4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-N-3708]

InvaGen Pharmaceuticals, Inc.; Withdrawal of Approval of an Abbreviated New Drug Application for Trandolapril Tablets

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration's (FDA or Agency) Center for Drug Evaluation and Research (CDER) is withdrawing approval of an abbreviated new drug application (ANDA) for trandolapril tablets. The basis for the withdrawal is that the holder of the ANDA has repeatedly failed to submit the required data to support a finding of bioequivalence for this ANDA. The holder of the ANDA has waived its opportunity for a hearing.

DATES: Withdrawal of approval is applicable [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

FOR FURTHER INFORMATION CONTACT: Jennifer Forde, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6228, Silver Spring, MD 20993-0002, 301-348-3035.

SUPPLEMENTARY INFORMATION:

FDA's Office of Generic Drugs (OGD) approved ANDA 078320, held by InvaGen Pharmaceuticals, Inc. (InvaGen), for a generic version of trandolapril tablets, 1 milligram (mg), 2 mg, and 4 mg, under the requirements of section 505(j) of the Federal Food, Drug, and Cosmetic

Act (FD&C Act) (21 U.S.C. 355(j)) and FDA's implementing regulations. OGD approved ANDA 078320 on June 12, 2007. In a notice published in the *Federal Register* of October 28, 2019 (84 FR 57736), CDER notified InvaGen of CDER's proposal to issue an order, under section 505(e) of the FD&C Act and § 314.150 (21 CFR 314.150), withdrawing approval of ANDA 078320 and all amendments and supplements to it on the grounds that InvaGen has failed to submit the required bioequivalence data necessary to demonstrate the bioequivalence of its drug product. In its October 28, 2019, notice of opportunity for a hearing (NOOH), CDER provided InvaGen with an opportunity to request a hearing to show why approval of ANDA 078320 should not be withdrawn.

As noted in the October 28, 2019, NOOH, FDA issued a letter to InvaGen on August 9, 2011, regarding ANDA 078320 because this drug product application was supported by bioequivalence studies with the bioanalytical analysis conducted by Cetero Research at the Houston, TX, site between April 1, 2005, and June 15, 2010. As FDA noted in its August 9, 2011, correspondence, inspection findings regarding Cetero Research's bioequivalence studies raised significant concerns about the validity of the reported results of the analytical studies conducted between April 2005 and June 2010 in support of drug applications, and as such, steps needed to be taken to demonstrate the bioequivalence of InvaGen's drug product approved under ANDA 078320. FDA informed InvaGen that ANDA 078320 needed to be supplemented by conducting new bioequivalence studies or re-assaying the samples from the original bioequivalence study. FDA recommended to InvaGen that the results of the requested bioequivalence studies or re-assays be submitted to ANDA 078320 within 6 months of the date of the August 9, 2011, letter.

Although the October 28, 2019, NOOH states that FDA did not receive a response from InvaGen to the August 9, 2011, letter from FDA, upon further review, additional correspondence between InvaGen and FDA has been identified. In a letter to FDA dated August 12, 2011, InvaGen requested a 6-month extension for submitting bioequivalence study data for ANDA 078320. On September 21, 2011, FDA issued a letter to InvaGen acknowledging InvaGen's August 12, 2011, request for an extension. In a letter to FDA dated September 6, 2012, InvaGen requested an additional 6-month extension to submit bioequivalence study data; and in a letter to FDA dated October 4, 2012, InvaGen requested that FDA consider and grant InvaGen's request for an extension. On October 23, 2012, FDA issued a letter to InvaGen granting InvaGen an extension until March 2013 to submit bioequivalence study data. InvaGen has not submitted the bioequivalence study data.

The additional correspondence noted above that was not identified in the October 28, 2019, NOOH does not alter the underlying basis of the October 28, 2019, NOOH. In the absence of information showing bioequivalence between the generic drug at issue and the reference listed drug (RLD), there is no basis for concluding that the Agency's finding of safety and efficacy supporting approval of the RLD can be used as a basis to support approval of the generic drug. Section 505(e) of the FD&C Act provides FDA the authority to withdraw approval of an ANDA in these circumstances.

In correspondence dated November 7, 2019, InvaGen requested withdrawal of the approval of ANDA 078320 under § 314.150(d). Because this application withdrawal is effectuated through the NOOH process (see 84 FR 57736), InvaGen's request to withdraw approval under § 314.150(d) is moot. In the November 7, 2019, correspondence, InvaGen also waived its opportunity for a hearing under § 314.150(a).

FDA finds that InvaGen has repeatedly failed to submit the required data to support a finding of bioequivalence for ANDA 078320. In addition, under 21 CFR 314.200, FDA finds that InvaGen has waived any contentions concerning the legal status of the drug product. Therefore, under section 505(e) of the FD&C Act, approval of ANDA 078320, and all amendments and supplements thereto, is withdrawn (see DATES). Introduction or delivery for introduction of this drug product into interstate commerce without an approved application is illegal and subject to regulatory action (see sections 505(a) and 301(d) of the FD&C Act (21 U.S.C. 355(a), 331(d))).

Dated: July 7, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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