

John C Saunders
04/20/01 06:33 AM

To: Jared G Kerr/AM/LLY@Lilly
cc: Anna Thornton/AM/LLY@Lilly, Jared G Kerr/AM/LLY@Lilly, Michele Sharp/AM/LLY@Lilly, Patrizia Cavazzoni/AM/LLY@Lilly
Subject: Re: South Africa Labeling Response: SmPC

The CPMP have given a positive opinion on the revised wording and this is now in the legal process with the EU commission - it will be approved ca 7/01) The text is as follows:

4.4. Special warnings and special precautions for use

Hyperglycaemia or exacerbation of pre-existing diabetes occasionally associated with ketoacidosis or coma has been reported very rarely, including some fatal cases. In some cases, a prior increase in body weight has been reported which may be a predisposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus.

4.8. Undesirable effects

Common (1-10%):

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 ≥ 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. For further information, see Section "Very Rare ($<0.01\%$)" below. (JCS note $<\geq$ symbols presented properly in MSWord, but don't copy / paste into notes.)

Very Rare ($<0.01\%$):

Hyperglycaemia or exacerbation of pre-existing diabetes occasionally associated with ketoacidosis or coma has been spontaneously reported very rarely, including some fatal cases (see also Section 4.4, Special warnings and special precautions for use).

Jared G Kerr



Jared G Kerr
18/04/01 19:32

To: John C Saunders/EMA/LLY@Lilly
cc: Patrizia Cavazzoni/AM/LLY@Lilly, Jared G Kerr/AM/LLY@Lilly, Michele Sharp/AM/LLY@Lilly, Anna Thornton/AM/LLY@Lilly
Subject: South Africa Labeling Response: SmPC

John:

I hope all is well with you and you had a nice vacation. We recently received a request from our South Africa affiliate concerning the wording of hyperglycemia in their label. The CDS states:

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Random plasma glucose levels \geq 200 mg/dL (suggestive of potential diabetes) as well as random levels \geq 160 mg/dL but $<$ 200 mg/dL (suggestive of potential hyperglycemia) in patients with baseline random glucose levels \leq 140 mg/dL have been seen occasionally in clinical trials.

The proposed comments from the South Africa MCC (MOH) is mostly from the SmPC section 4.4 "Special Warnings and special precautions for use".

Under "Warnings" - "Hyperglycemia or exacerbation of preexisting diabetes has been reported in very rare cases during ZYPREXA treatment. In some cases, a prior increase in body weight has been reported which may be a pre-disposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus." (South Africa MCC proposal)

Has the draft with the rappateur's comments on the SmPC specific to hyperglycemia been accepted and finalized? We need to determine our strategy regarding the South Africa MCC's proposal.
Thanks.

Sincerely,

Jared Kerr, MPH

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