Reviewer's report

**Title:** Utility of the sore throat pain model in the multiple-dose assessment of an acute analgesic: a double-blind, randomized, placebo-controlled study of flurbiprofen 8.75 mg lozenges

**Version:** 2  **Date:** 11 December 2013

**Reviewer:** Daniel Carr

**Reviewer's report:**

This report is a clearly conceptualized and articulate account of the extension of a well-established assay methodology previously employed to assess the efficacy of single doses, now extended to assess the efficacy of multiple doses over 24 hours. The first author has at least 25 years of experience with the acute sore throat model and has published results based upon this model in multiple peer-reviewed journals.

The above said, my ability to see how the present manuscript differed from an earlier one, that according to the cover letter had been modified in accordance with a reviewer's requests, was prevented by the absence of information in the cover letter concerning specific changes, nor any indication of same in the manuscript text itself.

As I read through the manuscript initially, my principal concerns as to analgesia for the placebo group, and detection of treatable bacterial tonsillo-pharyngitis, were only partially addressed. The free access to acetaminophen sufficed with respect to the former concern. As to the latter, the authors should insert an extra sentence indicating how patients whose throat cultures were positive for beta hemolytic streptococcus were directed to antibiotic therapy, or if not then why not. They should also indicate explicitly that (as I believe to be the case) such patients with positive throat cultures were maintained in the intent-to-treat group and the group results include these.

There are only a few additional comments to be addressed by the authors.

On page 7, first sentence under Assessment, the sudden introduction of the Practitioner's Assessment of Inflammation scale -- abbreviated as "PAIN" is confusing, particularly since the present report focuses upon pain and its treatment. Throughout the entire manuscript, the Practitioner's Assessment of Inflammation should be abbreviated in a way to minimize confusion with "pain". This referee would suggest the abbreviation "PrAoI".

As mentioned above, it is of interest to know whether patients were informed of the results of their throat culture and offered antibacterial treatment if they tested positive for beta hemolytic streptococcus.

Related to the section on Safety, pages 11-12, the Consort flow diagram...
indicates one patient left the active treatment arm of the trial due to an AE -- what was that?

In the Discussion, page 13, the authors describe a "major limitation" of the study as follows: "Approximately 40% of the patients reported the onset of throat symptoms in the previous 3 days (and five patients were inadvertently admitted with onset in the previous 4–5 days). These patients tended to dilute the differentiation between active medication and placebo as their throat symptoms improved naturally over the first 24 hours of the study (which was actually the 4th, 5th, or 6th day of these patients’ symptoms).” However, no results or statistical analyses are provided to support this observation about dilution -- please do so or remove this assertion.

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

Quality of written English: Acceptable

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

Declaration of competing interests:

'I declare that I have no competing interests.