4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2020-N-2143]

Determination That Bacitracin for Injection, 10,000 Units/Vial and 50,000 Units/Vial, Was Withdrawn From Sale for Reasons of Safety or Effectiveness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(FDA or Agency) has determined that bacitracin for injection, 10,000 units/vial and 50,000 units/vial, was withdrawn from sale for reasons of safety or effectiveness. The Agency will not accept or approve abbreviated new drug applications (ANDAs) for bacitracin for injection.

FOR FURTHER INFORMATION CONTACT: Sungjoon Chi, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6216, Silver Spring, MD 20993-0002, 240-402-9674, Sungjoon.Chi@fda.hhs.gov.

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 market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product: (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and (with certain exceptions) labeling as the listed drug, which is a version of the drug that was previously approved and (2) is bioequivalent to the listed drug. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

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approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (§ 314.162 (21 CFR 314.162)).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may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)).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.

Bacitracin for injection, 10,000 units/vial and 50,000 units/vial, is the subject of ANDA 060733 (originally NDA 6-483), held by Pharmacia and Upjohn Company (a subsidiary of Pfizer Inc.), and was initially approved on July 29, 1948. Bacitracin for injection is an antibiotic for intramuscular administration, the use of which is limited to the treatment of infants with pneumonia and empyema caused by staphylococci shown to be susceptible to the drug. However, in 1984, the Anti-Infective Drugs Advisory Committee concluded that intramuscular administration of bacitracin was not safe and effective. In addition, in April 2019, FDA's Antimicrobial Drugs Advisory Committee advised that the benefits of bacitracin for injection do not outweigh its risks for the drug's only approved indication.

Bacitracin for injection poses serious risks, including nephrotoxicity and anaphylactic reactions. Healthcare professionals generally no longer use bacitracin for injection to treat infants with pneumonia and empyema because other effective FDA-approved treatments are available that do not have these risks. Out of concern about these risks, on January 31, 2020, FDA requested that all application holders of bacitracin for injection voluntarily request withdrawal of approval of their applications under § 314.150(d) (21 CFR 314.150(d)). Two approved applications for bacitracin for injection had been withdrawn prior to January 31, 2020 (see 61 FR 40649, August 5, 1996, and 57 FR 6228, February 21, 1992) and therefore FDA did not need to request their withdrawal. In a letter dated February 7, 2020, Pfizer requested

withdrawal of approval of ANDA 060733 (originally NDA 6-483) for bacitracin for injection under § 314.150(d) and waived its opportunity for a hearing. In separate letters dated February 5, 2020, Akorn Inc. and Mylan ASI LLC requested that FDA withdraw approval of ANDAs 206719 and 090211, respectively, under § 314.150(d) and waived their opportunity for a hearing. Additionally, in separate letters dated February 7, 2020, X-GEN Pharmaceuticals, Inc. and Fresenius Kabi USA, LLC requested that FDA withdraw approval of ANDAs 064153 and 065116, respectively, under § 314.150(d) and waived their opportunity for a hearing. In the *Federal Register* of March 12, 2021 (86 FR 14127), FDA announced that it was withdrawing approval of ANDAs 060733 (originally NDA 6-483), 206719, 090211, 064153, and 065116, and all amendments and supplements thereto, effective March 12, 2021.

In a letter dated June 14, 2021, the only remaining application holder, Xellia Pharmaceuticals USA, LLC, requested that FDA withdraw approval of ANDA 203177 under § 314.150(d) and waived its opportunity for a hearing. In the *Federal Register* of July 11, 2022 (87 FR 41135), FDA announced that it was withdrawing approval of ANDA 203177, and all supplements thereto, effective July 11, 2022. Accordingly, the Agency has withdrawn approval of all ANDAs for bacitracin for injection.

After reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that bacitracin for injection, 10,000 units/vial and 50,000 units/vial, was withdrawn for reasons of safety or effectiveness. We have reviewed our files for records concerning the withdrawal of bacitracin for injection from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. Based on a thorough evaluation of this information, including information presented to FDA's Antimicrobial Drugs Advisory Committee and the recommendations of that committee, and an evaluation of the latest version of the drug product's labeling, we have determined that bacitracin for injection, 10,000 units/vial and 50,000 units/vial, would not be considered safe and effective

if it were introduced to the market today in the absence of new preclinical or clinical studies to address safety or effectiveness concerns identified during our review.

Accordingly, the Agency will remove bacitracin for injection, 10,000 units/vial and 50,000 units/vial, 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: September 9, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

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