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A legal update from Dechert's Mass Torts and Product Liability Group

Court Finds FDA's Regulation of Prescription Medications Preempts Failure-to-Warn Claims Against Pharmaceutical Companies

Introduction

In January 2006, the FDA promulgated regulations reshaping how prescription drug labels provide information to physicians and patients.[1] In the preamble to the FDA's Final Rule, the agency emphasized that FDA regulations—both old and new—preempt "conflicting or contrary State law." Four months later, a federal court in the Eastern District of Pennsylvania applied the FDA's Final Rule to the failure-to-warn claims made against two pharmaceutical manufacturers, and held that the plaintiff's claims were impliedly preempted. *Colacicco v. Apotex, Inc.*, Civ. No. 05-cv-5500, 2006 WL 1443357 (E.D. Pa. May 26, 2006).

Now, a second court has reached a similar conclusion in the much-publicized litigation against Pfizer, manufacturer of the COX-2 inhibitor drugs Celebrex® and Bextra®. District Judge Charles R. Breyer, of the Northern District of California, ruled that certain of the plaintiffs' failure-to-warn claims—those specifically asserting that Celebrex poses a cardiovascular risk—were preempted by the FDA's Final Rule.

In re Bextra and Celebrex Mktg. Sales Practices and Prod. Liab. Litig., No. M: 05-1699 CRB, 2006 WL 2374742 (N.D. Cal. Aug. 16, 2006) (hereafter "*In re Bextra*"). Notably, however, the court denied Pfizer's motion to dismiss the plaintiffs' fraudulent marketing claims relating to gastrointestinal risks, which had been included in the Celebrex label since the product entered the market. Thus, Judge Breyer's opinion provides pharmaceutical companies important insight into how courts may approach preemption of failure-to-warn and fraudulent marketing claims and can help companies to shape future litigation strategies.

Background: *In re Bextra*

In re Bextra arose from the development and marketing of Bextra and Celebrex, both of which belong to a class of medications known as COX-2 inhibitors. This new class of medications was designed with the hope of being more protective to patients' gastrointestinal system than older non-steroidal anti-inflammatory drugs ("NSAIDs"), while at the same time controlling their pain.

While NSAIDs may be an effective treatment in some patients for arthritis and other types of pain, they also have known gastrointestinal toxicities, which can lead to serious side effects such as perforations, ulcers, and bleeds. The plaintiffs alleged that Pfizer "aggressively marketed" Celebrex to consumers and various medical professionals in a deceptive manner by failing to warn of the medication's cardiovascular risks and minimizing its gastrointestinal side effects.

At its core, the plaintiffs' complaint asserted that Pfizer:

- Suppressed data regarding Celebrex's cardiovascular risk
- Falsely claimed that there were fewer gastrointestinal side effects with the medication

[1] Final Rule, Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Prods., 71 Fed. Reg. 3922 (Jan. 24, 2006) (to be codified at 21 C.F.R. §§ 201, 314, and 601) (effective date June 30, 2006).

- Falsely asserted that Celebrex provided superior pain relief to other traditional NSAIDs

Id. at *1.

With regard to an alleged cardiovascular risk, Celebrex's label included a warning for "aggravated hypertension," but did not warn of other cardiovascular risks. In May 1999, the FDA approved a revised label for Celebrex that, in the adverse events section of the label, reported the cardiovascular adverse events of angina pectoris, coronary artery disease, and myocardial infarction occurring in less than two percent of the studied patients.

The plaintiffs contended that a 2000 study of Celebrex, known as CLASS, revealed "a tendency" toward increased cardiovascular toxicity in patients taking the drug. The plaintiffs also claimed that Pfizer did not disclose to the FDA a June 1999 study that allegedly demonstrated an increased cardiovascular risk. According to the plaintiffs, if Pfizer had done so, then the FDA would have placed more significance on the cardiovascular data from CLASS and required different information to be provided to doctors and patients. *Id*. at *3.

In February 2001, the FDA concluded that CLASS showed no difference in the rate of serious adverse cardiovascular events for patients taking Celebrex versus patients taking other NSAIDs. Accordingly, the FDA did not require Pfizer to include a cardiovascular warning in its label. In fact, the company was allowed to state that there was no difference between the rate of serious adverse cardiovascular events for Celebrex when compared to other NSAIDs. *Id*.

The plaintiffs' claims against Pfizer did not rest solely on an alleged cardiovascular risk, but also included allegations that Pfizer's marketing campaign minimized the potential gastrointestinal side effects associated with Celebrex. Specifically, the plaintiffs asserted that Pfizer improperly marketed Celebrex as offering a superior gastrointestinal benefit to patients as opposed to other NSAIDs. Throughout its labeling history, Celebrex carried the warning that "serious gastrointestinal toxicity 'can occur at any time, with or without warning symptoms, in patients treated with non-steroidal anti-inflammatory drugs (NSAIDs)'." *Id*. at *3-*4.

