IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

PUBLIC CITIZEN, INC.
1600 20th Street, NW
Washington, DC 20009
(202) 588-1000

Plaintiff,

v.

FOOD AND DRUG ADMINISTRATION
5600 Fishers Lane
Rockville, MD 20854
(301) 827-2410

Defendant.

Case: 1:08-cv-00005
Assigned To : Kennedy, Henry H.
Assign. Date : 1/3/2008
Description: Admn. Agency Review

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

INTRODUCTION

1. Plaintiff brings this action pursuant to the Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. §§ 301-394, and the Administrative Procedure Act (APA), 5 U.S.C. §§ 702 and 706, to compel the United States Food and Drug Administration (FDA) to act on Public Citizen's petition seeking adequate warnings about the risk of tendon injury associated with fluoroquinolone antibiotics. On August 29, 2006, pursuant to 21 C.F.R. § 10.30, Public Citizen petitioned FDA to immediately add a "black-box" warning regarding the risks of tendinopathy and tendon rupture to the product labels of all fluoroquinolone antibiotics presently on the market in the United States, citing an alarming number of fluoroquinolone-induced tendon injuries reported to the agency. Public Citizen also urged FDA to mandate a "Dear Doctor" letter to warn physicians of these adverse effects and require the distribution of an FDA-approved Medication

Guide for all patients, to be dispensed when the prescriptions are filled. Although sixteen months have passed since Public Citizen filed its petition, FDA has neither granted nor denied the petition, nor has the agency taken action to adequately warn physicians and patients about the risk of fluoroquinolone-induced tendinopathy and tendon rupture. These stronger warnings to doctors and patients could lead to earlier intervention to stop tendon pain from progressing to frank tendon rupture by changing to other antibiotics. Therefore, to protect public safety and prevent needless injury, Public Citizen seeks a declaration that FDA has acted unlawfully by withholding action on Public Citizen's petition and an order requiring FDA to act thereon.

PARTIES

2. Plaintiff Public Citizen is a national, non-profit, public interest organization, headquartered in Washington, DC, with approximately 90,000 members. Since its founding in 1971, Public Citizen has worked before Congress, regulatory agencies, and in the courts to advance the interests of its members on a wide-range of consumer protection issues. In particular, Public Citizen's Health Research Group (HRG) promotes research-based, system-wide changes in health care policy and provides oversight concerning drugs, medical devices, doctors, hospitals, and occupational health. HRG works to ban or relabel unsafe or ineffective drugs, and publishes "Worst Pills, Best Pills News," a consumer guide to avoiding drug-induced death or illness. "Worst Pills, Best Pills News" has about 170,000 subscribers. Public Citizen and its members have been, and continue to be, injured by FDA's failure to act on Public Citizen's petition and to require adequate warning of the risk of fluoroquinolone-induced tendinopathy and tendon rupture, because such injuries could be prevented if doctors and patients were more aware of early warning signals. As long as fluoroquinolones are prescribed without

adequate warnings of the risk of these adverse effects, Public Citizen's members are at heightened risk of suffering fluoroquinolone-induced tendinopathy and tendon rupture.

3. The Department of Health and Human Services (HHS) is an agency of the federal government, and defendant FDA is an agency within HHS. By delegation from HHS, FDA is responsible for administration of the FDCA, 21 U.S.C. § 301 *et seq*. *See* 21 C.F.R. § 5.10. In particular, FDA regulates the content and format of prescription drug labeling. 21 C.F.R. 201. As set forth in more detail below, FDA has violated the law by failing to act on Public Citizen's petition seeking adequate labeling on fluoroquinolone antibiotics to inform the public about the risk of tendon injury associated with such drugs.

JURISDICTION

4. This Court has jurisdiction pursuant to 28 U.S.C. § 1331.

FACTS

5. Fluoroquinolones are antibiotic drugs that are widely prescribed for gastrointestinal, respiratory, and genito-urinary tract infections. Fluoroquinolones presently on the market in the United States include Ciprofloxacin (Cipro; Bayer); Enoxacin (Penetrex; Aventis); Gatifloxacin (Tequin; Bristol-Myers Squibb); Levofloxacin (Levaquin; Ortho-McNeil); Lomefloxacin (Maxaquin; Unimed); Moxifloxacin (Avelox; Bayer); Norfloxacin (Noroxin; Merck); and Ofloxacin (Floxin; Daiichi-Sankyo). Generic versions of two of these drugs, ciprofloxacin and ofloxacin, are also marketed in the United States.

6. Fluoroquinolones are drugs within the meaning of the FDCA, 21 U.S.C. § 321(g)(1), and new drugs within the meaning of 21 U.S.C. § 321(p).

7. The FDCA, 28 U.S.C. § 331, prohibits the introduction into interstate commerce of any drug that is misbranded. A drug is misbranded unless its labeling bears adequate warnings. 28 U.S.C. § 352(f).

8. Tendinopathy and tendon rupture associated with fluoroquinolone antibiotics has been observed since at least 1988. Since that time, reports of fluoroquinolone-induced tendon injuries have appeared repeatedly in the medical literature.

