

AstraZeneca BV, The Netherlands

Tel. +31 79 3632264

Fax +31 79 3632450

-----Oorspronkelijk bericht-----

Van:
Giddins Russell RE

Verzonden:
dinsdag 24 oktober 2000 14:33

Aan:
Vree Jeroen

CC:
Koomen Oscar; Dartee Wim WP

Onderwerp:
FW: Seroquel and Diabetes

Urgentie:
Hoog

Jeroen,

Could you please give me a call, to discuss how best to approach the assessor/agency, after you have had a review the attached note.

Many thanks,

Russell

From:
Geller Wayne

Sent:
23 October 2000 23:18

To:
Brecher Martin M; Giddins Russell RE

Cc:
De Vriese Geert; O'Brien Shawn SP; Dev Vikram VJ

Subject:
RE: Seroquel and Diabetes

Importance:

High

Dear Russell, Martin et al:

Please allow me to explain what has happened here. In early September I received a request from Dorothee Wientjens to respond to the Dutch Authorities regarding quetiapine and glucose metabolism. I sent Dorothee a copy of the recent Seroquel Safety Position Paper on DM and related disorders. This position paper followed the June 2000 SERM where it was presented as a discussion document. At the time, I did not consider sending the FDA response formulated this past summer. Only after receiving Russell's e-mail below did I realize that, in revising the document, I had inadvertently left a paragraph in which contradicted our summary and conclusions statements. Clearly the Dutch picked up on this discrepancy, hence their request to change the package label.

I now realize the mistake that I have made and apologize to all for having sent out this document. I agree with the earlier proposals to try and rectify the situation by providing the Dutch Authorities with the document sent earlier to FDA and to send a cover letter explaining the discrepancies. I, too, endorse Russell's position on future regulatory submissions and support measures aimed at timely, thorough internal review of documents going out to regulators.

As part of the corrective action plan, I would like to propose the following measures be taken in addition to those already discussed:

1. An immediate analysis of all reported cases of diabetes mellitus/hyperglycemia/diabetic ketoacidosis from mid-May 2000 through October 23, 2000

2. Re-review at the November 14/15 SERM meeting this topic with the new data

3. Correct the position paper to reflect our thinking on this issue shortly after the upcoming SERM meeting

Russell, I would appreciate your communicating these actions to the Dutch Health Authority, so that they are fully aware of this discrepancy and our plan for resolving this.

Please let me know what I can do to further assist in rectifying this matter.

Thanks and kind regards,

Wayne

-----Original Message-----

From:
Brecher Martin M

Sent:
Sunday, October 22, 2000 8:55 PM

To:
Giddins Russell RE; Geller Wayne

Cc:
De Vriese Geert; O'Brien Shawn SP

Subject:
RE: Seroquel and Diabetes

Russell. Wayne,

Who submitted the document to the Dutch agency?

Prior to reading the document sent to the Dutch I was of the opinion that our position was described in the FDA submission and that the FDA submission included all the cases described in the Dutch submission.WAYNE PLEASE CONFIRM.

If this is the case I agree with your suggestion Russell that we attempt to retrieve the situation by providing the Dutch with the FDA document as well as a cover document explaining why the FDA document provides the best analysis of the facts and trying to persuade them that the submission was an internal; document inadvertantly submitted.

I endorse all your views regarding future regulatory submissions.

This is a hot issue which requires immediate attention and priority.

Martin

From:

Giddins Russell RE

Sent:

Friday, October 20, 2000 12:27 PM

To:

Brecher Martin M; Geller Wayne

Cc:

De Vriese Geert; Lindstrom Diane DD; O'Brien Shawn SP; Czupryna Michael MJ; Duffy Paul PA - SAFA; Dev Vikram VJ; Butler George GC; Dartee Wim WP; Vree Jeroen; Koomen Oscar; Griffett Chris CR; Atkin Karen K; Arnold Barry BDC; O'Flynn Michael; Smith Mark MA MD; Witch Emma E

Subject:

Seroquel and Diabetes

Dear Martin and Wayne,

I tried to call you both but you were travelling.

We have now received another draft assessment report from the Dutch College, attached below. This assessment report however concerns Seroquel and Diabetes. The MEB are requesting us to add information regarding diabetes to the Warnings and Adverse events sections of the Dutch SPC.

<<
File: PhVigilance.pdf
>>

Please note that at the moment this a local Dutch initiative, but it may yet be linked into the recent draft assessment report for the MR SPC variation. Even if it is not linked, as The Netherlands is the Reference member state for Seroquel, the outcome will impact on the MR SPC and the other MR countries.

We need to prepare to respond to this new assessment report.

Please note that the request from the Dutch agency was prompted by the following submission that was sent to the Dutch agency:

<<
File: SeroquelSERMDMDKAPositionPaper.doc
>>

The document states that:

"While there were no reports of positive dechallenges and rechallenges, there is reasonable evidence to suggest that Seroquel therapy can cause impaired glucose regulation including diabetes mellitus in certain individuals. Consideration should be given to adding diabetes mellitus to the core data sheet based upon postmarketing and clinical trial safety data."

Having sent this to the Dutch College, it appears to me that we have offered a label change to the Dutch agency. I am unaware that we are in the process of revising the core datasheet in respect to this issue (this issue is not on the agenda for the upcoming SERM meeting). If it was not our intention to offer up such a change, we need to correct this false impression.

Jeroen/Oscar, could we retrieve the situation and clarify that the document was an internal discussion document and therefore has been sent out prematurely.

This also appears to contrast with the response that was recently sent to the FDA:

"Thus very few cases of diabetes mellitus (and related complications), hyperglycemia, and weight gain have been reported. AstraZeneca believes that
the current US Seroquel label accurately describes patient experiences to date of these conditions."

Martin, could you please let me know what the Medical function view is on this issue.

Please note that the document attached above was sent without the knowledge of Regulatory Affairs. As a result, I have a number of concerns:

1. It may appear to the Dutch agency that we are not keeping the SPC as up to date as we could, particularly when viewed against the SPC variation the we are currently progressing. We need to take great care with the impression of ourselves that we project to the Regulatory Agencies.

2. This document does not appear to have been through any internal review process and as such should not have been sent out to a Regulatory Agency. I recommend that internal discussion documents, such as those for SERM review, are marked as such until they have been properly reviewed and signed off.

3. If we "offer" a label change it must first be included in the core datasheet. All proposed label changes must go through the proper procedures and this involves Regulatory Affairs.

In future, documents to Regulatory Agencies should go via Regulatory Affairs and we should be kept informed of interactions with Regulatory Agencies.

Russell Giddins

Seroquel RAD