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Testimony Arthritis Advisory Committee and Drug Safety and Risk Management Advisory Committee: The FDA Must Reject Biologics License Application (BLA) 761130 for Tanezumab for the Treatment of Osteoarthritis

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I am Dr. Michael Carome, Director of Public Citizen's Health Research Group. I have no financial conflict of interest.

Public Citizen strongly opposes approval of tanezumab because the three phase 3 clinical trials that tested tanezumab in the intended target osteoarthritis-patient population demonstrated that the drug fails to provide clinically meaningful benefit compared with either placebo or oral non-steroidal anti-inflammatory drugs (NSAIDs), but does dramatically increase the rates of rapidly progressive osteoarthritis (RPOA), other types of serious joint damage, and total joint replacements in a dose- and duration-dependent manner. As a result, the risks of the drug far outweigh its benefits.

Public Citizen's March 10th comments submitted to the docket for this meeting provide much more detail.

Tanezumab: Unsafe for use in osteoarthritis patients

Regarding safety, we note the following:

- Tanezumab caused accelerated joint damage after as little as two 2.5-mg doses.
- Studies 1056, 1057, and 1058 demonstrated that tanezumab causes a dramatic, statistically significant, and clinically important increase in the rate of RPOA, other serious adverse joint events, and total joint replacements in a dose- and duration-dependent manner.
- Despite the robust risk-mitigation strategies employed in all three trials that were intended to minimize the risk of serious adverse joint events, an unacceptably high number of such events still occurred. In a real-world setting, where there would not be the same rigorous screening and monitoring of patients, the incidence of such serious adverse joint events almost certainly would be significantly higher.
- Per the Food and Drug Administration (FDA), there is “evidence that tanezumab can target healthy joints. Of the 33 CJSE [composite joint safety endpoint events] that occurred in joints with baseline radiographically healthy joints, 31 were in tanezumab-treated patients, and only two in naproxen-treated patients.”
- The proposed Risk Evaluation and Mitigation Strategy (REMS) is not sufficient to mitigate the risk of RPOA and would not ensure that the benefits of tanezumab outweigh the risks of RPOA. As the FDA noted, “stopping [tanezumab] after patients develop RPOA2 does

not appear to be effective in preventing further damage to the joints. In addition, the required precision and consistency of the medical imaging and interpretation do not appear feasible in practice.”

Conclusions

In closing, Public Citizen urges your committees to recommend that the FDA not approve the BLA for tanezumab.

A drug like tanezumab that accelerates the joint destruction of the underlying OA disease that it is intended to treat but lacks any evidence of clinically meaningful benefit in comparison to use of a placebo or oral NSAIDs obviously should never be approved by the FDA.

We therefore urge you to vote “no” on question 3. No REMS would ever be sufficient to minimize tanezumab’s risk of severe joint damage.

Finally, any further human studies of tanezumab in osteoarthritis patients would also be unethical.