Testimony Before the FDA's Meeting of the Pulmonary-Allergy Drugs Advisory Committee Regarding Gefapixant

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Public Citizen opposes FDA approval of gefapixant for the treatment of refractory or unexplained chronic cough in adults. The small effects of treatment with the drug do not provide substantial evidence of a clinically meaningful benefit for patients.

We agree with the FDA's assessment of the evidence supporting this application,[1] which is mainly based on the recount of cough data using a proprietary algorithm. Our concerns include the small treatment difference in cough frequency between groups, the lack of compelling additional data from the secondary endpoints, the large placebo response across all efficacy endpoints, and the potential unblinding of the trials due to taste disturbances.[2]

For example, while there was a small reduction in the frequency of cough of 15% in one trial and 17% in the other among patients taking gefapixant compared to those in the placebo group, these results reached statistical significance only in one of the two trials.[3] Moreover, the difference in the proportion of subjects who had a reduction in cough frequency of 50% or more, was only 6% between the two groups. The clinical meaningfulness of these results is further called into question by the FDA's post hoc analysis which suggested that compared to placebo treatment with gefapixant only resulted in a reduction of 1 to 2 coughs per hour.

As highlighted by the FDA, the secondary endpoints did not provide additional support of meaningful benefit for patients and "must be interpreted with caution." [4] For example, different analyses of the data demonstrated that there were generally only small differences between the two groups and only one patient reported outcome measure

[1] Food and Drug Administration. FDA briefing document. NDA 215010, drug name: gefapixant; Meeting of the Pulmonary-Allergy Drugs Advisory Committee. November 17, 2023. https://www.fda.gov/media/173850/download. Accessed November 17, 2023.
[2] *Id.* PDF p. 52-53.
[3] *Id.* PDF p. 46.
[4] *Id.* PDF p. 47.

reached statistical significance.[5] Importantly, the FDA found that there was no clear correlation between patients who reported that they were feeling better and those who were coughing less.

These small benefits stand in contrast to the disturbances in taste or loss of taste that lasted an average of 204 days.[6] They occurred in up to 65% of subjects in the treatment group compared to only 7% in the placebo group.

Because gefapixant is being considered for a novel therapeutic indication, there is limited experience on how to best measure and interpret the clinical meaningfulness of treatment effects.[7] However, based on the available data, there is no compelling evidence of meaningful clinical benefit from gefapixant treatment.

If the FDA were to approve gefapixant based on the very weak evidence of effectiveness, it would also set a concerning precedent for the evaluation of future treatments for chronic cough.

Patients with chronic cough deserve an effective treatment. Public Citizen therefore urges the committee to vote "No" on the voting question and strongly recommends that the FDA not approve gefapixant.

[5] *Id.* PDF p. 14, 39-43.
[6] *Id.* PDF p. 37.
[7] *Id.* PDF p. 9, 82.