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.	)	Civil Action No. _____

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

INTRODUCTION

1. Plaintiff Public Citizen brings this action pursuant to the Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 301 *et seq.*, 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 revised warnings on proton pump inhibitor (PPI) labeling. In a petition filed October 11, 2011, Public Citizen petitioned the FDA to 1) add "black box" warnings for four serious adverse events and additional safety information to all PPI product labeling; 2) require patient Medication Guides for all prescription PPIs; and 3) request that sponsors of all prescription PPI medications send a "Dear Doctor" letter to physicians and other providers that includes the black box warnings and other labeling changes described in the petition. Although more than two and a half years have passed since Public Citizen filed its petition, the

FDA has neither granted nor denied the petition, and has not required adequate warnings on PPIs. To protect public safety and prevent needless death and injury, Public Citizen seeks a declaration that the FDA has acted unlawfully by withholding action on Public Citizen's petition and an order requiring the FDA to act thereon.

PARTIES

2. Plaintiff Public Citizen is a national non-profit, public interest organization headquartered in Washington, DC, with approximately 300,000 members and supporters nationwide. 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 150,000 subscribers. Public Citizen and its members have been, and continue to be, injured by the FDA's failure to act on Public Citizen's petition. As long as PPIs are prescribed and taken in their over-the-counter (OTC) form without adequate warnings, Public Citizen's members are at risk of suffering adverse effects of these drugs.

3. The Department of Health and Human Services (HHS) is an agency of the federal government, and the FDA is an agency within HHS. The FDA is responsible for administration of the FDCA. In particular, the FDA regulates the content and format of prescription drug labeling. *See* 21 C.F.R. § 201. As set forth in more detail below, the

FDA has violated the law by failing to act on Public Citizen's petition seeking adequate warnings on PPIs.

JURISDICTION

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

FACTS

5. PPIs, which suppress stomach acid, are one of the most widely used classes of drugs in the United States, with 131 million prescriptions dispensed in 2013. PPIs on the market include Nexium (esomeprazole), Dexilant (dexlansoprazole), Prilosec (omeprazole), Zegerid (omeprazole and sodium bicarbonate), Prevacid (lansoprazole), Protonix (pantoprazole), Aciphex (rabeprazole), Vimovo (esomeprazole and naproxen), Prevpac (lansoprazole, amoxicillin, and clarithromycin), Prilosec OTC, Zegerid OTC, Prevacid 24HR, Nexium 24HR, and generic counterparts.

6. The approved uses for prescription PPIs include treatment of gastroesophageal reflux disease (GERD), erosive and ulcerative esophagitis, peptic ulcer and *H. pylori* eradication, pathological hypersecretory conditions, and upper-gastrointestinal bleeding prophylaxis in critically ill patients and those taking nonsteroidal, anti-inflammatory drugs. However, PPIs are often prescribed outside of their approved uses. A 2009 study found that more than two-thirds of people on PPIs were not prescribed them for an approved use.

7. PPIs 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).

8. The FDCA, 21 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. *Id*. § 352.

9. Evidence shows that PPIs pose serious safety risks about which their labeling does not warn.

10. Evidence shows that use of PPIs for one month or more can cause patients to become dependent on the drugs, resulting in symptoms coming back after discontinuation of the drugs. This rebound effect is caused by an increase in the level of acid production in the stomach that occurs after stopping PPIs, in what is known as rebound acid hypersecretion (RAHS). RAHS is currently not mentioned in PPI labeling.

11. Long-term and multiple daily-dose PPI therapy has been associated with an increased risk of osteoporosis-related fractures of the hip, wrist, or spine. Particularly in the osteoporotic elderly population, this risk carries with it the potential for significant morbidity and, in some cases, mortality. In 2010, the FDA required a labeling change for PPIs to include this fracture risk, but the FDA does not require the warning on OTC drugs, and it has not required a black box warning concerning this risk.

12. Long-term PPI use has also been associated with an increased likelihood of certain serious infections, such as Clostridium difficile-associated diarrhea (CDAD) and community-acquired pneumonia. These conditions can be fatal, particularly in elderly and vulnerable populations. Approximately six months after Public Citizen submitted its petition, the FDA issued a Drug Safety Communication warning of the increased risk of CDAD with PPI use. The FDA later instructed manufacturers to add a warning of the risk of CDAD to the *Highlights* and *Warnings and Precautions* sections of all PPI

labeling. However, the FDA has not required a black box warning about the risk of CDAD. Moreover, PPI labeling still does not mention the pneumonia risk.

13. Another serious problem associated with long-term PPI use is severe hypomagnesemia. Magnesium levels as low as those seen in the published case series can cause fatal cardiac arrhythmias and other life-threatening complications. Although PPI labeling mentions hypomagnesemia in the *Highlights* section, FDA has not required a black box warning regarding the risk.

14. On August 23, 2011, pursuant to 21 U.S.C. § 352 and 21 C.F.R. §§ 10.30 and 201.56, Public Citizen sent a petition to the FDA urging the FDA to require black box warnings on PPI labeling about RAHS, fracture risk, infection risk, and magnesium deficiency risk. The FDA docket management division received the petition on October 11, 2011, and gave it docket number FDA-2011-P-0741.

15. As relevant here, the petition also urged the FDA to require all PPI labeling to: include appropriate information on potential interactions between PPIs and the drug mycophenolate mofetil; include a warning in the *Warnings and Precautions* section on the potential for Vitamin B12 deficiency; include information in the appropriate section about the potential for drug-induced acute interstitial nephritis; and, if the PPI is approved for the treatment of GERD, include specific recommendations in the *Indications* section for length of treatment.

16. In addition, the petition urged the FDA to require the distribution of FDA-approved patient Medication Guides to be dispensed when prescriptions are filled, and to request that the sponsors of all prescription PPI medications send a “Dear Doctor” letter to physicians and other providers. Since the petition, the FDA has required that

Medication Guides be provided with all but one prescription PPI-containing product. However, these guides—like the product labeling—do not contain all of the warnings sought in the petition.

17. Public Citizen's petition provided sufficient grounds for the FDA to require black box warnings on PPI labeling about RAHS, fracture risk, infection risk, and magnesium deficiency risk, as well as for the FDA to require the other relevant labeling changes and distribution of information discussed in the petition.

18. On April 3, 2012, the FDA sent a letter to Public Citizen, indicating that the FDA had not yet reached a decision on issues in the petition because the petition "raises complex issues requiring extensive review and analysis by Agency officials."

19. To date, the FDA has neither issued a decision on Public Citizen's petition nor required adequate warnings on PPI labeling. The FDA has failed to act despite the large increase in recent years in prescriptions for PPI drugs and the seriousness of the adverse effects about which Public Citizen petitioned the agency.

20. The considerable danger to public health caused by the FDA's failure to require adequate warnings on PPI labeling counsels in favor of expeditious action on Public Citizen's petition. The pace of the FDA's decisional process is lagging unreasonably in light of the nature and extent of the public health interests harmed by the FDA's delay.

CLAIMS FOR RELIEF

21. The 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).

22. The 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 the FDA's failure to act on Public Citizen's petition;

B. Order the FDA to issue a decision on Public Citizen's petition within 30 days of declaring the 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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