UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF KENTUCKY
BOWLING GREEN DIVISION
CASE NO. 1:07-CV-176-R

DENNIS MORRIS PLAINTIFF

v.

WYETH, INC., et. al. DEFENDANTS

MEMORANDUM OPINION

This matter comes before the Court on Defendant PLIVA, Inc.'s Motion to Dismiss based on Federal Preemption (Docket #60). Defendants Teva Pharmaceuticals USA, Inc. and UDL Laboratories Inc. have joined this motion (Docket #64). Plaintiff Dennis Morris has filed a response (Docket #81). Defendant Morton Grove Pharmaceuticals, Inc. has joined Defendant PLIVA Inc.'s motion (Docket #85). Defendants have filed a reply (Docket #86) and Plaintiff has responded to Defendant Morton Grove Pharmaceuticals, Inc.'s motion (Docket #89). This matter is now ripe for adjudication. For the reasons that follow, Defendants' Motion to Dismiss is **GRANTED**.

BACKGROUND

Metoclopramide is a prescription drug used to treat gastric reflux symptoms. It is the generic equivalent of Reglan, the listed drug for metoclopramide.[1] Plaintiff Dennis Morris ("Morris") took metoclopramide from March 1993 to October 2005. Morris alleges that his use of metoclopramide caused him to develop severe and persistent Tardive Dyskinesia ("TD"). TD is a drug-induced neurological disease affecting a patient's brain chemistry, and loosely

[1]A listed drug, or reference listed drug, is the new drug already approved by the FDA that serves as the basis for the generic drug manufacturer's abbreviated application. *See* 21 U.S.C. §355(j); 21 C.F.R. § 314.3.

resembles Parkinson's Disease.

Morris filed a complaint in federal court asserting various products liability, negligence, and breach of implied warranty claims under Kentucky law against both the brand and generic manufacturers of metoclopramide. Central to all of his claims is the assertion that Defendants failed to adequately warn Morris of the long-term negative effects of ingesting metoclopramide.

In its June 2008 Order, the Court dismissed all of Morris' claims against Defendant Schwarz Pharma, Inc., a brand manufacturer of Reglan, because Morris did not allege that he consumed a product manufactured by Schwarz as required under Kentucky's Products Liability Act. The Court also dismissed any claims against Defendant Wyeth Inc., the original successor in interest to Reglan, for the injures caused by a generic drug manufacturer's product. Because Morris alleged in his complaint that he consumed a product manufactured by Wyeth, those claims still remain against Wyeth.

Defendants PLIVA Inc. ("Pliva"), Teva Pharmaceuticals USA Inc. ("Teva"), UDL Laboratories Inc. ("UDL"), and Morton Grove Pharmaceuticals, Inc. ("Morton Grove") are all generic drug manufacturers that manufactured and distributed metoclopramide. These Defendants now move to dismiss all the claims alleged against them based on federal preemption.

STANDARD

"When considering a motion to dismiss pursuant to Rule 12(b)(6) of the Federal Rules of Civil Procedure, the district court must accept all of the allegations in the complaint as true, and construe the complaint liberally in favor of the plaintiff." *Lawrence v. Chancery Court of Tenn.*, 188 F.3d 687, 691 (6th Cir. 1999) (citing *Miller v. Currie*, 50 F.3d 373, 377 (6th Cir. 1995)).

The Supreme Court's recent decision in *Bell Atlantic Corporation v. Twombly* clarified the pleading standard necessary to survive a Rule 12(b)(6) motion to dismiss. *Assn' of Cleveland Fire Fighters v. City of Cleveland*, 502 F.3d 545, 548 (6th Cir. 2007). *Twombly* does not "require heightened fact pleading of specifics, but only enough facts to state a claim to relief that is plausible on its face." *Bell Atl. Corp. v. Twombly*, 127 S. Ct. 1955, 1974 (2007). A plaintiff must allege sufficient factual allegations to give the defendant "fair notice concerning the nature of the claim and the grounds upon which it rests." *Twombly*, 127 S. Ct. at 1965.

Pursuant to Rule 12(b)(6), a court may consider the complaint, matters of public record, orders, and exhibits attached with the complaint in deciding a motion to dismiss. *See Barany-Snyder v. Weiner*, 539 F.3d 327, 332 (6th Cir. 2008). In so doing, the court "need not accept the plaintiff's legal conclusions or unwarranted factual inferences as true." *Id.* (citing *Commercial Money Ctr., Inc. v. Illinois Union Ins. Co.*, 508 F.3d 327, 336 (6th Cir.2007)).

