Reviewer's report

Title: A double-blind, randomized, placebo-controlled study assessing the efficacy and tolerability of desvenlafaxine 10 and 50 mg/d in adult outpatients with major depressive disorder

Version: 1 Date: 27 November 2012

Reviewer: Nicholas Mitchell

Reviewer's report:

Re:

“A double-blind, randomized, placebo-controlled study assessing the efficacy and tolerability of desvenlafaxine 10 and 50 mg/d in adult outpatients with major depressive disorder”

Thank you for inviting me to review this article. Overall, this is a very professionally written article, reflecting a generally well-designed clinical trial.

Please find my comments and suggestions below.

Major Compulsory Revisions:
None

Minor Essential Revisions:
1. In the inclusion criteria, I would be interested to know how the DSM-IV diagnosis of MDD was established (i.e. through clinical interview, checklist, SCID).

2. The authors specify in Figure 1 that 3 individuals were excluded for concomitant medication use. I would like to know what medications were considered for exclusion criteria, and if patients were allowed to use particular types of medications (i.e. benzodiazepines or hypnotics) during the trial period.

3. Similarly, 33 individuals were excluded based on comorbid conditions. I would like to know what psychiatric disorders were used as exclusion criteria and which were not.

Discretionary Revisions:
1. It may be worth mentioning in the final paragraph of the background section that this study was not designed to compare between the doses of desvenlafaxine used. This is mentioned in the conclusions, but given the number of comparisons made between the treatment groups in the results section, it would benefit the reader to have it pointed out earlier.

2. Were patients with uncontrolled hypertension excluded? If so, specifically mentioning this would be beneficial given concerns with other SNRIs.
3. Were any measures taken at the follow-up visit that occurred 7 to 14 days after the end of the trial period? If not, this may represent a limitation of the trial as separation from placebo may have occurred outside of the 8 week trial period.

4. In the conclusions, the authors note that a high placebo response rate is associated with failure to separate from placebo in clinical trials. I think that it is notable that the authors attempted to control for this by excluding individuals with a large placebo response at baseline, and still had a large placebo response during the trial period.

Sincerely,

Dr. Nicholas Mitchell

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare I have no competing interests.