Reviewer's report

Title: Early identification of patients at risk for substantial weight gain during Olanzapine treatment for schizophrenia, schizophreniform, or schizoaffective disorder

Version: 1 Date: 25 March 2008

Reviewer: Douglas Noordsy

Reviewer's report:

This report describes a post-hoc analysis of 2 Lilly datasets involving patients with schizophrenia randomly assigned to olanzapine treatment to evaluate early predictors of substantial weight gain at 26-34 weeks. This report is clear and well written. It presents the hypotheses, methods, results, limitations and conclusions in a methodical, precise and balanced way. I lack the expertise to fully evaluate the statistical methodology, but it appears sound.

- Major Compulsory Revisions
  NONE

- Minor Essential Revisions
  1. RESULTS, 2nd paragraph, second sentence should read: “…was a gain of 5.2 kg at Week 28 (Figure 1B).”

- Discretionary Revisions
  2. METHODS, Variables, page 6 and DISCUSSION, Limitations, page 17 refer to the fact that the available data for evaluating long-term weight gain (26-34 weeks) are within the 21 to 39 week range when weight gain has been reported to plateau in previous studies. You might point out that data that exceeded the 21-39 week range would be more valuable than data that fall within that range, as they would give greater confidence that the period of primary weight gain had passed.

  3. METHODS, Statistical Methodology, last paragraph, page 9: It is not clear from the explanation provided why an evaluation of missing values for weight at week 30 would generate 100 different datasets in order to account for uncertainty in missing values. This section attempts to prepare the reader for RESULTS, Evaluating potential impact of dropouts on the results, where the notion of multiple datasets is not mentioned. The last paragraph of this section on page 14 describes the results of this analysis, in which the correlation between weight change at 3 weeks (measured) and weight change at 30 weeks (imputed) is reported to be higher than in the primary analysis. Although the purpose and importance of this analysis is clear, it is not clear how calculation of correlation of imputed data to the data it was extrapolated from is valid. I would anticipate
many readers coming from a clinical perspective will struggle with this concept. The manuscript also describes this imputed data in terms that make it sound like real data, which is confusing.

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of outstanding merit and interest 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:**

In the past 5 years, Dr. Noordsy has been a consultant to, a speaker for, or has received research support from: Eli Lilly, Janssen, Bristol Myers Squibb, AstraZeneca, Pfizer and Forest Pharmaceuticals.