Reviewer's report

Title: Prospective Open-Label Study of Add-on and Monotherapy Topiramate in Civilians with Chronic Nonhallucinatory Posttraumatic Stress Disorder

Version: 1 Date: 1 July 2004

Reviewer: Phebe Tucker

Reviewer's report:

Accept article, after both discretionary revisions and minor essential revisions (labeled). This is, I believe, an article of importance in its field

Questions:

1. Is the question posed by the authors new and well defined?

The question is well defined in the abstract: will a prospective, open-label study confirm therapeutic effects of topiramate in chronic, nonhallucinatory PTSD observed in a prior study? Thus, although not entirely new, it further explores this treatment question in a more focused design, excluding hallucinatory PTSD which had a less robust effect in the author’s prior study, and improving on use of assessment instruments.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?

The methods are generally well described, although a few points need to be addressed:

- Although informed consent was obtained, it would be important to clarify why obtaining IRB approval may not have been necessary, even a less formal centralized IRB approval consistent with chart reviews of clinical treatments. Did subjects sign an informed consent document? Although these steps may not be absolutely necessary for a clinical population in a private practice setting, the methods section should address this issue. (major compulsory revision)

- On page 6, shouldn’t secondary measures also include cluster C and D symptoms? (minor essential revision)

- On page 6 in second full paragraph, please clarify more the “response” and “full response” criteria for reduction of nightmares. It is a bit confusing because you are using response for PCL-C in the previous paragraph as 30% reduction of symptoms. (minor essential revision)

- It would be helpful to give the baseline and end PCL-C symptom levels for total and subclusters. (minor essential revision)

- On page 10, eliminate reference to quetiapine, an atypical antipsychotic, which does not fit in with the discussion of anticonvulsants. (discretionary revision)

- On page 10-11, in discussion of side effects, it might be helpful to mention that topiramate does not have the side effects associated with SSRI’s often used/approved in PTSD (sexual dysfunction, weight gain, sleep disturbance, etc.) (discretionary revision)
3. Are the data sound and well controlled?
   · This is not a placebo-controlled study, but uses an appropriate, validated rating scale to assess PTSD.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   · I can’t assess statistics adequately, but ANOVA on bottom of page 7 may need more clarification (p-value, etc.) (discretionary revision)

5. Are the discussion and conclusions well balanced and adequately supported by the data? Yes, and limitations are candidly discussed.

6. Do the title and abstract accurately convey what has been found?
   Yes, they are focused

7. Is the writing acceptable?
   The article is generally very well written and interesting. A few points:
   · References (minor essential revisions)
     i. I would cite a more recognized epidemiologic work for prevalence of PTSD, such as Kessler’s study (Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB (1995): Posttraumatic stress disorder in the National Comorbidity Survey. Archives of General Psychiatry 52:1048-1060.)
   · On page 5, eliminate reference to Table 1 from Methods; it is already appropriately mentioned in Results, Patient Characteristics. (discretionary revision.)
   · On page 7, list the % reduction of subscale symptoms beside each cluster rather than as a range (minor essential revision)
   · Table 1: spell out years, and label comorbid disorders with N and % in the far right column. (minor essential revision)
   · Table 4: spell out days and put labels over far right column. (minor essential revision) 
   · Figure legend: Eliminate “and response rate”—I believe figure shows symptom reduction rather than response rate. (minor essential revision)

Is review by expert statistician necessary: Perhaps. I cannot assess the ANOVA and its description on page 7. Perhaps other reviewers can.

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Declaration of competing interests:
I have received research funding from Ortho-McNeil Pharmaceuticals, Inc., to conduct research in this same area. I have also received some honoraria for consultant work and as participant in Speaker's Bureau for Ortho-McNeil Pharmaceuticals, Inc.