Reviewer’s report

Title: Safe Prescribing of Non-Steroidal Antiinflammatory Drugs in Patients with Osteoarthritis. An Expert Consensus Addressing Benefits and Gastrointestinal as well as Cardiovascular Risks

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Reviewer: Neville Yeomans

Reviewer’s report:

There have been a number of expert consensus statements about increasing the safety of NSAID prescribing published in the last decade, as the authors acknowledge. However, there is new information in this one and it does tackle the risks to the GI tract in a much more comprehensive way (adding in the risks to intestine and colon much better than previous publications), adds a little new information about rheumatological issues and some updating of literature about the cardiovascular risks of the two families of NSAID. My specific comments, though, are as follows (not in order of importance but more in order of appearance in the MS):

1. The abbreviation ns-NSAID in the abstract needs defining (even though 'non-selective' appears by itself in the background para.

2. p.5, para 2, the final sentence beginning 'Although': The opening clause in this sentence 'Although ... yet to be defined' does not belong semantically with the remainder of the sentence, which refers to H. pylori. If should be moved to the following paragraph.

3. p.5, para 3: The paper referred to in reference 39 as evidence for an increasing incidence of lower GI complications does mention coding difficulties for this diagnosis. Without clear evidence from another source or country, it would be safer to just say an apparently increasing trend.

4. Methods: The literature review performed for the consensus conference was truncated at October 2011. How did the writing group incorporate data that were published since then to the recommendations arrived at by all those at the meeting? Some later papers are cited in this manuscript, but did the consensus group have a chance to evaluate them?

5. p.19, para 4, 1st line: 'inhibitors were associated' not 'was'.

6. p.28, last para: The authors say that the 2013 CNT meta-analysis 'confirmed that ... high-dose naproxen is associated with less vascular risk than other NSAIDs'. That is what the CNT authors concluded, it is true, but the conclusion is unsafe. There were <20 CV endpoints in the naproxen patients, and the comparison with the other NSAIDs was INDIRECT: Drug A vs placebo, then Drug B vs placebo, extrapolated to conclusions (non-randomized) about Drug A vs Drug B. On these grounds and others, the FDA declined earlier this year to amend the naproxen CV labeling. I think the authors should be more guarded
about the strength of this conclusion at the present time. As they point out, the PRECISION trial will hopefully give a more robust answer when the last patient completes follow up at end 2015.

7. While the algorithm in Figure 1 is a commendable effort to give guidance for managing these patients, and obviously records accurately the consensus at the meetings, it is of course just guidance for patients at two ends of a continuum. One would hope most clinicians would recognise this, and realise that they will have to interpolate for the majority of their patients, this nonetheless seems a fundamental caveat to specifically add to the paper.

**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###