Reviewer's report

Title: Onset of Efficacy and Tolerability Following the Initiation Dosing of Long-Acting Paliperidone Palmitate: Post-Hoc Analyses of a Randomized, Double-Blind Clinical Trial

Version: 2 Date: 17 November 2010

Reviewer: Catherine A. Harrington

Reviewer's report:

Major Revisions
1. Please determine the composite incidence of any EPS symptom. Although there was a low incidence of individual events, an overall estimate of any EPS symptoms would be useful in evaluating overall tolerability. Also, add information on changes in the rate of use of anti-EPS medication, if no changes, please state that.
2. Add information on any serious adverse events that may have occurred or state that none occurred.

Minor Revisions
1. Add a sentence to the Design section on page 5 that summarizes the exclusion criteria for the original study.
2. There is an extra period in the second from the last sentence on page 6.
3. Anxiety appears to be dose related. Please mention this in the results or discussion section.

Discretionary Revisions
1. The lead sentence in paragraph 1, page 5 starting with "An early... is duplicative. The idea was already clearly stated earlier in the background section. Perhaps add a sentence in this same paragraph clarifying the benefit of deltoid injection (e.g. better absorption) over gluteal (e.g. less pain).
2. A composite for any sexual disorder events might also be illuminating but a 36 day time period is probably too short to evaluate the effect of hyperprolactemia.
3. On page 8 in the discussion on baseline use of concomitant medications (e.g., benzodiazepines) an overall rate of use is reported. Was there a difference at baseline between placebo and treatment groups in rate of use?
4. While investigators must decide on "treatment-relatedness" when making a decision to withdraw treatment in the face of an adverse event for an individual patient, this is not a reliable assessment for evidence based decision-making and should not be reported.

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 own very small stock positions in Johnson and Johnson and Abbott.