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LETTER TO THE EDITOR

Comment on: "Cost-Utility Analysis of Duloxetine in Osteoarthritis: A US Private Payer Perspective"

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Dear Editor,

We would like to alert you to the fact that, after careful review of the article by Wielage et al. [1] published recently in the journal, we noticed several data inaccuracies.

1. The pain level of patients in the different publications is not mentioned. We know from clinical trial experience with tapentadol that patients had moderate to severe pain (most even severe pain). The pain level of patients in studies with duloxetine, naproxen and celecoxib might have been lower; at least we would extrapolate this from the dosages used. Based on this, we doubt if the comparators are appropriate. The patient who uses naproxen (or even cyclooxygenase [COX]-II) is not similar to someone who uses strong opioids.
2. The article does not make clear whether tapentadol immediate release (IR) or extended release (ER) is being compared. In Sect. 2.2, the authors mention comparisons between tapentadol ER and oxycodone controlled release (CR) (similar efficacy, better tolerability for tapentadol, lower discontinuation rate than oxycodone [2, 3]). The ER formulation of tapentadol would be the right one to use in the chronic condition osteoarthritis (OA). However, the high dosage shown in Table 1 indicates that this does not refer to tapentadol ER (according to the Summary of Product characteristics [SmPC], the highest dosage recommended is 500 mg). The dosage mentioned in Table 1 seems to reflect the tapentadol IR dose for pricing purposes. This very high dosage leads to the unfavourably high result for tapentadol in the cost-effectiveness plane, which we cannot accept.
3. The dosing for oxycodone ER is not comparable with the dosing for tapentadol. Comparing the World Health Organization Defined Daily Dose (WHO-DDD), which is 400 mg for tapentadol and 75 mg for oxycodone, this would be a factor of 5.3 (which is also reflected in the clinical trials where oxycodone was used as active comparator [3]). The very low dosage used for oxycodone (10–30 mg) would be suitable for patients with mild to moderate pain, whereas the dosage of 600 mg for tapentadol is beyond even that used in severe pain and therefore these are not comparable.
4. As a follow-up to the above, Table 1 uses some results from the tapentadol ER trials (e.g. "initial 3 months discontinuation" [3]) but the data presented in the table are mixed with inappropriate assumptions (utility measures are the same as for tramadol).
5. Table 1: proton pump inhibitor (PPI) use for all opioids is high: 21 %. Why is this higher than for nonsteroidal anti-inflammatory drugs (NSAIDs) and what is the source of these data? As the main adverse events for opioids are nausea, vomiting and constipation (which cannot be treated with PPIs), we do not see a causal relationship between opioid treatment and use of PPIs at all.
6. Table 1: How are "discontinuation drug costs" defined? Why are they so high for tapentadol compared with other therapies? In our clinical trials, the

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percentage of patients discontinuing the study are lower than for oxycodone [2]. This should lead to lower costs, not to higher.

7. Table 1 shows the same opioid abuse rates for tapentadol and oxycodone—data from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) system [4] suggest otherwise.
8. Table 3 indicates that opioid abuse costs approx. $US5,471 based on data from 2003 to 2007. If the model used tapentadol IR, rather than tapentadol ER, as the comparator, it fails to account for the fact that tapentadol ER is available as a tamper-resistant formulation in the USA and the opioid abuse costs (penalty for tapentadol in the model) are not accurately reflected.
9. There are inconsistencies within the text. The authors state, in the Discussion section, that data for tapentadol are assumed to be the same as for oxycodone because "No studies were available for tapentadol […]". However, publications for tapentadol (Afilalo et al. [1], Lange et al. [1] and Wild [1]) are listed in the reference list (references [36–38] in the original paper). The available data should be reflected appropriately in the analysis.

Importantly, these data inaccuracies have led to very negative results for tapentadol, a strong opioid analgesic that was included in the study.

We respectfully would like to ask the journal to comment on these inaccuracies and their effects on the research results and conclusions. We would kindly ask that a revised analysis be conducted and/or that a correction/erratum be published in accordance with International Committee of Medical Journal Editors (ICMJE) requirements.

Conflicts of interest Both authors are employees of Grünenthal GmbH, Aachen, Germany.

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