

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

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[Docket Nos. FDA-2006-P-0081 (formerly Docket No. 2006P-0178) and FDA-2005-P-0369 (formerly Docket No. 2005P-0023)]

Determination That TEQUIN (Gatifloxacin) Was Withdrawn From Sale for Reasons of Safety or Effectiveness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and Drug Administration (FDA) has determined that TEQUIN (gatifloxacin) Tablets, Injection, and Oral Suspension, were withdrawn from sale for reasons of safety or effectiveness. This determination means that FDA will not accept or approve abbreviated new drug applications (ANDAs) for gatifloxacin oral tablets, injection, or oral suspension that refer to any previously approved dosage forms and strengths of TEQUIN (gatifloxacin).

FOR FURTHER INFORMATION CONTACT: Elena Cohen, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6228, Silver Spring, MD 20993-0002, 301-796-3602.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as

the “listed drug,” which is a version of the drug that was previously approved under a new drug application (NDA). ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of an NDA. The only clinical data required in an ANDA are data to show that the drug that is the subject of the ANDA is bioequivalent to the listed drug.

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(j)(7)), which 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 generally known as the “Orange Book.” 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of the drug’s NDA or ANDA for reasons of safety or effectiveness, or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (section 505(j)(7)(C) of the act; § 314.162 (21 CFR 314.162)).

FDA will not approve an ANDA if the listed drug has been withdrawn from sale for safety or effectiveness reasons (section 505(j)(4)(I) of the act). Under § 314.161(a)(1) (21 CFR 314.161(a)(1)), the agency must determine whether a listed drug was withdrawn from sale for reasons of safety or effectiveness before an ANDA that refers to that listed drug may be approved. A drug that has been withdrawn from the market for safety or effectiveness reasons is not a listed drug (21 CFR 314.3(b)). FDA may not approve an ANDA that does not refer to a listed drug. FDA currently has pending one or more ANDAs that refer to TEQUIN (gatifloxacin).

Bristol-Myers Squibb Co. (BMS) is the holder of three NDAs¹ for TEQUIN tablets, injection, and oral suspension as listed in the following table:

¹ On December 17, 1999, FDA approved NDAs 21–061 and 21–062 for community-acquired pneumonia, acute bacterial exacerbation of chronic bronchitis, acute bacterial

TABLE 1.—APPROVED TEQUIN PRODUCTS

NDA No.	Active Ingredients	Strength	Dosage Form/Route
21-061	Gatifloxacin	200 milligrams (mg)	Tablet; oral
21-061	Gatifloxacin	400 mg	Tablet; oral
21-062	Gatifloxacin	Equivalent to 10 mg/milliliter (mL) (200 mg)	Injectable; injection
21-062	Gatifloxacin	400 mg/40 mL (10 mg/mL)	Injectable; injection
21-062	Gatifloxacin in dextrose 5% in plastic container	200 mg/100 mL (2 mg/mL)	Injectable; injection
21-062	Gatifloxacin in dextrose 5% in plastic container	400 mg/200mL (2 mg/mL)	Injectable; injection
21-678	Gatifloxacin	200 mg/5 mL	Suspension; oral

TEQUIN is an antibacterial drug indicated for the treatment of infections due to susceptible strains of designated microorganisms in the following conditions: Acute bacterial exacerbation of chronic bronchitis; acute sinusitis; community-acquired pneumonia; uncomplicated skin and skin structure infections; uncomplicated and complicated urinary tract infections; pyelonephritis; uncomplicated urethral and cervical gonorrhea; and acute, uncomplicated rectal infections in women.

