Reviewer’s report

Title: Antihistamine Effects and Safety of Fexofenadine: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Version: 2 Date: 22 May 2019

Reviewer: Emanuel Raschi

Reviewer's report:

The authors revised the systematic review, by proving data on population (actually healthy volunteers), risk of bias (low/uncertain), and funnel plots.

The conclusion remains a major concern. In their rebuttal letter, the authors reply that heterogeneity is low when comparing fexofenadine with second-generation antihistamines; however, this statement does not appear to be supported by the data presented in the text (99% of heterogeneity for efficacy, figures 2 and 3; 79% in figure 6b; 76% in figure 7b; 96% in figure 9b). The heterogeneity on sedative effect (a key conclusion) is not shown in figure 5b, and odds ratio is largely driven by a single study (Howarth 1999).

Taken together, these data on healthy volunteers do not allow to draw the conclusions stated by the authors in the abstract and in the full text. the first sentence in the discussion should be also corrected ("Our meta-analysis indicates that fexofenadine has positive antihistamine effects and safety profile in patients with indications requiring antihistamines").

As suggested in the first revision, this systematic review highlights the need to perform well-designed head-to-head studies in people with therapeutic indications requiring antihistamines.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

None relevant to the content of the study

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my
report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal