Reviewer’s report

Title: A Cost-Consequences analysis of the effect of Pregabalin in the treatment of peripheral Neuropathic Pain under medical practice conditions in Primary Care settings.

Version: 2 Date: 25 May 2010

Reviewer: Gillian Hall

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While I agree that a comparison of the outcome of specific treatments versus routine practice could be helpful in NeP, I feel that in the papers current format we cannot fully understand and so interpret the results.

• Major Compulsory Revisions

1. The methods are not sufficiently clear to allow us to understand the cohorts. Without going into great depth we do need to understand how the study was conducted, in a stepwise fashion: how the physicians were selected; what population the patients were drawn from; at what stage patients came into the study etc. Otherwise the potential for bias is not clear.

2. A large proportion of patients had PGB. Is this normal in Spain or is it due to the study design? If the second, how will this affect the results.

3. Your comparator was prescribed a mixture of treatments, some considered appropriate for NeP and others not. You need to be able to justify this. You also need to be very clear about this in both your discussion and abstract. I was surprised that no TCAD/other AED than gabapentin was among those commonly used as a second line treatment. The non-PGB group was small so the inappropriately treated patients will make a great difference. A clearer methods section will help clarify how this happened.

4. You say the differences in baseline characteristics will bias results against PGB but the alternative cohort had more previous use of AEDs and TCADs so may include more refractory patients.

5. Table 5 reports within treatment comparison of baseline and change to follow-up for a range of costs, including secondary care and tests. As most of the patient investigations are completed around the time of diagnosis do the p-values tell us anything? Patients had to have six months history of pain but they may not have consulted for this period or investigations may have taken some weeks.

6. The paper reports that the PGB cohorts had significantly greater cost reductions. They did, but this appears to be due to greater pre-PGB costs rather than lower costs post-treatment. Both comparisons should be provided. This should be discussed. Does this difference in pre-treatment cost suggest some residual bias? Could there be differences in health care coverage?

7. The methods state that significant results were adjusted but the tables only
have one value. Which is it? What covariates were included in the model? It is normal to adjust all appropriate comparisons as non-significant results can become significant! Therefore all comparisons of change in pain and cost should be adjusted with both results reported.

8. The three NeP conditions included have very different short-term prognoses. Can they be looked at separately? If not this needs to be discussed.

Minor Essential Revisions

9. The results are repeated in the discussion on a number of occasions, they should be removed. Similarly the objective is stated both in the introduction and methods. Figure 2 would be improved by a clear title.

Level of interest: An article of importance in its field

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

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have received funding for research and payment for consultancy from a number of pharmaceutical companies and charities and have no direct stock holding in any pharmaceutical company.