Reviewer's report

Title: Clinical effectiveness and cost-effectiveness of pegvisomant for the treatment of acromegaly: a systematic review and economic evaluation

Version: 1 Date: 18 October 2008

Reviewer: Philippe Chanson

Reviewer's report:

The article «Clinical effectiveness and cost-effectiveness of pegvisomant for the treatment of acromegaly: a systematic review and economic evaluation » by Moore et al. presents the results of a review on effectiveness of pegvisomant in patients with acromegaly and proposes an evaluation of the cost-effectiveness in terms of economic criteria. The Authors conclude that the drug is highly effective but consider that its cost must be reduced by one-third to be cost-effective.

The review is complete and discussion is well-conducted

Major comments

1- Page 12. The paragraph on GH levels needs to be discussed in light of the interference of pegvisomant with GH assays, that may explain that some results may be artefactual due to the absence of discrimination between the drug and GH with some assays; moreover, many variations in GH levels observed during the use of this drug are likely explained by the hook-effect related to the amount of pegvisomant, (Paisley et al. Eur J Endocrinol 2007). All these points need to be explicitly indicated in the paper as it has major consequences on the use of GH assays in patients with acromegaly treated with pegvisomant (GH assays are probably not to be recommended) and also on the interpretation of the course of GH levels during the treatment.

2- Pages15 and 16. Even if theses studies were published after the end of collection of the studies by the Authors there are now data on QoL during pegvisomant which may help to refine, if useful, the model

3-Page 16. Concerning the non-responders and the fact that it is « unrealistic that no-responder patients would persist with pegvisomant… » , it must be kept in mind that even if not normalized, some patients (which proportion ?) may greatly benefit from treatment and would ask to continue the treatment for long time…This points to the fact that in the treatment of acromegaly, particularly in cost-benefit analysis studies, one need to take into account the patients who are clearly improved by the treatment…even if not « normalized » in terms of hormonal control…pushing, in some cases, to continue what appears to be an unsuffciently active treatment.

4- Page 19. With regard to our previous remarks in §1, the sentence « Increased GH incompletely blocked by PEG might exacerbate… » is too speculative and
needs to be amended. This sentence might also lead the Reader to think that the Authors did not understand the mechanism of action of the drug: indeed, whatever the levels of GH, as soon as the GH receptor is blocked, there is no reason to have effects related to GH... even if GH levels are high.

Minor comments

1- Figure 5. If data were extracted from the meta-analysis papers of Dekkers et al. J Clin Endocrinol Metab 2008 and/or Holadaway et al. Eur J Endocrinol 2008, this needs to be acknowledged.

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

My clinical department and lab have received research and educational unrestricted grants from Pfizer, Ipsen and Novartis. I am a member of the International Advisory Board on Acromegaly sponsored by Novartis and I received fees for speaking from Pfizer, Novartis and Ipsen.