4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2011–N–0021]

AbbVie Inc., et al.; Withdrawal of Approval of Abbreviated New Drug Applications for Prescription Pain Medications Containing More than 325 Milligrams of Acetaminophen

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing approval of 7 abbreviated new drug applications (ANDAs) for prescription drug products containing more than 325 milligrams (mg) of acetaminophen. The holders of these ANDAs have waived their opportunity for a hearing.

DATES: Effective [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

FOR FURTHER INFORMATION CONTACT: Rachel Turow, Center for Drug Evaluation and Research (CDER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6236, Silver Spring, MD 20993-0002, 301-796-5094.

SUPPLEMENTARY INFORMATION: In the Federal Register of January 14, 2011 (76 FR 2691), FDA announced its plans to reduce the maximum dosage unit strength of acetaminophen in prescription drug products. The notice announced FDA's conclusion that, based on a reevaluation of the relative risks and benefits of prescription acetaminophen products, fixed-combination prescription drugs containing more than 325 mg of acetaminophen per dosage unit (tablet, capsule, or liquid) do not provide a sufficient margin of safety to protect the public against the serious risk of acetaminophen-induced liver injury. Accordingly, we asked product sponsors to limit the maximum amount of acetaminophen per dosage unit to 325 mg and, for

those products containing more than 325 mg of acetaminophen per dosage unit, to submit requests that FDA withdraw approval of their applications under § 314.150(d) (21 CFR 314.150(d)). FDA asked that all such requests be made before January 14, 2014, after which date the Agency planned to initiate proceedings under section 505(e) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 355(e)) to withdraw approval of any prescription drug products containing more than 325 mg of acetaminophen per dosage unit that remained on the market.

FDA did not receive a request for withdrawal of approval of an application containing more than 325 mg of acetaminophen per dosage unit from one sponsor. In addition, FDA received requests for withdrawal of approval of five applications for products containing more than 325 mg of acetaminophen per dosage unit for which sponsors either submitted requests under § 314.150(c) or failed to cite a relevant regulatory provision. FDA contacted all of these sponsors on multiple occasions to ask that they submit a request that FDA withdraw approval of their applications under § 314.150(d), but they failed to respond.

With respect to the application for which FDA received no request for withdrawal, FDA initiated proceedings under § 314.150(a) and (b) to withdraw approval. With respect to the requests for withdrawal of approval submitted under § 314.150(c), the Agency notes that because FDA has made a determination under § 314.150(a) that approval of these applications should be withdrawn for reasons of safety, application holders may not withdraw their applications under § 314.150(c). The text of § 314.150(c) expressly precludes withdrawal of an application under the subsection if FDA has made a safety determination under § 314.150(a). Similarly, when a request for withdrawal is made without a citation to any regulation, FDA does not consider it to be appropriately notified that an application holder has voluntarily waived the opportunity for a

hearing. Accordingly, FDA decided to proceed with withdrawal of approval of applications for which sponsors either submitted requests under § 314.150(c) or failed to cite a relevant regulatory provision under the withdrawal procedures outlined in § 314.150 (a) and (b).

Thus, in a notice published in the Federal Register on March 27, 2014 (79 FR 17156), the Director of CDER offered an opportunity for a hearing on a proposal to issue an order, under section 505(e) of the FD&C Act and 21 CFR 314.150(a), withdrawing approval of 6 ANDAs for products containing more than 325 mg of acetaminophen for which the ANDA holders did not voluntarily request to withdraw their applications under § 314.150(d). The ANDA holders were provided an opportunity to request a hearing to show why approval of their ANDAs should not be withdrawn. None of the ANDA holders requested a hearing in response to the notice.

The ANDAs listed in table 1, other than ANDA 040148, were the subject of the March 27, 2014, Federal Register notice. Because the holders of these ANDAs failed to request a hearing by April 28, 2014, they are considered to have waived their opportunity for a hearing under § 314.200(a)(2) and FDA is now withdrawing approval of their applications.

