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Client Alert

FDA & Life Sciences Practice Group

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First Circuit Finds Federal Preemption of State Tort Claims That Conflict With A Medication's FDA-Approved Labeling & Warnings

An opinion issued by the U.S. Court of Appeals for the First Circuit on February 20, 2015 held that the Federal Food, Drug, and Cosmetic Act ("FDCA") preempted claims that Lexapro's U.S. Food and Drug Administration (FDA) approved drug labeling misleads California consumers and violates state laws against false advertising and unfair competition.[1] In doing so, the Court focused on interpreting *Wyeth v. Levine*, 555 U.S. 555 (2009) in light of *PLIVA Inc. v. Mensing*, 131 S.Ct. 2567 (2011). The Court held that these two cases "draw [a line] between [labeling] changes that can be independently made… and changes that require prior FDA approval."[2] Based on its analysis of FDA's prescription drug labeling regulations, the Court determined that a manufacturer can make certain labeling changes independently and without prior FDA approval only when new information is presented which was not available at the time of FDA's review and approval of the labeling at issue. Accordingly, "*Wyeth* effectively reserves the launch of new drugs to the expertise of FDA, but then preserves a wide scope for the states in requiring manufacturers to respond to information not considered by the FDA."[3] A state law duty to initiate a change "is therefore not by its nature a second guess of an FDA judgment."[4] Because the Plaintiffs failed to allege the existence of new information, and argued instead that the requested labeling change should be based on information FDA already considered, the Court determined that the Plaintiffs' tort claims based in state law were preempted under the FDCA.[5]

Background

Lexapro, the medication at issue in the case, is an FDA-approved antidepressant manufactured by Forest Laboratories, Inc. FDA first approved Lexapro in 2002 to treat depression in adults. In 2008, FDA approved Lexapro to treat major depressive disorder in adolescents. Plaintiffs argued that Lexapro was no more effective for adolescents than a placebo because FDA approved Lexapro for adolescent use on the basis of only two clinical trials that displayed statistically significant, but very limited efficacy, and extrapolation from adult data. Plaintiffs alleged that Lexapro's FDA-approved labeling overstated the medication's efficacy for adolescents because Forest supposedly manipulated Lexapro's efficacy data, and the efficacy data did not actually show a true statistically significant difference

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from placebo, thereby misleading California consumers by omitting material efficacy information, in violation of California's Consumer Legal Remedies Act ("CLRA"), False Advertising Law ("FAL"), and Unfair Competition Law ("UCL").[6] Forest denied the claims. The District Court dismissed the claims, finding them barred by California's safe harbor doctrine, which prohibits the courts from condemning actions permitted by the legislature, including Congress.[7] Having made its determination on the safe harbor provision, the District Court did not reach the issue of preemption. On appeal, the Circuit Court affirmed the dismissal on the basis of federal preemption without considering California's safe harbor doctrine.

Basis for Preemption

In considering the question of federal preemption, the Circuit Court first reviewed FDA's "onerous and lengthy" approval process for prescription medications and the reach of FDA's decision-making authority. The Court noted that, under the FDCA and during its review and evaluation of new and supplemental applications, the Agency not only exercises its discretion to determine whether the scientific data are "sufficient to establish effectiveness" and provide "substantial evidence that the drug will have the effect it purports or is represented to have," but reviews the medication's proposed labeling as well. Specifically, FDA must determine, "based on a fair evaluation of all material facts," that the proposed labeling is not "false or misleading in any particular."[8] Upon approval, the medication may only be sold with its approved labeling.[9]

The Court next evaluated the means by which manufacturers can change their product's labeling under the FDCA, recognizing two pathways. The first requires FDA approval of a proposed change to the product labeling before distributing the product with the changed labeling.[10] The second—the Changes Being Effected ("CBE") regulation—permits a manufacturer to make certain changes to product labeling prior to FDA approval, but only if newly acquired information supports the modification.[11]