The plaintiffs claimed that "[a]lthough Pfizer was well aware that Celebrex had no proven superiority over competing drugs, and in fact had serious side effects, including gastrointestinal complications . . . Pfizer nevertheless pushed Celebrex to market on false claims of improved gastrointestinal safety while downplaying its other risks." Purchaser Plfs.' Resp. in Opp. to Pfizer's Mot. to Dismiss Purchase Claims Master Celebrex Compl., 2006 WL 1436596, at 11 (N.D. Cal. May 5, 2006) (hereafter "Plfs.' Opp.").

Over Pfizer's objections, the court permitted the plaintiffs to file what became known as a "Purchase Claims Master Celebrex Complaint" for a national class of "end-payors." The plaintiffs sought relief for having purchased and/or paid for Celebrex. *In re Bextra*, 2006 WL 2374742, at *1. Among other grounds, Pfizer moved to dismiss the complaint on the basis that the claims were preempted by the Food, Drug, & Cosmetics Act ("FDCA") and its supporting regulations. *Id*. at *2.

The Court's Decision on Failure-to-Warn Claims

The plaintiffs' allegations against Pfizer centered around the contention that the company impermissibly marketed Celebrex without disclosing the drug's cardiovascular risks to doctors and patients.[2] As Judge Breyer noted, "Plaintiffs are asserting, in effect, that Pfizer should have included an additional warning on the Celebrex label and in the Celebrex advertising—a warning not required by the FDA." *Id.* at *4.

It was precisely these types of claims, however, that the FDA's Final Rule sought to preempt. Simply put, the plaintiffs' attempt to impose liability on Pfizer because it did not include a cardiovascular warning was barred because the proposed warning had been considered and rejected by the FDA as "scientifically unsubstantiated." *Id.* at *9-*10.

In reaching its conclusion, the court focused on three issues:

- The FDA was vested with the authority to determine whether conflicting and contrary state laws would interfere with the fulfillment of the FDA's goals and purposes

- The FDA's position on preemption was entitled to deference even when it was stated in a preamble

[2] In an attempt to avoid the preemption issue altogether, the plaintiffs asserted that their allegations had nothing to do with the validity of the FDA-approved Celebrex label. Rather, they were challenging the "improper promotion" of Celebrex "in a manner inconsistent with the approved label." Plfs.' Opp., 2006 WL 1436596, at 19. Yet, in later briefing, the plaintiffs argued that state law might require manufacturers to place additional risk information in their labels. *In re Bextra*, 2006 WL 237472, *4.

and represented a position different from one previously taken by the agency

- The court must defer to an agency's view of its own regulations when the interpretation is not clearly erroneous

Addressing the issue of FDA authority, the plaintiffs asserted that because the FDA's primary purpose was to "protect consumers from dangerous products," and not to concern themselves with the issue of how drugs are purchased and priced, the FDA was without authority to opine that an actual conflict between FDA regulations and a cause of action by third-party payors. Plfs.' Opp., 2006 WL 1436596, at 23-24. The plaintiffs argued that because the FDCA did not provide a monetary remedy for third-party payors, Congress must not have intended the FDA to have authority over the plaintiffs' claims. *In re Bextra*, 2006 WL 237472, at *7.

However, multiple courts have determined that Congress made a clear delegation of authority to the FDA to administer the FDCA, and "such responsibility implies the authority and expertise to determine which state laws conflict with its regulations." *Id.* (citations omitted). In other words, while the FDCA itself may not directly speak to issues concerning third-party payors, the plaintiffs' claims could impact the FDA's ability to implement its own regulations in such a way that would prevent it from achieving its purposes and objectives. *See* Final Rule, 71 Fed. Reg. at 3933-36. Thus, the court found that the FDA had sufficient authority to determine when state law conflicts with FDA regulations.

The plaintiffs further argued that even if such authority existed, the FDA's position on preemption was entitled to no deference because it was merely part of the Final Rule's preamble and not the regulation itself. Moreover, they contended that the FDA's position was inconsistent with previous agency interpretations. Plfs.' Opp., 2006 WL 1436596, at 25-27; *In re Bextra*, 2006 WL 2374742, at *7. Brushing aside the claim that statements made in a preamble are without effect, the court turned to the issue of an agency's evolving interpretation of its own regulations.

As even the court noted, the FDA had taken the position in the 1970s and 1990s that its labeling regulations established only minimum standards, while the agency now claimed that the regulations established both a floor and a ceiling. *In re Bextra*, 2006 WL 2374742, *7 (citations omitted). While the court acknowledged the FDA's current position was a "180-degree reversal of its prior position," it pointed to the Supreme Court's recognition that an agency's interpretation of its own regulations "may change over time as the agency gains more experience with the interrelationship between its regulations and state laws." *Id.* at *8 (citations omitted).