In January 2003, FDA received revised product labeling relating to several approved supplements for TEQUIN (gatifloxacin). This revised labeling deleted references to TEQUIN injection, 10 milligrams/milliliter (mg/mL) (200 mg), indicating that this product was no longer being marketed; therefore, the product was moved from the prescription drug product list to the “Discontinued Drug Product List” section of the Orange Book. In response to

sinusitis, uncomplicated urinary tract infections, complicated urinary tract infections, pyelonephritis, and uncomplicated gonorrhea. The December 17, 1999, approval letter also stated that indications for uncomplicated skin and skin structure infections were approvable pending the submission of certain postmarketing data. For administrative purposes, the agency assigned administrative NDAs 21-404 (TEQUIN Tablets) and 21-405 (TEQUIN Injections) for the treatment of uncomplicated skin and skin structure infections. BMS provided a complete response, and upon approval on October 17, 2002, NDAs 21-404 and 21-405 were retired by FDA. The approvals and all other submissions for the treatment of uncomplicated skin and skin structure infections were incorporated in the original NDAs, 21-061 and 21-062. NDAs 21-404 and 21-405 are not listed in the Orange Book, but can be found through a search at *Drugs@FDA*.

a citizen petition from Apotex Corp. (Docket No. FDA-2005-P-0369),² FDA stated, in the **Federal Register** of February 3, 2006 (71 FR 5858), that TEQUIN injection, 10 mg/mL (200 mg), was not withdrawn for reasons of safety and effectiveness.

On May 1, 2006, Public Citizen Research Group submitted a citizen petition (Docket No. FDA-2006-P-0081),³ under 21 CFR 10.30, requesting that FDA immediately ban TEQUIN because of the increased risk of dysglycemia (hypoglycemia, low blood sugar, and hyperglycemia, high blood sugar) in humans. Public Citizen states that it reached its conclusion based on: (1) The relatively high numbers and rates of gatifloxacin-associated dysglycemia adverse event reports calculated from data collected by FDA's Adverse Event Reporting System (AERS) and Health Canada's Adverse Drug Reaction Monitoring Program; (2) a study by Park-Wyllie et al., published in March 2006 in the *New England Journal of Medicine*, that showed that patients (diabetic and nondiabetic) receiving gatifloxacin had approximately 17 times the odds of having a hyperglycemic episode and 4 times the odds of having a hypoglycemic episode compared to those taking macrolide antibiotics; and (3) the relatively high numbers and rates of gatifloxacin-associated dysglycemic events in the manufacturer's safety studies in uninfected patients and other studies in infected patients, including clinical trials, cohort studies, case-control studies, postmarketing surveillance studies, and case reports.