In addition, table 1 includes ANDA 040148 for which the ANDA holder submitted a timely voluntary request for withdrawal under 314.150(d) and waived its opportunity for a hearing. However, ANDA 040148 was erroneously omitted from the March 27, 2014, Federal Register notice (79 FR 17163) announcing withdrawal of approval of 108 ANDAs. FDA is now withdrawing approval of ANDA 040148 as well.

Table 1 – ANDAs for Which FDA Is Withdrawing Approval

Application No.	Drug Product(s)	Applicant or Holder
ANDA 40117	Vicodin HP (Acetaminophen and Hydrocodone Bitartrate Tablets), 660 mg/10 mg	AbbVie Inc., 1 N. Waukegan Rd., North Chicago, IL 60064
ANDA 88058	Vicodin (Acetaminophen and Hydrocodone Bitartrate Tablets), 500 mg/5 mg	AbbVie Inc.
ANDA 89736	Vicodin ES (Acetaminophen and Hydrocodone Bitartrate Tablets), 750 mg/ 7.5 mg	AbbVie Inc.
ANDA 89166	SYNALGOS-DC-A (Acetaminophen**,** Caffeine, and Dihydrocodeine Bitartrate Capsules), 356.4 mg/30 mg/16 mg	Leitner Pharmaceuticals LLC, 340 Edgemont Ave., Bristol, TN 37620
ANDA 40366	Acetaminophen and Hydrocodone Bitartrate Oral Solution, 500 mg/15 milliliters (mL); 7.5 mg/15 mL	Nesher Pharmaceuticals USA LLC, 13910 St. Charles Rock Rd., Bridgeton, MO 63044
ANDA 040148	Acetaminophen and Hydrocodone Bitartrate Tablets, 500 mg/10 mg	Watson Laboratories, 311 Bonnie Circle, Corona, CA 92880
ANDA 040637	Acetaminophen, Caffeine, and Dihydrocodeine Bitartrate Tablets, 712.8 mg/60 mg/32 mg	West-Ward Pharmaceutical Corp., 435 Industrial Way West, Eatontown, NJ 07724

With respect to the ANDAs listed in table 1 (with the exception of ANDA 040148), for the reasons discussed in the January 14, 2011, and March 27, 2014, notices, the Director of CDER, under section 505(e)(2) of the FD&C Act and under authority delegated to her by the Commissioner of Food and Drugs (the Commissioner), finds that new evidence of clinical experience, not contained in the applications listed in table 1 and not available at the time the applications were approved, shows that prescription drugs containing more than 325 mg of acetaminophen per dosage unit are not safe for use under the conditions of use that formed the

basis upon which the applications were approved (21 U.S.C. 355(e)(2)). Therefore, approval of the applications for the drug products listed in table 1 of this document (with the exception of ANDA 040148), and all amendments and supplements thereto, is withdrawn (see DATES). Distribution of these products in 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) and 331(d)).

With respect to ANDA 040148 listed in table 1, under § 314.150(d), and under authority delegated to the Director of CDER by the Commissioner, approval of ANDA 040148 and all amendments and supplements thereto, is withdrawn (see DATES).

The safety issue discussed in this document and the March 27, 2014, and January 14, 2011, Federal Register notices is limited to products containing more than 325 mg of acetaminophen per dosage unit. Thus, the withdrawal of approval of products containing more than 325 mg of acetaminophen per dosage unit listed in table 1 does not change the approval status of any products with 325 mg or less of acetaminophen per dosage unit that were approved under the same application. In addition, the withdrawal of approval of products containing more than 325 mg of acetaminophen per dosage unit does not change the approval status of products with 325 mg or less of acetaminophen per dosage unit that refer to or rely on the withdrawn products. For example, this withdrawal action will not affect the approval status of an ANDA for a product that contains 325 mg or less per dosage unit that references a product listed in table 1, but for which FDA approved a suitability petition for a lower strength under section 505(j)(2)(C) of the FD&C Act and § 314.93 (21 CFR 314.93)).

Dated: July 14, 2014.

Peter Lurie,

Associate Commissioner for Policy and Planning.

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