

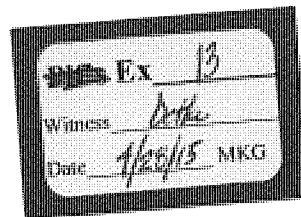


Pierre V Tran/AM/LLY
11/11/2002 08:44 PM

To Walter Deberdt/AM/LLY@Lilly
cc David G Perahia/EMA/LLY@Lilly, Dick Veldhuis/EMA/LLY@Lilly, Ilker Yalcin/AM/LLY@Lilly, John H April/AM/LLY@Lilly, Lily Zahed/AM/LLY@Lilly, Michael Detke/AM/LLY@Lilly, Richard Bump/AM/LLY@Lilly

bcc

Subject Re: comments on SUI clinical expert report



Walter,
Thanks for taking the time to review the SUI CER and offer your valuable comments.
Pierre
Walter Deberdt

Walter Deberdt
11/11/2002 06:44 PM

To: Richard Bump/AM/LLY@Lilly, Ilker Yalcin/AM/LLY@Lilly
cc: John H April/AM/LLY@Lilly, Michael Detke/AM/LLY@Lilly, David G Perahia/EMA/LLY@Lilly, Pierre V Tran/AM/LLY@Lilly, Dick Veldhuis/EMA/LLY@Lilly, Lily Zahed/AM/LLY@Lilly
Subject: comments on SUI clinical expert report

Richard, Ilker,

As you may know I'll work together with David and John on the MDD CER. So I read with much interest (during the rainy weekend) the SUI CER. I have written my comments in red in the attached document. I appreciated very much all the hard work that must have gone in this review and besides the few items that I'm listing here below I'm convinced you have made a very useful document which is nice to read (when it's raining outside).

I read through this document in a 'naive' condition: I don't know much about SUI and I just started working on duloxetine. I thought this could be useful for you since CPMP members don't know much about SUI and duloxetine neither. I also took the approach that the CER should be readable as a stand alone document, because the CPMP members may not want to look up numbers and % in the Summaries or in the Study Reports.

As you can see in my comments in the CER, I fear that the pharmacokinetics section in the actual wording shows too much doubt and uncertainty.

In the efficacy section one should pay attention to the difference between SBAT in I-QOL compared to the other studies, and the possible explanations for this difference, since this is the European phase III study. CPMP is likely to be sensitive on this.

Knowing a bit the CPMP sensitivity for maintenance of effect and relapse rates, I'd add some discussion on these.

I think it is important to discuss the early discontinuations due to AE in relationship to uptitration like in SAAW, compared to the other studies; especially if these early DC/AEs were making the difference between the 'European' SBAT study and the other studies.

Discontinuation symptoms are a big deal in MDD (thanks to ourselves with Prozac promotion). Mike, can you confirm that for MDD we would propose a gradual tapering? It would seem logic that if we propose this for MDD, we would recommend it also for SUI.

Finally, I'd be glad to discuss these and other topics in more detail with you. I'm sure I would learn from such a discussion. So, if you have some time for this, please send me an invitation when it is convenient for you. Many thanks,

Walter Deberdt
Sr. Clinical Research Physician

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