ANALYSIS

I. Federal Preemption

Federal preemption doctrine is based on the Supremacy Clause of the United States Constitution. *State Farm Bank v. Reardon*, 539 F.3d 336, 341 (6th Cir. 2008). The Supremacy Clause provides that the Constitution, federal law, and all treaties "shall be the supreme Law of the Land; and the Judges in every State shall be bound thereby, any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. CONST. art. VI, cl. 2. The Supreme Court has interpreted the Supremacy Clause to include "both federal statutes themselves and federal regulations that are properly adopted in accordance with statutory authorization." *Reardon*, 539 F.3d at 341 (citing *City of New York v. FCC*, 486 U.S. 57, 63 (1988)).

Federal preemption can take several forms. "Federal law may preempt state law either expressly or impliedly." *Id.* (citing *Fidelity Fed. Sav. & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 152-53 (1982)). "Express preemption exists where either a federal statute or regulation contains explicit language indicating that a specific type of state law is preempted." *Id.* at 421-42. The Supreme Court has recognized at least two types of implied preemption: "field preemption" and "conflict preemption." *Gade v. Nat'l Solid Wastes Mgmt. Ass'n*, 505 U.S. 88, 98 (1992). Field preemption is inferred "where the scheme of federal regulation is so pervasive as to make reasonable the inference that Congress left no room for the States to supplement it." *Id.* (internal quotations omitted). Conflict preemption occurs where compliance with both federal and state regulation is physically impossible, or "where state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Id.* (internal citations and quotations omitted).

Defendant generic manufacturers base their federal preemption argument on conflict preemption. They argue that under federal law generic manufacturers cannot unilaterally alter their labeling. Therefore, state laws that impose heightened warning labels are in direct conflict with federal law.

In response, Plaintiff Morris asserts that conflict preemption does not apply because the purpose of both federal and state regulation is to protect the health and safety of the public. Therefore, state regulation of generic manufacturers is consistent with federal law. Morris also argues that conflict preemption is precluded by Defendants' failure to abide by federal regulations designed to protect public health. Morris maintains that Defendants had knowledge of safety information that was contrary to that contained in the metoclopramide label and failed

to both propose a label change with the FDA as required by federal law and inform the medical community about the safety information. Morris argues that it would be contrary to public policy to grant federal preemption in a scenario such as this because it would create an incentive for generic manufacturers to withhold adverse information from the FDA.

A discussion of federal regulation of generic manufacturers is necessary to determine whether Morris' state law claims are preempted.

II. Federal Regulation of Generic Drugs

The Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 301 *et seq.*, charges the Food and Drug Administration ("FDA") with the responsibility of approving the introduction of new drugs on the market. *See* 21 U.S.C. § 355; *Riegel v. Medtronic, Inc.*, 128 S.Ct. 999, 1002 (2008). A manufacturer seeking to market a new drug must submit a New Drug Application ("NDA") with the FDA. 21 U.S.C. § 355(b). The NDA requires, among other things, that the manufacturer supply the agency with "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use" and "specimens of the labeling proposed to be used for such drug." 21 U.S.C. § 355(b)(1). A new drug's labeling is significant because it "'embraces advertising or descriptive matter that goes with the package in which the [new drug is] transported' in addition to any label that may be placed directly on a pill bottle." *Colacicco v. Apotex, Inc.*, 521 F.3d 253, n.1 (3d Cir. 2008) (quoting *Kordel v. United States*, 335 U.S. 345, 350 (1948)). The FDA can refuse to approve the NDA if the manufacturer fails to provide "adequate tests" or there is "insufficient information" to ensure the new drug's safety and effectiveness. 21 U.S.C. § 355(d).

The NDA procedure applies to new drugs manufactured and distributed by brand

manufacturers. In contrast, generic manufacturers seeking to market a generic drug must submit an Abbreviated New Drug Application ("ANDA") with the FDA. 21 U.S.C. § 355(j). Congress codified the ANDA procedure with the passage of the Drug Price Competition and Patent Term Act (the Hatch-Waxman Amendments) in 1984. The legislative history of the Drug Price Competition and Patent Term Act reveals that the purpose of amending the FDCA to include the ANDA procedure was to help Americans facing rising drug prices by increasing the availability of low costing generic drugs. *See, e.g., Drug Price Competition and Patent Term Act: Hearing on H.R. 3605 Before the Subcomm. On Health and the Env't of the H. Comm. on Energy and Commerce*, 98 the Cong. 1-2 (1983) (statement of Rep. Henry A. Waxman).

