Reviewer's report

Title: Efficacy of ambroxol lozenges for pharyngitis: a meta-analysis

Version: 3 Date: 27 March 2013

Reviewer: Christian de Mey

Reviewer's report:

06.Aug.2012, I was invited to review a first version (V1) of the paper "Efficacy of ambroxol lozenges for pharyngitis: a meta-analysis" by Chenot J-F, Weber P, and Friede T. 13.Aug.2013 I filed an extensive review (CdM-R1), which concluded: "the present publication presents a pooled analysis of data that already were reported extensively 4 years ago (ref 12); the publication does not lead to effect estimates that are essentially different from those already reported; however, the present paper is deficient in several important methodological aspects, particularly those pertinent to the evaluation of the clinical relevance of the observed effects and the assessment of the quality of the available study reports".

13.Dec.2012, I was invited to review a second version (V2) of the paper. Surprisingly, V2 and the authors' comments accompanying V2 failed to address most of the CdM-R1 comments. 21.Dec.2013 I filed a new extensive review (CdM-R2), which concluded "In summary: the revision failed to address and/or to resolve several of the concerns raised in my review of the first version of the manuscript. The publication presents a pooled analysis of data that already were reported extensively 4 years ago (ref 14); the present publication does not lead to effect estimates that are essentially different from those already reported; however, the present paper is deficient in several important methodological aspects, particularly those pertinent to the evaluation of the clinical relevance of the observed effects and the assessment of the quality of the available study reports; additionally, the paper concludes ill-substantiated claims for instance with regard to the likely superiority of alternative medications, although such claims were neither investigated nor reported in any of the publications that were analysed".

21.Mar.2013, I have been invited to review a third version (V3) of the paper. V3 is accompanied by a reply to CdM-R1 and CdM-R2. I have reviewed V3 and these replies to CdM-R1 and CdM-R2 and report this review in the present. An extensive review report is attached (V3_Comments-CdM). The attached is an essential part of the present review.

In summary: the second revision (version V3 of the manuscript) failed to address and/or to resolve several of the concerns raised in my previous reviews.

The publication presents a pooled analysis of data that already were already reported extensively 5 years ago (ref 14); the present publication does not lead to effect estimates that are essentially different from those already reported, but
there is unresolved disagreement between the present paper and past trial reports with regard to the interpretation of the clinical relevance of the observed treatment effects. In my previous reviews I presented suggestions that might be taken into account when making such assessments. The authors reject such approaches without presenting any sound alternative. In this way, their evaluation is nothing more, albeit nothing less than their personal opinion. There is reason and interest to raise considerations about the relevance of treatment effects above such weak level of evidence. The paper might have contributed to the debate that is urgently needed between investigators and external reviewers to meet such challenge; unfortunately, it failed in this regard also since the authors raise ill-founded doubt not only on the quality of the trial reports, but also on the trials themselves, on the credibility of the investigators and trial report authors and on my professional integrity as the invited reviewer of their manuscript. In view of my efforts in reviewing the three versions of this manuscript with meticulous care and identifying several mistakes and inaccuracies, of which some have been now corrected, I find the latter particularly uncalled for.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

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 confirm to be the author of two publications that have been subject of the publication’s review. I confirm that the work leading to these publications was honoured by a CRO-agreement with the marketing authorisation holder of the medication presently evaluated. This work was ended five years ago.

I made the present assessment on my own responsibility and on my own means. My effort in reviewing this manuscript is not subject to any incentive either present or future by or from any of the parties concerned, incl. the authors and the marketing authorisation of the medication evaluated in the manuscript.

My evaluation is not influenced by any personal or financial relationship with other people or organizations. I have no financial competing interests; I also have no non-financial competing interests that may cause them embarrassment were they to become public after the publication of the manuscript.