Reviewer's report

Title: Impact of ethnicity on efficacy and safety during treatment with olanzapine in schizophrenia, schizophreniform or schizoaffective disorder

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Reviewer: R E E Ferner

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BMC ethnic differences in effects of olanzapine

The authors have examined a series of six trials that together included 980 patients, 605 of whom were white.

1. The study is of interest, because of the possibilities that the efficacy or safety of anti-psychotic drugs may differ between white and black populations. A previous systematic review of ADRs suggested this might be so: ‘the RR of hyperglycaemia in Black compared with non-Black patients was 1.55 (95% CI 0.95, 2.53); and the RR of diabetes mellitus in non-White compared with White patients was 1.35 (95% CI 0.95, 1.92).’ [RR = relative risk; Ormerod et al. Ethnic Differences in the Risks of Adverse Reactions to Drugs Used in the Treatment of Psychoses and Depression: A Systematic Review and Meta-Analysis. Drug Safety 2008;]. The diagnosis and prognosis may anyway differ in different ethnic groups.

2. The authors do not explicitly state how the studies identifying their criteria [duration > 6 months, at least one masked treatment arm with oral olanzapine, dose between 5 and 20 mg]. The recent Cochrane review included 50 studies that randomised “approximately 9100 people. All but eight included studies were double blind. Seventeen studies were sponsored by pharmaceutical companies producing olanzapine and 14 studies were sponsored by pharmaceutical companies marketing the comparing substances, 15 studies had a neutral sponsor. Four studies did not provide data on sponsoring.” [Olanzapine versus other atypical antipsychotics for schizophrenia (Review) Komossa K]. This suggests that many relevant studies may have been omitted from the analysis.

3. Ethnicity was dichotomized, but the authors do not say how patients were assigned to one group or the other. There is no consideration of the effects of the simplifying assumption that ethnicity is ‘black and white.’

4. It is not clear from this paper whether the patients had been exposed to atypical antipsychotic medicines before the olanzapine treatment. Since these were comparative trials, for example, against quetiapine or aripiprazole, it is likely that there were prior exposures, and that the weight and glucose measures were not obtained prior to any exposure. There remains, therefore, the possibility that patients were pre-selected as ‘tolerant’ of atypicals, and do not represent an
inception cohort.

5. Nearly half the patients discontinued treatment prior to the end of the relevant 24–28 week trials. The analysis in this paper is said to be ‘intention to treat,’ and for some parameters, a last-observation-carried-forward analysis was made. However, with such a large number of drop-outs, the uncertainties must be substantial, and might have been subject to a sensitivity analysis.

6. The authors seem to have assumed that studies were homogenous. The absence of confidence intervals around any estimates makes it very hard to judge whether the findings were anyway due to low power, or truly indicate no effect. Figure 4 shows ‘statistically significant’ results at two of 15 time-points. It would have been more useful to look at the area-under-the-curve for weight change −v− time. A statistical review is needed.

7. Figures 5–7 are dull and add little.

8. There is no explicit consideration of the occurrence of overt diabetes.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

'I declare that I have no competing