Reviewer’s report

Title: Safety and tolerability of donepezil 23 mg in moderate to severe Alzheimer’s disease

Version: 1 Date: 1 February 2011

Reviewer: Ben Seltzer

Reviewer’s report:

Review of

This is a comprehensive review of the safety and tolerability of the recently approved 23 mg/day formulation of donepezil with some additional analysis of data from 2 previous clinical trials where the temporal relationship between dose initiation and AEs could also be studied.

This is important and useful information which deserves to be published. The data are presented in clear and appropriate fashion.

1. Minor Essential Rwevisions

The authors should simply make clear that 1) this study greatly expands the safety assessment of the 23 mg/day study and is not just repeating information that has already been presented and 2) this paper includes an analysis of 2 previous trials because of the more fundamental question it raises, viz., what is the relationship between dose transitions and AEs. They have to distinguish, at various points in the text, between “this paper,” which has two methodologies and two data sets, and what they frequently term “this study,” which is actually reference 3. So, for example, the first sentence of the Discussion should read “Both the 23 mg/d …. used in the study of Farlow et al....” Similarly, under Patient Disposition, “Of 1467 patients in the 10 mg/day vs 23 mg/day study who were randomized....” And, under Objectives, “the primary objective of the study of Farlow et al....” In other words, make it clear that this paper is an analysis of three different trials, not just an appendix to reference 3.

2. Discretionary revisions

A few other minor points:

The paragraph under Methods that describes the analysis of references 8 and 9 needs to be a little clearer. I think the first sentence is missing a verb.

Last sentence, second paragraph of Discussion, say “previous studies did not
specifically examine the temporal relationship….”

Patients receiving memantine scored lower than those on donepezil alone, but was the difference statistically significant?

At the very end, do the authors want to speculate on what might be an appropriate titration from 10 mg to 23 mg to cut down initial AEs?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

Within the past 5 years, I have received honoraria for speaking from Eisai/Pfizer, Forest, and Novartis; and research support from Eisai/Pfizer and Novartis.