Focusing on *Mensing*'s reasoning that a manufacturer can only be required under state law to do what it can do independently under federal law, the First Circuit determined that *Mensing* limited *Wyeth* to "situations in which the drug manufacturer can, 'of its own volition,…strengthen its label in compliance with its state tort duty.'"[12] The Court explained how drawing the line at this point lets FDA be the exclusive judge of safety and efficacy information provided to it. The Court determined that *Wyeth* circumscribes the initial evaluation and approval of labeling for prescription medications as solely FDA's territory.[13]

Applying *Mensing* and *Wyeth*, the Court ruled that Plaintiffs needed to allege a labeling deficiency that Forest could have remedied through the CBE pathway. Because the CBE supplement should only be used to change the labeling to reflect "newly acquired information," and FDA had considered the information that Plaintiffs claimed the manufacturer had supposedly manipulated or over-stated, the Court found that Plaintiffs failed to allege any new information that warranted a labeling change under the CBE provision. Without new information to justify a change to Lexapro's labeling under the CBE pathway, Forest could not have independently changed its labeling.

Analysis

This decision is significant for the renewed life it breathes into preemption as a defense for brand pharmaceutical companies. After *Wyeth*, the plaintiffs' bar sounded the death knell for preemption as a viable defense. The First Circuit's decision, as well as others, shows that this view is incorrect.[14] Indeed, *Mensing* refocused the preemption inquiry on a straightforward legal question: could the manufacturer have used the CBE pathway to unilaterally change its labeling in the way the plaintiff contends state law required? The CBE regulation does not permit any and all labeling changes, but rather only ones that meet its legal standards. If, as in the Lexapro case, the plaintiff challenges the adequacy of the FDA-approved labeling language based on information that was available to FDA when it approved

the labeling, the claim is preempted, because a manufacturer may not use the CBE regulation to second guess a FDA determination. By the same reasoning, even if the information relied on by the plaintiff post-dates FDA's labeling determination, preemption may still apply because the information, despite being new, may not rise to the level required by the CBE regulation to justify the labeling change advocated by the plaintiff. For example, scattered adverse event reports may not provide substantial enough evidence of a causal association to justify a new warning.[15] By making clear that the key issue under *Mensing*—whether the manufacturer could have used the CBE pathway to do what state law supposedly required—applies equally to claims against brand manufacturers, the First Circuit decision clarifies and reinvigorates preemption as a defense for brand manufacturers.

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We will continue to monitor developments in this area and will provide updates to you as developments arise. Please contact us if there is anything we can do to help you in related matters.

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[1] *In re Celexa & Lexapro Mktg. Sales Practices Litig. (Marcus v. Forest Labs., Inc.)*, 2015 WL 727970 (C.A.1 (Mass.)) (*Hereinafter* "In re Celexa & Lexapro").
[2] *Id.* at 7.
[3] *Id.*
[4] *Id.*
[5] *Id.*
[6] Cal Civ. Code § 1750 et seq.; Cal. Bus. & Prof. Code §17500 et seq.; Cal. Bus. & Prof. Code § 17200 et seq.
[7] *See In re Celexa & Lexapro Mktg. Sales Practices Litig. (Marcus v. Forest Labs., Inc.*), No. 13-11343-NMG, 2014 WL 866571 (D. Mass. March 5, 2014).
[8] 21 U.S.C. § 355(d)(7); 21 C.F.R. §314.125(b)(6).
[9] *See* 21 U.S.C. §§ 331(c), 333(a), and 352(a),(c).
[10] 21 C.F.R. § 314.70(b)(2)(v)(A).
[11] 21 C.F.R. § 314.70(c)(6)(iii).
[12] *In re Celexa & Lexapro* at 6.
[13] *Id.* at 7.
[14] *See e.g., Glynn v. Merck Sharp & Dohme Corp. (In re Fosamax (Alendronate Sodium) Prods Liab. Litig.*, 951 F.Supp. 2d 695 (D.N.J. Apr. 10, 2013).
[15] Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 49,603, 49,604 (Aug. 22, 2008).