



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2021-N-0030]

Determination That BELVIQ (Lorcaserin Hydrochloride) Tablets, 10 Milligrams, and BELVIQ XR (Lorcaserin Hydrochloride) Extended-Release Tablets, 20 Milligrams, Were Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) has determined that BELVIQ (lorcaserin hydrochloride) tablets, 10 milligrams (mg), and BELVIQ XR (lorcaserin hydrochloride) extended-release tablets, 20 mg, were withdrawn from sale for reasons of safety or effectiveness. The Agency will not accept or approve abbreviated new drug applications (ANDAs) for lorcaserin hydrochloride tablets, 10 mg and 20 mg.

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SUPPLEMENTARY INFORMATION: Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to seek approval to market a generic version of a previously approved drug product. In general, to obtain approval, the ANDA applicant must show, among other things, that the generic drug product has the same active ingredient(s); dosage form; route of administration; strength; conditions of use; and, with certain exceptions, labeling as the listed drug. In addition, the ANDA applicant must show that the generic drug product is bioequivalent to the listed drug.

Section 505(j)(7) of the FD&C Act requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the “Approved Drug Products With Therapeutic Equivalence

Evaluations,” which is known generally as the “Orange Book.” Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug’s new drug application (NDA) or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

BELVIQ (lorcaserin hydrochloride) tablets, 10 mg, is the subject of NDA 022529, and BELVIQ XR (lorcaserin hydrochloride) extended-release tablets, 20 mg, is the subject of NDA 208524, both held by Eisai Inc. (Eisai), and initially approved on June 27, 2012, and July 15, 2016, respectively. BELVIQ and BELVIQ XR are indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index of:

- 30 kilograms per square meter (kg/m^2) or greater (obese); or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes).

After reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that BELVIQ (lorcaserin hydrochloride) tablets, 10 mg, and BELVIQ XR (lorcaserin hydrochloride) extended-release tablets, 20 mg, were withdrawn for reasons of safety or effectiveness.

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 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.

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 (see <https://www.fda.gov/drugs/drug-safety-and-availability/safety-clinical-trial-shows-possible-increased-risk-cancer-weight-loss-medicine-belviq-belviq-xr>). On February 13, 2020, FDA announced it had asked Eisai to voluntarily withdraw BELVIQ and BELVIQ XR from the U.S. market (see <https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-withdrawal-weight-loss-drug-belviq-belviq-xr-lorcaserin-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.

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.

Dated: February 26, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

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