Testimony Before the Food and Drug Administration's Pharmacy Compounding Advisory Committee Regarding Adding Lorcaserin Hydrochloride to the List of Drug Products Withdrawn or Removed from the Market Because They Have Been Found to be Unsafe or Not Effective

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June 8, 2022

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

Public Citizen urges the Pharmacy Compounding Advisory Committee to endorse the Food and Drug Administration's (FDA's) proposal to add all drug products containing lorcaserin hydrochloride to the list of drug products that have been withdrawn or removed from the market because they have been found to be unsafe or not effective and that therefore may not be compounded under the exemptions provided by Section 503A(a) or Section 503B(a) of the Food, Drug, and Cosmetic Act (the Withdrawn or Removed List (codified at 21 C.F.R. § 216.24)).

The correct vote on this matter could not be more obvious. On March 4, 2021, the FDA published a notice in the Federal Register announcing that the agency had determined that Belviq (lorcaserin hydrochloride) tablets, 10 mg, and Belviq XR (lorcaserin hydrochloride) extended-release tablets, 20 mg — which were initially approved by the FDA on June 27, 2012, and July 15, 2016, respectively, as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in certain adults who were overweight or obese — were withdrawn from sale for reasons of safety or effectiveness and that the agency would not accept or approve abbreviated new drug applications (ANDAs) for lorcaserin hydrochloride tablets, 10 mg and 20 mg.[1]

The following excerpts from the FDA's March 4, 2021, notice indicate that these lorcaserin hydrochloride products were withdrawn from sale specifically for reasons of safety:

> In 2012, the Agency required the drug manufacturer to conduct a randomized, double-blind, placebo-controlled clinical trial to evaluate the risk of cardiovascular problems. The Cardiovascular and Metabolic Effects of Lorcaserin in Overweight and Obese Patients--Thrombolysis in Myocardial Infarction 61 (CAMELLIA-TIMI 61) clinical trial was conducted to fulfill this requirement. An analysis of the CAMELLIA-TIMI 61 trial results suggests an imbalance in cancer in humans. Although chance effect cannot be ruled out, the imbalance persisted throughout multiple analysis approaches. The clinical findings corroborated by the evidence from the animal models informed the Agency's assessment that the risk outweighs any potential benefits for the current indications. These findings were considered clinically meaningful and could not be adequately addressed through labeling. Additional evidence would be necessary to investigate this

[1] 86 FR 12697-12698.

> signal; however, the Agency has determined that it is unlikely that the necessary safety endpoints (i.e., cancer and reproductive safety) can be readily or ethically investigated in a clinical trial. Because preclinical or clinical studies would first need to be conducted to address these concerns, the Agency has determined that this drug product would not be considered safe and effective if it were reintroduced to the market.
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> FDA issued a Drug Safety Communication on January 14, 2020, alerting the public that results from a clinical trial assessing the risk of heart-related problems show a possible increased risk of cancer with BELVIQ and BELVIQ XR… On February 13, 2020, FDA announced it had asked Eisai to voluntarily withdraw BELVIQ and BELVIQ XR from the U.S. market... On February 13, 2020, Eisai submitted a request to FDA to withdraw approval of NDA 022529 for BELVIQ and NDA 208524 for BELVIQ XR under 21 CFR 314.150(d) and waived its opportunity for a hearing. As requested by Eisai, the Agency issued a Federal Register notice on September 17, 2020 (85 FR 58063), withdrawing approval of the applications for BELVIQ (lorcaserin hydrochloride) tablets, 10 mg, and BELVIQ XR (lorcaserin hydrochloride) extended-release tablets, 20 mg, effective September 17, 2020.
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> Accordingly, the Agency will remove BELVIQ (lorcaserin hydrochloride) tablets, 10 mg, and BELVIQ XR (lorcaserin hydrochloride) extended-release tablets, 20 mg, from the list of drug products published in the Orange Book. FDA will not accept or approve ANDAs that refer to this drug product.

Importantly, the Pharmacy Compounding Review Team for the Center for Drug Evaluation and Research's Office of New Drugs (OND) appropriately recommended that all drugs containing lorcaserin hydrochloride be included on the Withdrawn or Removed List. In support of this recommendation, the OND observed the following:

(1) Lorcaserin products were withdrawn from the market for safety reasons, with the primary safety concern being the drug's increased risk of malignancy that was observed in both the postmarketing trial data from the CAMELLIA-TIMI 61 trial and nonclinical studies.

(2) Although the mechanism by which lorcaserin hydrochloride is associated with malignancy is unknown, the OND is not aware of data or information suggesting that the increased risk of malignancy is restricted to particular drug products containing the active pharmaceutical ingredient lorcaserin hydrochloride.[2]

Public Citizen therefore urges you to protect public health by voting in favor of the FDA's proposal that "Lorcaserin hydrochloride: All drug products containing lorcaserin hydrochloride" be added to the Withdrawn or Removed List under sections 503A and 503B of the Food, Drug, and Cosmetic Act.

Moreover, moving forward, the FDA should not delay initiating the notice and comment rulemaking process for amending FDA regulations at 21 C.F.R. § 216.24 once the agency has published a determination that a drug product was withdrawn from sale for reasons of safety.

[2] Food and Drug Administration. FDA briefing document: Pharmacy Compounding Advisory Committee (PCAC) meeting. June 8, 2022. https://www.fda.gov/media/158541/download. Accessed June 3, 2022.

Instead, to better protect public health, whenever the FDA issues a notice announcing such a determination, the agency simultaneously should issue a notice of proposed rulemaking proposing to amend the Withdrawn or Removed List under FDA regulations at 21 C.F.R. § 216.24 to include that drug product.