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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2008-N-0321]

Hospira, Inc., et al.; Withdrawal of Approval of One New Drug Application and Two Abbreviated New Drug Applications

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing approval of one new drug application (NDA) and two abbreviated new drug applications (ANDAs) for edetate disodium injection. The holders of these applications have agreed in writing to permit FDA to withdraw approval of the applications and have waived their opportunity for a hearing.

DATES: Effective [insert date of publication in the FEDERAL REGISTER].

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: FDA informed the holders of the following applications that the agency believes a potential problem associated with edetate disodium is sufficiently serious that the following drug products should be removed from the market:

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Application No.	Drug	Applicant
NDA 11-355	ENDRATE (edetate disodium) Injection	Hospira, Inc., 275 North Field Dr., Lake Forest, IL 60045-5046
ANDA 40-376	Edetate Disodium Injection	Apotex Inc., 150 Signet Dr., Toronto, Ontario, Canada M9L 1T9
ANDA 40-437	Edetate Disodium Injection	Bioniche Pharma, 272 E. Deerpath Rd., suite 304, Lake Forest, IL 60045

Edetate disodium is indicated for the treatment of hypercalcemia and for the control of ventricular arrhythmias associated with digitalis toxicity. Hospira, Inc. (Hospira), Apotex Inc. (Apotex), and Bioniche Pharma (Bioniche) have agreed in writing to permit FDA to withdraw approval of their respective applications (listed in the table of this document), and to voluntarily remove their respective products from the market, under § 314.150(d) (21 CFR 314.150(d)).

On January 16, 2008, FDA issued a public health advisory to alert patients and healthcare professionals about important safety information concerning the drug edetate disodium (see “FDA Public Health Advisory: Edetate Disodium (Marketed as ENDRATE and Generic Products),” available on the Internet at http://www.fda.gov/cder/drug/infopage/edetate_disodium/default.htm). As noted in the January 16, 2008, Public Health Advisory, there have been cases where children and adults have died when they were mistakenly given edetate disodium instead of edetate calcium disodium (calcium disodium versenate) or when edetate disodium was used for indications other than those approved by FDA. FDA asked Hospira, Apotex, and Bioniche to voluntarily remove their products (listed in the table of this document) from the market because of safety concerns.

Hospira's NDA 11-355 for ENDRATE was initially approved in 1959 solely on the basis of safety. The 1962 amendments to the Federal Food, Drug, and Cosmetic Act (the act) required that drugs be shown to be effective as well. To accomplish this, FDA initiated the Drug Efficacy Study Implementation (DESI) review to evaluate the effectiveness of drugs that had been previously approved on safety grounds alone. In its DESI review of edetate disodium, FDA concluded that edetate disodium was effective for the treatment of hypercalcemia and for the control of ventricular arrhythmias associated with digitalis toxicity, the two approved indications for the drug (35 FR 437, January 13, 1970).

In a letter dated September 17, 2007, FDA informed Hospira that the agency was reevaluating the safety and efficacy of ENDRATE (edetate disodium) Injection based on reports of fatal medication errors and reports of serious adverse reactions associated with this product. In its September 17, 2007, letter, FDA asked Hospira for additional information related to the safety of ENDRATE (edetate disodium) Injection.

On September 19, 2007, FDA sent letters to Apotex and Bioniche for ANDAs 40-376 and 40-437, respectively, requesting the same information for generic versions of edetate disodium.

In a letter dated October 1, 2007, Hospira provided the postmarketing safety information FDA requested on ENDRATE (edetate disodium). In its October 1, 2007, letter, Hospira stated that "[b]ased on the limited indications for ENDRATE (edetate disodium) and the availability of alternate medical products that offer a superior risk-benefit profile," Hospira determined that "the product is not medically necessary."

In a letter dated December 7, 2007, under § 314.150(d), FDA asked Hospira to waive its opportunity for a hearing (otherwise provided for under part 314 (21 CFR part 314)) to permit FDA to withdraw approval of NDA 11-355, and to voluntarily remove ENDRATE (edetate

disodium) from the market. In a letter dated December 20, 2007, Hospira concurred with FDA's determination to withdraw approval of NDA 11-355, ENDRATE (edetate disodium), under § 314.150(d); waived its opportunity for a hearing; and agreed to voluntarily remove ENDRATE from the market. Hospira initiated a recall of the product.

In separate telephone conversations on April 8, 2008, FDA asked Apotex and Bioniche, under § 314.150(d), to permit FDA to withdraw approval of ANDAs 40-376 and 40-437, respectively, for generic versions of edetate disodium, and to waive their opportunity for a hearing. Apotex and Bioniche, in letters dated April 9, 2008, and April 17, 2008, respectively, agreed to withdraw their ANDAs under § 314.150(d). Both Apotex and Bioniche indicated that alternative drug products that offer a superior risk-benefit profile are currently available for the approved indications for edetate disodium injection. Both Apotex and Bioniche waived their opportunity for a hearing (otherwise provided under part 314). In its April 9, 2008, letter, Apotex stated it has never marketed ANDA 40-376. In its April 17, 2008, letter, Bioniche agreed to voluntarily remove its edetate disodium product from the market.

Therefore, under section 505(e) of the act (21 U.S.C. 355(e)), § 314.150(d), and under authority delegated to the Director, Center for Drug Evaluation and Research, by the Commissioner of Food and Drugs, approval of the applications listed in the table of this

document, 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 act (21 U.S.C. 355(a) and 331(d)). On the basis of the circumstances described in this document that led to the withdrawal of approval of the applications listed in the table of this document, the agency will remove these products from the list of drug products with effective approvals published in FDA's "Approved Drug Products With Therapeutic Equivalence Evaluations," referred to as the "Orange Book."

Dated: 5.15.08
May 15, 2008.

Douglas C. Throckmorton

Douglas C. Throckmorton

Douglas C. Throckmorton,
Director,
Center for Drug Evaluation and Research

Deputy

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