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Letters to the editor
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Diacerein and arthrosis treatment

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Dear Dr. Burkhard Leeb:

Thank you for your letter published in *Medwave* regarding our article titled "Is diacerein an alternative for osteoarthritis treatment?" [1]. Your letter provides us with complementary information regarding the registration status of diacerein in Europe, specifically as related to the recommended suspension of marketing authorization made by the European Medicines Agency (EMA), as a result of patient cases of severe diarrhea and hepatic alterations.

Regarding this point, we feel it important to review the latest EMA recommendations [2], which allow, under very specific conditions, the use of diacerein in treating arthrosis. The established conditions include the following: patients under 65 years old; no hepatic comorbidity; and treatment prescribed by physicians with experience in arthrosis therapies. In clinical practice, these indications highly restrict therapeutic applications, particularly since most arthrosis patients are seniors. However, this would not constitute an absolute contraindication for diacerein use.

Regarding the statement that diacerein would be positioned as a first-line pharmacological therapy for arthrosis [3], we feel that current evidence and clinical guidelines do not support the first-line application of this medicine. This is especially so when considering the risk-benefit ratio, where treatment can have little to no effect on disease symptoms and a high risk for side effects.. The Friendly Summary of Body of Evidence using Epistemonikos (FRISBEE) method reuses information cited in existing systematic reviews, but it also recombines the accumulated evidence in a new meta-analysis. Based on the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach, meta-analyses provide a new summary of findings, i.e., an optimal presentation of both desired and undesired effects, together with confidence levels for existing evidence. The development and validation of these procedures have been rigorous, demonstrating the superiority of this approximation against other ways of presenting research results [4], [5], [6], [7]. While we do consider the appreciations of the ongoing clinical trials to be correct, and, to a certain degree, accuracies related to a greater probability of finding an effect with more than four weeks of monitoring, we believe that the conclusion we made in our abstract is unaffected by taking these considerations into account.

Regarding the incoherency between the text and table summarizing our results, this is an error that we thank you for detecting. We will provide an erratum to correct this point. The correct message is that communicated in the table, i.e., low confidence for pain and moderate confidence for functionality. Considering this, the key messages would be as follows:

- Diacerein could result in a slight decrease of pain in patients with arthrosis, but the confidence level for the evidence is low.
- Diacerein probably does not improve functionality in patients with arthrosis, although the confidence level for the evidence is moderate.
- A frequent adverse side effect of diacerein is diarrhea, with a high confidence level for the evidence.

We have several comments regarding the possibility that the two clinical trials might modify current evidence. In the first trial [8], instead of outright exclusion, an alternative would be to evaluate the results and evaluate if there are outcome differences when used for more or less than one month (i.e., conduct a sensitivity analysis). We must remember that these hypotheses are always physiopathological and pharmacodynamical theories, but the real clinical impact is debatable and should be evaluated through evidenced-based health assessments. In turn, the second trial [9] does not directly respond to the question, rather providing a proposal for new research (and an eventual FRISBEE) that compares diacerein against some other intervention (e.g., non-steroidal anti-inflammatories, paracetamol, etc.). This is precisely the most interesting clinical question regarding diacerein.

Finally, we thank you for your comments on our FRISBEE summaries. We are happy to know that our friendly format has been well received, and we also thank you for your comments on possible improvements. One of our primary objectives is to formalize a process for "evidence-based medicine" that is familiar to and understood by all decision makers in healthcare. We would like to take this opportunity to mention that we are working on a different type of article – one that provides a greater methodological emphasis on evaluating discrepancies in reviews and sensitivity analyses and that gives greater detail on these variables. This new focus will be first applied to the most controversial or interesting reviews.

Notes

From the editor
The author originally submitted this article in Spanish and English. The Journal has not copyedited this English version.

Declaration of conflicts of interest
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