Author's response to reviews

Title: Pregabalin versus gabapentin in partial epilepsy: a meta-analysis of dose-response relationships

Authors:

Philippa Delahoy (philippa.delahoy@pfizer.com)
Sally Thompson (sally.thompson@pfizer.com)
Ian C Marschner (ian.marschner@mq.edu.au)

Version: 2 Date: 12 October 2010

Author's response to reviews:

October 13th, 2010

Miss Angelina Ilievska MSc (on behalf of Dr Ravindra Garg)
Editor
BMC Neurology

Dear Miss Ilievska,

We are delighted that BMC Neurology has, in principle, accepted our manuscript entitled “Pregabalin and gabapentin in partial epilepsy: a comparison of dose-response curves” for publication. Thank-you!

In response to the editorial requirements of BMC Neurology, I can confirm that:

(1) The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines have been followed.

(2) The title has changed to “Pregabalin versus gabapentin in partial epilepsy: a meta-analysis of dose-response relationships” (also in accordance with PRISMA guidelines).

(3) An Authors’ contributions section has been included before the Acknowledgements and Reference list.

We have also addressed the comments and queries provided by your two reviewers. A response for each comment is detailed below. We hope that these amendments meet with your approval.

Response to Reviewer #1

Criticism 1: In the conclusion it is stated that pregabalin is likely to be more effective than gabapentin at approximately equivalent doses, but it should be stated more clearly that this is true at comparable effective doses.

Response: In the “Objective” and “Conclusion” subsections of the Abstract, the phrase “approximately equivalent” has been replaced by “comparable effective”.

Criticism 8: Do the title and abstract accurately convey what has been found?
Title:
Response: The title of the manuscript has been changed as detailed above in our response to the editorial requirements of BMC Neurology and PRISMA.

Response to Reviewer #2
Criticism 1: Discretionary revision: I think that it would be very interesting to analyse tolerability data.
Response: Unfortunately, the scope of the review mandated by the available data was to assess the relative efficacy of pregabalin and gabapentin based upon two endpoints. An assessment of the relative tolerability of these agents will be best answered when data from the ongoing randomized, controlled trial become available.
Criticism 2: Why has meta-analysis not been done for those patients who withdrew from the study because of adverse effects?
Response: The results do, in part, take into account patients who withdrew from the study because of adverse effects. The base-case analysis (intention-to-treat last observation carried forward) includes data from those patients who subsequently withdrew from the studies. One of our sensitivity analyses (analysis of responders) was an intention-to-treat missing equals failure analysis whereby patients who withdrew were classified as non-responders. We accept that these analyses consider patients who withdrew for any reason, not solely due to adverse effects. We feel that the decision to analyze the data as a function of any type of withdrawal best reflects the realities of clinical practice.
Criticism 3: Major Compulsory Revisions: In the discussion I would explain the reason for why there is a lack of a dose-effect relationship.
Response: Our interpretation of the data was that the magnitude of the clinical response and change-from-baseline in SFD increased with each dose of pregabalin and gabapentin. Of note, on page 14, we also discuss the difference in dose-response between low dose vs mid/high dose PGB and GBP as potentially due to pharmacokinetic differences and the saturable absorption of gabapentin.
Criticism 4:
Furthermore, in Table 1, I would report the length of studies (both titration and double-blind maintenance) because this may have consequences on efficacy and tolerability.
Response: This request has been fulfilled.

We would like to extend our gratitude to the referees who have helped us improve our manuscript.

Kind regards
Philippa Delahoy, BSc (Hons)
Pfizer Australia,
38-42 Wharf Road,
West Ryde,
NSW 2114,
Australia
Tel: + 61 2 9850 3333
Fax: + 61 2 9850 3111
E-mail: philippa.delahoy@pfizer.com

E-mail addresses of the other authors:
sally.thompson@pfizer.com
ian.marschner@mq.edu.au