The ANDA procedure establishes an expedited FDA review process. The manufacturer must demonstrate that the generic drug it seeks to market is approved as a listed drug, meaning that the new drug product on which the generic drug is based already has FDA approval. 21 U.S.C. § 355(j)(2)(A)(i); 21 C.F.R. § 314.3. The manufacturer must show that the generic drug has the same active ingredients and is "bioequivalent" to the listed drug. 21 U.S.C. § 355(j)(2)(A)(ii)-(iv). Most important for this case, the manufacturer must supply "information to show that the labeling proposed for the [generic] drug is *the same as* the labeling approved for the listed drug . . . except for changes required because of differences approved under a petition filed under subparagraph (C) or because the [generic] drug and the listed drug are produced or distributed by different manufacturers." 21 U.S.C. § 355(j)(2)(A)(v) (emphasis added).

Federal regulations require that a generic drug's "labeling (including the container label, package insert, and, if applicable, Medication Guide) proposed for the drug product must be *the same as* the labeling approved for the reference listed drug, except for changes required because

of differences approved under a petition filed under § 314.93[2] or because the drug product and the reference listed drug are produced or distributed by different manufacturers." 21 C.F.R. § 314.94(a)(8)(iv) (emphasis added). The FDA can refuse to approve an ANDA if the information submitted by the manufacturer is "insufficient to show that the labeling proposed for the drug is *the same as* the labeling approved for the listed drug . . ." 21 C.F.R. § 314.127(a)(7) (emphasis added). The FDA can also withdraw the approval of an ANDA if "the labeling for the drug product that is the subject of the abbreviated new drug application is no longer consistent with that for the listed drug . . ." 21 C.F.R. § 214.150(b)(10).

The distribution of "misbranded" drugs is prohibited under the FDCA. 21 U.S.C. § 331(a),(b). A listed or generic drug is deemed misbranded if "its labeling is false or misleading in any particular." 21 U.S.C. § 352(a). Several enforcement mechanisms are available to the FDA to ensure that misbranded drugs remain off the market. For example, the FDA has authority to initiate injunction proceedings, *id.* at § 332, criminal prosecutions, *id.* at § 333(a), and the seizure of misbranded drugs, *id.* at § 334. *Colacicco*, 521 F.3d at 260.

Post-approval, a brand manufacturer obtaining NDA approval has the ability to submit additional information to the FDA to change the new drug's label "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction" or "[t]o add or strengthen an instruction about dosage administration that is intended to increase the safe use of the drug product." 21 C.F.R. § 314.70(c)(6)(iii)(A), (C). This regulation is known as the "changes being

[2]Section 314.93 governs "[a] person who wants to submit an abbreviated new drug application for a drug product which is not identical to a listed drug in route of administration, dosage form, and strength, or in which one active ingredient is substituted for one of the active ingredients in a listed combination drug, must first obtain permission from FDA to submit such an abbreviated application." 21 C.F.R. § 314.93(b).

effected," or "CBE" regulation. *Id.* The CBE regulation does not apply to the ANDA procedure. In 1992, the FDA issued a final rule that addressed the applicability of the CBE regulation to the ANDA procedure. Abbreviated New Drug Applications, 57 Fed. Reg.17950-01 (April 28, 1992). The FDA explained:

> FDA received no comments on this provision, but has amended the provision to adopt references to statutory, rather than regulatory, provisions or to explain what information should be provided. However, the agency wishes to remind ANDA applicants that, as noted in paragraph 4 above, the labeling for an ANDA product must, with few exceptions, correspond to that for the reference listed drug.

