UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS
1 COURTHOUSE WAY
BOSTON, MASSACHUSETTS 02210

F. DENNIS SAYLOR IV
DISTRICT JUDGE

December 13, 2019

Stacy Cline Amin, Chief Counsel
Office of the Chief Counsel
Food and Drug Administration
10903 New Hampshire Avenue
White Oak 32, Room 4379
Silver Spring, MD 20993-0002

RE: *In re Zofran (Ondansetron) Products Liability Litigation*
MDL no. 1:15-md-2657-FDS

Dear Ms. Amin:

I am a United States District Judge for the District of Massachusetts. I am presiding over a Multidistrict Litigation (MDL) proceeding entitled *In re Zofran (Ondansetron) Products Liability Litigation*, MDL no. 1:15-md-2657-FDS.

I am submitting this letter in connection with the citizen petition filed by GlaxoSmithKline LLC on November 1, 2019, pursuant to 21 C.F.R. § 10.30, docket no. FDA-2019-P-5151-0001.

Overview of the Litigation

The MDL proceeding involves more than 400 individual lawsuits against GlaxoSmithKline LLC, all of which allege that the ingestion of Zofran (ondansetron) by pregnant women caused birth defects in their children. Although the claims are asserted under a variety of theories under the laws of a variety of states, in substance, all of the claims allege that GSK failed to warn of the dangers of ingesting Zofran during pregnancy.

Background: Approval and Proposed Label Changes

I understand the following facts to be true:

A predecessor of GSK, Glaxo, Inc., sponsored the original new drug application for Zofran. On January 4, 1991, the FDA approved the marketing and sale of Zofran for the prevention of nausea and vomiting induced by chemotherapy or radiation therapy and post-

operative nausea and vomiting. The 1991 approval was for an injection formulation; in 1992, 1995, 1997, and 1999, the FDA approved additional formulations.

Zofran has not been approved for nausea and vomiting in pregnancy. Nonetheless, it has been used off-label for that purpose with some frequency.

The FDA has considered possible label changes to Zofran for use during pregnancy on three subsequent occasions: (1) beginning in December 2010, when the FDA sent GSK a Prior Approval Supplement Request indicating that the FDA was aware of the common use of Zofran during pregnancy and requested that GSK "review and analyze available published and unpublished literature on the use of ondansetron during pregnancy and lactation, with a focus on the presence or absence of adverse pregnancy and/or neonatal outcomes"; (2) beginning in January 2013, when an individual named James P. Reichmann submitted a citizen petition asking the FDA to revise the Zofran label to provide pregnancy warnings and requesting that it reclassify the drug's pregnancy risk category from B to C, D, or X; and (3) beginning on September 22, 2015, when Novartis (which had acquired the rights to Zofran from GSK) submitted to the FDA a proposed update including several changes to the "Risk Summary" section of the label to advise against using Zofran during pregnancy and warn of potential risks to a developing fetus.

On the first two occasions, the FDA did not require any changes to the label. Certain relatively limited changes were approved in September 2016 in response to the Novartis request.

The Federal Preemption Dispute

Plaintiffs contend that the Zofran label failed to provide adequate warnings of the dangers of ingesting the drug during pregnancy, and that GSK was obliged under the laws of various states to provide such a warning. GSK contends that the state-law failure-to-warn claims are preempted by federal law.

As you may know, the preemption issue has arisen in other product-liability litigation involving pharmaceuticals. The Supreme Court recently issued an opinion in *Merck Sharpe & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668 (2019), clarifying some of the relevant legal principles.

GSK has moved for summary judgment in its favor as to all cases on the basis of federal preemption. It has based that motion, in substantial part, on the fact that the FDA did not require substantial labeling changes in response to the Reichmann petition and the Novartis proposal.

Plaintiffs have opposed the motion, alleging among other things that GSK improperly withheld certain information from the FDA concerning the dangers of ingesting Zofran during pregnancy at the time of the initial approvals, and continued to do so thereafter.

The motion for summary judgment remains pending as of this writing.

The GSK Citizen Petition

I understand that GSK filed a citizen petition with the FDA on November 1, 2019. The petition requests that "[the] FDA either refrain from taking action to alter Zofran's pregnancy-related labeling or take action to alter the labeling in light of [certain information], as the Agency deems appropriate." With the petition, GSK submitted a variety of exhibits; it contends that those exhibits include all the information that plaintiffs allege was wrongfully withheld on earlier occasions.

The Status of the Litigation

At the time GSK filed the citizen petition, the first individual trial in the MDL proceeding had been scheduled to begin on January 13, 2020. Because the citizen petition could potentially affect the resolution of the preemption dispute, and therefore the outcome of the entire litigation, both parties sought to postpone the trial date for at least several months. I have set a new trial date of May 4, 2020.

The Purpose of This Letter

The purpose of this letter is both (1) to advise you of the status of the litigation, and the relationship of the petition to that litigation, and (2) to request that the FDA resolve the matter as expeditiously as possible, consistent with the agency's statutory and regulatory duties, including its overarching duty to protect the safety of the public.

I trust and expect that the FDA will make its decision based on the relevant scientific and medical criteria, and according to the law, without regard to its potential impact on the litigation. In particular, I trust that the FDA will not take into account whether any decision may be helpful to the plaintiffs or the defendant, or to my ability to resolve the dispute. I ask only that the FDA resolve the matter, however it is resolved, without undue delay.

I express no view as to the merits of the petition, as a matter of substance or procedure, or what decision, if any, the FDA should make. I likewise express no view as to the effect, if any, on the litigation of any particular action or inaction by the agency.

Finally, and to be clear, by this letter I am not invoking the referral process set forth in 21 C.F.R. § 10.25(c), and express no view as to whether such a referral may or may not be appropriate, now or in the future.

Conclusion

I very much appreciate your consideration of this letter. I am providing a copy of this letter to the Division of Docket Management for inclusion in the docket of the FDA proceeding. I am also directing the clerk of court to place a copy of this letter on the docket in the MDL proceeding, so that it will be part of the record of the litigation.

Thank you.

Sincerely yours,

F. Dennis Saylor IV

FDS/dh

Cc: Christine Bono, Deputy Clerk, United States District Court, District of Massachusetts
Division of Dockets Management, United States Food and Drug Administration