9. In August 1996, Public Citizen successfully petitioned FDA to place a warning regarding the risk of tendinitis and tendon rupture on the package inserts of all fluoroquinolones. Although it was thought that such a warning would effectively educate physicians and patients about this adverse event, a simple non-bolded warning buried in the list of possible adverse reactions to fluoroquinolones has proved inadequate. Fluoroquinolone-induced tendon injuries continue to occur at an alarming rate.

10. From November 1997 through December 31, 2005, the FDA adverse event database received reports of 262 cases of tendon ruptures; 258 cases of tendinitis; and 274 cases of other tendon disorders in patients using fluoroquinolone antibiotics. Because only a small fraction of adverse events typically are reported to FDA, the actual number of injuries attributable to fluoroquinolones is considerably higher. Analysis of the entire FDA adverse event database reveals that fluoroquinolones are implicated significantly more often in tendon ruptures than any other class of drugs. There has been no change in the rate of fluoroquinolone-induced tendon ruptures reported to FDA since December 31, 2005. From January 2006 through March 31, 2007, the FDA adverse event database received reports of 74 additional cases of tendon ruptures

in patients using fluoroquinolone antibiotics for a total of 336 cases of tendon rupture reported since November 1997.

11. FDA issued a statement in the October 1996 issue of its Medical Bulletin to all manufacturers of fluoroquinolones requesting a revision of the package inserts to include a new paragraph in the "Warnings" section acknowledging the risk of tendonitis and tendon rupture in patients using fluoroquinolones. The warning is among a list of other potential side effects and is in plain, non-bold type. Although the warning is accurate, it is buried in a long list of potential adverse reactions. Fluoroquinolone-induced tendon ruptures persist despite the re-labeling of the package insert in 1996. A more pronounced black-box warning would better alert physicians and patients of this complication.

12. On August 29, 2006, pursuant to 21 C.F.R. § 10.30, Public Citizen filed a petition with FDA, docket no. 2006P-0371, urging FDA to immediately add a black-box warning regarding the risks of tendinopathy and tendon rupture to the product labels of all fluoroquinolone antibiotics presently on the market in the United States. Public Citizen also urged FDA to mandate a "Dear Doctor" letter to warn physicians of these adverse effects and require the distribution of an FDA-approved Medication Guide for all patients, to be dispensed when the prescriptions are filled.

13. In support of its petition, Public Citizen presented an analysis of the FDA adverse event database to document the relationship between fluoroquinolone use and tendon injury.

14. On February 26, 2007, FDA responded to Public Citizen's petition, indicating that FDA had not yet reached a decision because the petition "raises complex issues requiring extensive review and analysis by Agency officials."

15. On August 29, 2006, the Office of the Illinois Attorney General (IL AG) sent a letter to FDA in support of Public Citizen's petition. The IL AG had submitted a similar petition to FDA on May 18, 2005, docket no. 2005P-0205. On November 16, 2005, FDA responded to the IL AG's petition, indicating that FDA had not yet reached a decision because the petition "raises complex issues requiring extensive review and analysis by Agency officials." To date, FDA has not ruled on the IL AG's petition of May 2005 petition.

16. Public Citizen's petition provides sufficient grounds for FDA to order enhanced labeling of fluoroquinolone antibiotics pursuant to 21 C.F.R. § 201.57(c)(1).

17. To date, FDA has not issued a decision on Public Citizen's petition, nor has it taken action to require adequate warnings of the risk of fluoroquinolone-induced tendinopathy and tendon rupture. Specifically, FDA has failed to require a black-box warning and enhanced provider information and, in addition, has failed to mandate an FDA-approved Medication Guide for patients. FDA has failed to act despite the significant and continuing reports to the agency of tendon injury linked to the use of fluoroquinolone antibiotics.

18. The considerable danger to public health occasioned by FDA's failure to require adequate warnings of the risk of fluoroquinolone-induced tendinopathy and tendon rupture counsels in favor of expeditious action on Public Citizen's petition. The pace of FDA's decisional process is lagging unreasonably in light of the nature and extent of the public health interests prejudiced by FDA's delay. Without FDA action on Public Citizen's petition to add adequate warnings to the labels of fluoroquinolone antibiotics, Public Citizen's members will continue to suffer injury or the threat of injury because they are at risk of being prescribed fluoroquinolone antibiotics and

suffering tendon damage or tendon rupture as a result. With adequate warnings, they could prevent the evolution of tendonitis into tendon rupture.

CLAIMS FOR RELIEF

1. FDA's failure to act on Public Citizen's petition constitutes agency action unlawfully withheld or unreasonably delayed and violates the Administrative Procedure Act, 5 U.S.C. § 706(1).

2. FDA's failure to act on Public Citizen's petition is not in accordance with law and violates the Administrative Procedure Act, 5 U.S.C. § 706(2)(A).

WHEREFORE, Plaintiff requests that this Court:

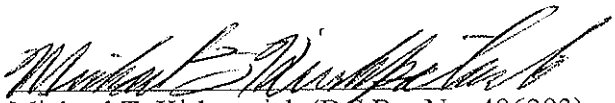
A. Declare unlawful FDA's failure to act on Public Citizen's petition;

B. Order FDA to issue a decision on Public Citizen's petition within 30 days of declaring FDA's failure to act unlawful;

C. Award Public Citizen its reasonable costs and attorney's fees under 28 U.S.C. § 2412; and

D. Grant all other appropriate relief.

Respectfully submitted,



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Dated: January 3, 2008