Id.[3] The Court understands this to mean that the FDA applies the statutory provisions of the NDA procedure to the ANDA procedure, but declines to apply the regulatory provisions of the

---

[3]In response to a comment recommending that generic manufacturers be allowed to add heightened warnings or precautions to their label, the FDA explained:

> As for accepting ANDA's with additional warnings or precautions, section 505 (j)(2)(A)(v) and (j)(3)(G) of the act requires that the applicant's proposed labeling be the same as that of the reference listed drug unless: (1) The labeling differences are due to an approved petition under section 505(j)(2)(C) of the act (otherwise referred to as a "suitability petition"); or (2) the drug product and the reference listed drug are produced or distributed by different manufacturers. (See 21 U.S.C. 355 (j)(2)(A)(v) and (j)(3)(G).) Thus, the exceptions in section 505 (j)(2)(A)(v) and (j)(3)(G) of the act are limited. In addition, under the patent and exclusivity provisions of the act, the ANDA labeling may be required to carry fewer indications than the reference listed product's labeling or to have other labeling differences. In the preamble to the proposed rule, the agency described various types of labeling differences that might fall within the permitted exceptions. An ANDA applicant is required to include in its ANDA a side-by-side comparison of the applicant's proposed labeling with the currently approved labeling for the reference listed drug. The agency will carefully review all differences annotated by the applicant in determining if such differences fall within the limited exceptions permitted by the act.

Abbreviated New Drug Applications, 57 Fed. Reg.17950-01 (April 28, 1992).

NDA procedure, such as the CBE regulation, to the ANDA procedure.[4] Thus, a manufacturer of generic drugs may only unilaterally change its label to reflect "differences in expiration date ... or omission of an indication or other aspect of labeling protected by patent." 21 C.F.R. § 314.94(a)(8).

III. Federal Preemption under the ANDA Procedure

Only a handful of federal district courts have considered the issue of whether federal preemption applies to state failure-to-warn claims involving generic drugs approved under the ANDA procedure. *See Laisure-Radke v. Par Pharmaceutical, Inc.*, 2006 WL 901657 (W.D. Wash. March 29, 2006); *Mensing v. Wyeth, Inc.*, 562 F.Supp.2d 1056 (D. Minn. 2008); *Gaeta v. Perrigo Pharmaceuticals Co.*, 562 F.Supp.2d 1091 (N.D. Cal. 2008); *Masterson v. Apotex, Corp*., 2008 WL 3262690 (S.D. Fla. August 7, 2008); *Bolin ex rel. Bolin v. SmithKline Beecham Corp.*, 2008 WL 3286973 (S.D. Fla. August 7, 2008); *Valerio ex rel. Valerio v. SmithKline Beecham Corp.*, 2008 WL 3286976 (S.D. Fla. August 7, 2008). In the majority of these cases, the district court found in favor of federal preemption. *Cf. Laisure-Radke*, 2006 WL 901657 (denying motion for summary judgment based on preemption).

The Court finds the *Mensing* decision instructive. In *Mensing*, the district court determined that a generic drug manufacturer may not unilaterally strengthen a drug label without prior FDA approval. *Mensing*, 562 F.Supp.2d at 1061-62. The court reached its determination

[4]The FDA's different regulatory provisions under the NDA and ANDA procedures is what distinguishes the issue before the Court from the federal preemption case currently pending before the United States Supreme Court. *Wyeth v. Levine*, currently pending before the Supreme Court, involves the preemption of state failure-to-warn claims involving branded drugs approved under the NDA approval process. Brief of Petitioner at 8-10, 30, Wyeth v. Levine, No. 06-1249 (2008).

based on the FDA's comments regarding its regulation of the ANDA procedure. In particular, the court focused on the FDA's comments in implementing the Hatch-Waxman Amendments stating that the exceptions to the requirement that a generic label be "the same as" the listed drug label are limited, *id.* at 1062, the statutory scheme allowing the FDA to withdraw an ANDA if the generic drug label "is no longer consistent with that for the listed drug," *id*., the FDA's negative responses to comments to proposed ANDA regulations asking that ANDA applicants be allowed to deviate from the listed drug labeling to add contraindications, warnings, precautions, adverse reactions, and other safety-related information, *id.*, and the court's determination that the CBE regulation does not apply to generic manufacturers, *id.* at 1064. The court concluded that plaintiff's state law failure-to-warn claims are conflict preempted by federal law because generic manufacturers cannot unilaterally heighten their labels to conform with state law. *Id.* at 1065.

In contrast, the district court in *Laisure-Radke v. Par Pharmaceutical, Inc*. reached the opposite conclusion based on its determination that the CBE regulation does apply to generic manufacturers. *Laisure-Radke*, 2006 WL 901657 *4-5. The court reasoned that because the CBE regulation applies to changes to "an approved application," without any distinction between an approved NDA or ANDA, the regulation applies to both. *Id.* at *4. Thus, there was no conflict between federal and state law because generic manufacturers could heighten the warnings on their labels post-approval. *Id.* at *5-6.