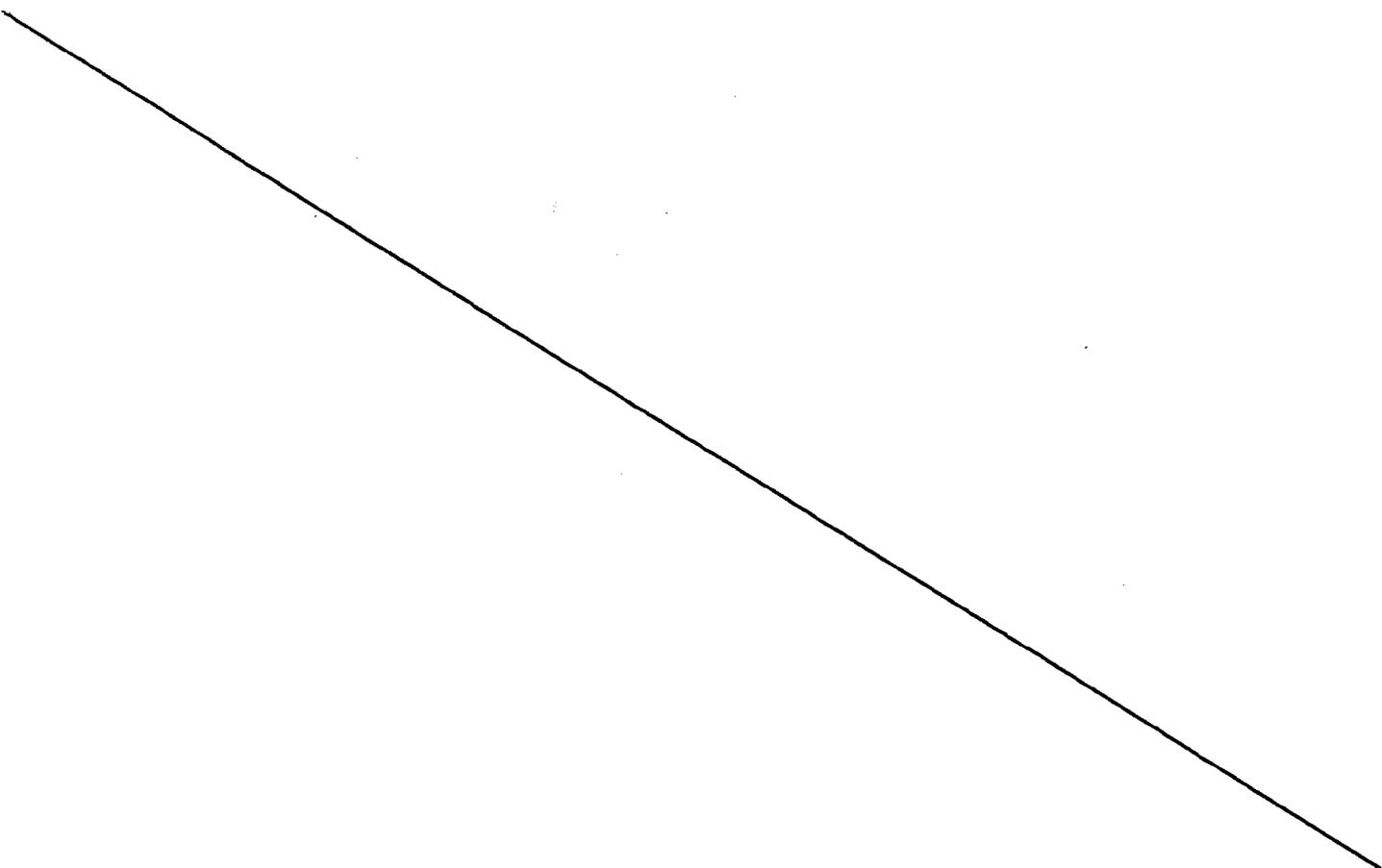
In June 2006, BMS announced that it would no longer market TEQUIN. In light of pending ANDAs and the citizen petition, FDA examined whether

² This citizen petition was originally assigned docket number 2005P-0023/CP1. The number was changed to FDA-2005-P-0369 as a result of FDA's transition to its new docketing system (*Regulations.gov*) in January 2008.

³ This citizen petition was originally assigned docket number 2006P-0178. The number was changed to FDA-2006-P-0081 as a result of FDA's transition to its new docketing system (*Regulations.gov*) in January 2008.

all TEQUIN products, including TEQUIN (gatifloxacin) injection, 10 mg/mL (200 mg), were withdrawn from the market for reasons of safety or effectiveness. After considering the citizen petition and reviewing agency records concerning the drug product, analyses of AERS reports, and relevant literature, FDA has determined under § 314.161 that TEQUIN was withdrawn from sale for reasons of safety or effectiveness. Accordingly, the agency will remove all TEQUIN products from the Orange Book (§ 314.162). FDA will not accept or approve ANDAs that refer to these drug products.

Therefore, the agency has determined, under § 314.161, that all dosage forms and strengths of TEQUIN (gatifloxacin) listed in the table of this document were withdrawn from sale for reasons of safety. TEQUIN (gatifloxacin) will be removed from the list of drug products published in the Orange Book. FDA will not accept or approve ANDAs that refer to any dosage form or strength of TEQUIN (gatifloxacin).



Dated: 9/2/08
September 2, 2008.



Jeffrey Shuren,
Associate Commissioner for Policy and Planning.

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