

From:

From: Melville, Margaret G
Sent: Thursday, December 12, 2002 10:51 AM
To: Fitton, Lesley R; Ney, Christine A; Schwartz, Jack A; Brecher, Martin; Jones, Martin AM; Oldham, Alex; Street, Paul R; Trumble, Sharon M; Fox, Mahogany; Limp, Gerald L; Leong, Ronald; Warner, Linda (Safety)
Subject: FW: Seroquel Diabetes Issues - Changes to Zyprexa PI in Australia
Dear All,

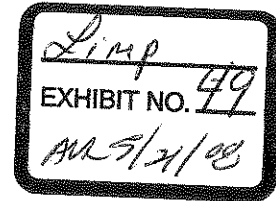
Please find the below information regarding a recent Dear Dr. Letter issued in Australia for Olanzapine. You will note, as Paul does, that they have been able to put their findings in context with the first sentence -- diabetes incidence is increased in schizophrenic patients.

The issuance of a Dear Dr. Letter was the first step in the cascade of events in Japan. Mahogany, please do keep us in the loop as we feel this is a hot topic.

We will review the glucose issue in a Safety and Evaluation Meeting on December 16, but currently there is no language regarding glucose dysregulation in the Core Data Sheet. At this time any language regarding glucose dysregulation must be imposed by Health Authorities.

Best Regards,

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

From: Street, Paul R
Sent: Tuesday, December 10, 2002 2:37 PM
To: Trumble, Sharon M; Groves, Angela J; Jonsson, Marianne; Cronin, Kathryn E; Melville, Margaret G; Parish, Caroline; Grafford, Kerstin
Cc: Fox, Mahogany
Subject: Seroquel Diabetes Issues - Changes to Zyprexa PI in Australia

Colleagues

Mahogany Fox (Regulatory Affairs, AZ Australia) has kindly provided a copy of a Dear Doctor Letter dated 30 September that was issued by Lilly concerning glucose dysregulation with olanzapine (Zyprexa). This action has apparently been taken proactively by Lilly, rather than as a response to a specific Health Authority request. The following addition to the text in the 'Precautions' section of the PI has been agreed:

'There is an increased prevalence of diabetes in patients with schizophrenia. As with some other antipsychotics, exacerbation of pre-existing diabetes has been reported very rarely. Hyperglycaemia, diabetic coma and diabetic ketoacidosis have been reported in very rare cases, sometimes in patients with no reported history of hyperglycaemia (see ADVERSE EVENTS). Appropriate clinical monitoring is advisable in diabetic patients' 'Note that very rare refers to an incidence <0.01%'

The Dear Doctor Letter cites four publications to substantiate the statements regarding the increased prevalence of diabetes in the schizophrenic population. A tabulation of 'diabetes warnings' from Australian PI was also provided for other atypicals (clozapine and risperidone) and typicals (chlorpromazine; droperidol; flupenthixol; fluphenazine; haloperidol; primozide; thioridazine; trifluoperazine and zuclopenthixol).

The other changes to the PI are:

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 glucose levels >11 mmol/L (suggestive of diabetes) was 1.0% compared to 0.9% with placebo. The incidence of non-fasting plasma glucose levels >8.9 mmol/L but <11 mmol/L (suggestive of hyperglycaemia) was 2.0% compared to 1.6% with placebo.'

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Adverse events identified from post marketing surveillance

'Metabolic - Very rare (<0.01%) exacerbation of pre-existing diabetes

I hope this helps. Please let me know if you need any more information

Regards

Paul

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