Reviewer’s report

Title: The Sertindole Safety Survey: a retrospective analysis under a named patient-use program in Europe

Version: 2 Date: 3 March 2008

Reviewer: Tilman Steinert

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This paper presents the results of the survey of all patients treated with sertindole after its suspension from the market in 1998. The objective of the controlled prescription was predominantly to determine the safety of the drug.

This kind of studies must obligatorily be published whatever results it yields. Otherwise a serious publication bias would result, which gives reason to serious concerns just recently. An open-access journal is a good place to publish such a paper and thus I suggest to do so. However, I would suggest some revisions, particularly regarding the presentation of the results and the discussion.

major compulsory revisions:

1) Methods, inclusion criteria: This aspect is the most unclear (see below, too). Probably, the inclusion criteria comprised those patients who had initiated sertindole before 1998 and continued it as part of the NPU programme (by the way, British English should be used, the authors write program) on the one hand and those who initiated after the suspension and primarily entered into the NPU programme on the other hand. This is what I assume, but I am not sure from the descriptions given. Anyway, this should be described more clearly and gives rise to much confusion (see below).

2) Results, p.9, last par.: the division into the 'Before' and 'After' group is not described enough clearly, see above. Line before the last: 'its' instead of 'it'. The associated table (3) is not self-explanatory in this respect and it is difficult to understand for the reader what the figures report.

3) P.10, 2nd par. 'At the time of their last physician visit (at market suspension November 1998) more than half of the patients were still being treated with sertindole'. This is quite confusing. Why was the last visit at market suspension? After reading the method I thought that Nov. 1998 was the beginning, not the end of the study period! How could patients be included who were already discontinued in Nov. 1998? Either this is wrong or the inclusion criteria are not adequately described (see above!). The related table (4), again, is not sufficiently self-explanatory at all (actually, the reader has to study the text extensively in order to understand what is meant with the right columns and their headings).

4) P. 10., continued: Market suspension accounted for one third of patients who stopped sertindole: Again, obvious contradiction with inclusion criteria as described in p.6
5) Safety chapter: Taking into account that this was the main objective of the entire study, the results presented here are too rough and superficial. What about 4 'other' deaths? In the discussion is mentioned that the 3 sudden deaths were patients with multiple previous treatments, but certainly it would be of interest to read much more details about these patients with fatal events.

6) Table 6: Again, the information about SAEs should be reported in much more detail. It is rather unsatisfactory to report 50 out of 87 adverse events as 'others' ('others' should account for not more than 20 %).

10) Table 7 maybe is superfluous and the information could be given as two lines of text. Keeping in mind 9) , I have doubts whether the heading (most frequent SAEs) is correct at all for QTc Prolongation.

minor essential revisions:

1) The abstract should contain more results. Not even the number of included patients is mentioned. Since most interest of this study was placed on cardiac adverse events, a result should be mentioned in the abstract also.

2) Background: This chapter is well written. But in the last par. it should be described more precisely what happened after the market suspension in November 1998: Under which conditions could patients continue sertindole, and under which conditions was it possible to start it after 2000?

3) Tables: The headings of all tables are 'table 1'. The right numbers should be inserted.

4) Discussion: Most of it is a repetition of the results more than a discussion. The first sentence, again, is in clear contrast with the inclusion criteria. E.g., torsades de pointes were not reported â## but could that be expected in routine ECGs? Probably not. How probable is it that torsades de pointes accounted for the cases of sudden death? How were their ECGs?

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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:

Some years ago I received travel costs and salary for a presentation about sertindole at the ECNP congress from the Lundbeck company.