Finally, the plaintiffs maintained that the FDA's position on preemption was not entitled to judicial deference because it was plainly erroneous and inconsistent with the regulations. *Id.* Judge Breyer rejected this argument by pointing to the Final Rule. As the FDA noted, it retains final authority to disapprove a product label and may order a manufacturer to cease distribution of the drug and pursue an enforcement action against a manufacturer who violates FDA regulations. *Id.* (citations omitted). The FDA took the view that any state law requiring additional or different warnings could have the effect of diminishing warnings the FDA has approved by requiring manufacturers to include information in the product label that the FDA would consider "false and misleading" and result in a misbranded product. *See* Final Rule, 71 Fed. Reg. 3922, 3935.

The FDA expressed the concern that product liability suits would "directly threaten[] the agency's ability to regulate manufacturer dissemination of risk information for prescription drugs in accordance with the act" by holding manufacturers liable for failing to provide warnings that the FDA had considered and rejected or eroding the warning's effectiveness by "over-warning." *Id.* at 3922, 3934-35. Thus, the court could not conclude that the FDA's position was incorrect as the agency was in a better position to determine what state laws would encourage manufacturers to propose defensive labels that "upset the FDA's careful balance of statutory objectives." *In re Bextra*, 2006 WL 2374742, *9.

For these reasons, the FDA's position was entitled to deference and the plaintiffs' failure-to-warn claims concerning an alleged cardiovascular risk were preempted. *Id.* at *9-*10.

The Court's Decision on Fraudulent Marketing Claims

While the court granted Pfizer's motion to dismiss the failure-to-warn claims relating to an alleged cardiovascular risk, Judge Breyer denied Pfizer's motion to dismiss the allegations of a fraudulent scheme to minimize the gastrointestinal side effects associated with Celebrex. In doing so, the court focused on two issues:

- Pfizer could not support its assertion that its submission of advertisements to the FDA for pre-approval, and the FDA's ensuing silence with re-

gard to those advertisements, "necessarily determined" that the advertisement was not deceptive

- The FDA's silence with respect to preemption of lawsuits challenging false claims in prescription drug advertisements provided evidence that no actual conflict existed

Id. at *11.

The plaintiffs claimed that Celebrex advertisements were false and misleading because they exceeded the labeled and approved gastrointestinal benefits and minimized the established risks. *Id.* (citation omitted). Pfizer argued that because it submitted its Celebrex advertisements for FDA approval, and the FDA did not object to its advertising, the FDA had "necessarily determined" that the advertisements were both accurate and struck a fair balance between the risks and the benefits of the medication.

The court, however, rejected this position. Instead, Judge Breyer found that Pfizer had not produced sufficient information that would allow him to determine that the FDA pre-approval process was an affirmative determination establishing that Celebrex advertisements were not misleading. *Id.* For this reason, the court could not agree that an actual conflict had been established.

In *dicta*, the court offered the view that the FDA's silence was significant in this circumstance. If the FDA believed that its regulations preempt state laws, then the FDA would say so. Here, the FDA had been silent on the subject of reviewing promotional materials and preemption. This silence suggested to the court that the FDA did not intend preemption to apply in those circumstances. *Id.* (citation omitted).

Conclusion

Both the *In re Bextra* and *Colacicco* decisions offer tremendous insight into how courts might interpret the FDA Final Rule's preemption language. Together, these decisions demonstrate that a regulatory body's interpretation of its own regulations should be—and will be—accorded judicial deference. Plaintiffs may read the cases to say that while failure-to-warn claims are preempted, fraudulent marketing claims are not. To synthesize these this way would, however, be over-reading them.

The *Bextra* court's decision should be read much more narrowly, particularly as the court specifically noted that the record before it was limited solely to information contained in the parties' pleadings and provided through judicial notice at a motion to dismiss stage. Thus, its decision was not based on a fully developed record that could more clearly elucidate that the core of the plaintiffs' fraudulent marketing claims posed an actual conflict with the FDA's Final Rule.

In addition, the FDA's Final Rule will offer pharmaceutical companies additional protection against future failure-to-warn and fraudulent marketing claims once the new labels described in the Final Rule are adopted. The FDA has stated that if a company has used the "Highlights" section of the new label consistently with the FDA's guidance on "brief summaries," then any failure-to-warn claims focusing on a pharmaceutical company's advertising will be preempted when the allegations concern a failure to include any information the substance of which appears *anywhere* in the labeling. Final Rule, 71 Fed. Reg. 3922, 3936. *See also* FDA, Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements, 69 Fed. Reg. 6308 (Feb. 2004).

It should be understood, however, that the FDA's Final Rule is not a panacea to all plaintiffs' failure-to-warn and fraudulent marketing claims. Pharmaceutical companies facing such litigation must be prepared to embrace the benefits bestowed by the FDA's position on preemption, while recognizing that courts may be looking for express statements of intent to preempt, even in the context of promotional materials.

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