Reviewer's report

Title: Greater Incidence of Depression with Zolpidem, Zaleplon, Eszopiclone, and Ramelteon than with Placebo

Version: 5 Date: 22 May 2007

Reviewer: Ripu Jindal

Reviewer's report:

General
I believe that any examination of an association must include discussion of limitations of the study. There is a need to establish temporal relationship and all alternative explanations should be ruled out before causality can be inferred. I see that the author has removed causation from the title. I do not see efforts to discuss alternative explanations for the association.

In the end, I did not reach the same conclusions that Dr. Kripke did. He concludes his paper, "when premonitory insomnia occurs preventive treatments such as antidepressant drugs, depression oriented cognitive behavioral therapy and bright light may be preferred." Dr. Kripke's analyses of the data have yielded provocative results. They just need to be followed by controlled studies. We do not have the data (to report to the patients or even the physicians) to recommended prophylactic antidepressant treatment, and sleep restriction as ways to prevent depression. In the last few years we have learned that antidepressant do increase the risk of suicide in some patients. However, the risk benefit analyses continues to favour use of antidepressants in the treatment of depression. I do not believe that we have the data to conduct a risk benefit analysis of prophylactic use of antidepressant agents.

I agree with Dr. Kripke that the FDA and the pharmaceutical manufacturers are good target audience for this paper. I do not think that patients and general practitioners are the right audiences for the paper. The results can be used to secure funding for further studies but not to make treatment recommendations.

The author has mentioned the mood elevating effect of sleep deprivation. I believe such an effect is only transient. The effect of long term sleep deprivation on mood is largely unknown. I would like the author to clarify the issue of sleep deprivation. Recommending the use of sleep deprivation as well as sedating antidepressant such as trazodone, seems contradictory.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

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What next?: Reject because scientifically unsound

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
**Statistical review**: No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I do not have any competing interest