The Court declines to adopt the reasoning of *Laisure-Radke*. The Court bases its decision on its reading of the CBE regulation and the corresponding FDA final rules that reiterate that a generic drug manufacturer's label must be "the same as" the listed drug's label. The Court also relies on statements made by the FDA since the *Laisure-Radke* decision. For

example, the FDA recently stated in the supplementary information section of a proposed rule that: "CBE changes are not available for generic drugs approved under an [ANDA] application under 21 U.S.C. 335(j). To the contrary, a generic drug manufacturer is required to conform to the approved labeling for the listed drug." Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848 (January 16, 2008) (to be codified at 21 C.F.R. pt. 314, 601, 814).[5]

Plaintiff Morris makes several arguments against preemption. First, Morris argues that if Defendant brand manufacturers are not liable under Kentucky law and Defendant generic manufacturers are not liable under federal preemption, this creates a "federal void" in which no one is responsible for the injuries Morris allegedly suffered. Such a void, Morris argues, would be contrary to both federal and state regulatory schemes designed to protect public health.

The Court believes this is an overstatement. Misbranded drugs bearing inadequate labels are illegal under federal law and the FDA has authority to prohibit their distribution through various enforcement mechanisms. In addition, several liability options remain available to

---

[5] The FDA also takes the position that the CBE regulation necessitates federal preemption of state law. The FDA's proposed rule states:

> If finalized as proposed, this rule codifies longstanding agency policy and understanding with respect to §§ 314.70(c)(6)(iii), 601.12(f) and 814.39(d). To the extent that state law would require a sponsor to add information to the labeling for an approved drug or biologic without advance FDA approval based on information or data as to risks that are similar in type or severity to those previously submitted to the FDA, or based on information or data that does not provide sufficient evidence of a causal association with the product, such a state requirement would conflict with federal law. In such a situation, it would be impossible to market a product in compliance with both federal and state law, and the state law would "stand[] as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress," Hines, 312 U.S. at 67.

Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848 (January 16, 2008).

Morris. The Court's ruling applies only to federal preemption of failure-to-warn claims against generic manufacturers. Morris' products liability claims against brand manufacturer Wyeth remain under state law, as do Morris' design defect claims.

Next, Morris argues that a generic manufacturer is required under federal law to continually update the FDA by notifying the agency of adverse event reports and post-market surveillance. Morris alleges that Defendant generic manufacturers had safety information showing that continual use of metoclopramide led to an increased risk of TD and failed to propose a labeling change. Thus, Morris argues that the issue of whether or not Defendant generic manufacturers properly complied with FDA regulations impacts the Court's federal preemption determination.

The Court declines to adopt this reasoning. Whether or not the generic manufacturers failed to notify the FDA, and in turn the medical community, about safety information regarding metoclopramide and TD has no bearing on the Court's federal preemption determination or Morris' state law claims. Generic manufacturers are required to maintain and present adverse reporting information to the FDA. *See* Protecting the Identities of Reporters of Adverse Events and Patients; Preemption of Disclosure Rules, 60 Fed. Red. 16962-01 (April 3, 1995) (to be codified at 21 C.F.R. pt. 20). The FDA has the authority to withdraw a manufacturer's ANDA should the generic manufacturer fail to do so. *Id.* Therefore, it is the proper role of the FDA, not the Court, to determine whether Defendants have failed to comply with FDA reporting requirements.

Finally, Morris argues that public policy favors denying federal preemption. If Defendants prevail on their federal preemption claim, then Morris contends that they will have

little incentive to report adverse events. Because the FDA is largely dependent on the self-reporting by manufacturers, the tort system is better able to enforce reporting failures than the FDA. Defendants respond that Congress took this into consideration in enacting the Hatch-Waxman Amendments and decided that the benefit of providing access to less expensive generic drugs outweighed the potential risks that may result. The Court agrees, declining to reinterpret federal law on public policy grounds alone.

CONCLUSION

For the foregoing reasons, the Defendants' Motion to Dismiss is **GRANTED**.

An appropriate order shall issue.

Thomas B. Russell

Thomas B. Russell, Judge
United States District Court

October 24, 2008