wiley

ARTICLE

Court to Weigh Viability of State Suits over Generics

The National Law Journal
March 14, 2011

On March 30, the U.S. Supreme Court will hear argument in three consolidated cases involving injury allegedly caused by generic versions of the prescription drug Reglan (metoclopramide): *Pliva v. Mensing*, U.S., No. 09-993, *Actavis Elizabeth LLC v. Mensing*, U.S., No. 09-1039, and *Actavis Inc. v. Demahy*, U.S., No. 09-1501. This controversy will again require the Court to reconcile overlapping federal and state standards for regulating prescription-drug label warnings.

In its landmark decision in *Wyeth v. Levine*, 129 S. Ct. 1187 (2009), the Court held that state-law-based products liability claims based on inadequate labeling of branded prescription drugs did not conflict with, and were not pre-empted by, the U.S. Food and Drug Administration's authority under the Federal Food, Drug, and Cosmetic Act to regulate drug labeling. Justice John Paul Stevens' opinion for the court – observing that primary responsibility for labeling rested with manufacturers – reasoned that manufacturers could comply with both federal and state jury-imposed labeling standards because FDA regulations permitted pioneer manufacturers like Wyeth to make certain safety-related labeling changes without prior FDA approval.

In the generic-metoclopramide cases, the Court must decide whether the nonpre-emption result of *Wyeth* extends to claims against generic manufacturers, whose ability to modify labels under federal law is far more restricted. The stakes are high for generic manufacturers and potentially also for innovator biopharmaceutical companies still reeling from *Wyeth*. The possibility that the Court – with two new members – could revise or limit *Wyeth*, decided just two years ago,

Authors

Bert W. Rein
Founder
202.719.7080
brein@wiley.law

Practice Areas

Food & Drug

also makes this one of the more interesting cases to watch during the current term.

In the decisions below, the U.S. courts of appeals for the 5th and 8th circuits found the plaintiffs' claims not pre-empted. *Mensing v. Wyeth Inc.*, 588 F.3d 603 (8th Cir. 2009); *Demahy v. Actavis Inc.*, 593 F.3d 428 (5th Cir. 2010). The 8th Circuit ruled that a generic manufacturer was, at a minimum, able to propose a labeling change or request that the FDA send a "Dear Doctor" letter advising health care professionals of new safety information, and that this ability to "take steps to warn its customers" averted any conflict between federal and state law – a position the government endorsed in its amicus brief opposing certiorari. *Mensing*, 588 F.3d at 608-10; U.S. Brief at 18-20. It further observed that if manufacturers were reluctant to make such suggestions, "they could have simply stopped selling the product." *Mensing*, 588 F.3d at 611.

The 5th Circuit went even further, holding that, in addition to proposing labeling changes and "Dear Doctor" letters, generic manufacturers, like pioneer manufacturers, could implement certain safety-related changes unilaterally as "changes being effected," subject to the FDA's subsequent approval, further foreclosing a pre-emption defense. *Demahy*, 593 F.3d at 439, 444. It also held that the requirement that a generic drug's label be "the same as" the branded drug that it copied applied only at the time the application was approved and that the labeling could deviate from branded labeling thereafter to enhance safety. Id. at 436-37.

Differing Regulatory Regimes

The generic petitioners rely heavily on the differing regulatory regimes governing innovator drugs and generic drugs. To gain approval of an innovator drug, an applicant must conduct studies and submit reports and labeling that establish the safety and efficacy of that drug when used under labeled conditions. A generic drug applicant, by contrast, may piggyback on the branded-drug application and obtain FDA approval simply by establishing that its drug is bioequivalent to the branded drug that it imitates and by using labeling that is, with nonsubstantive exceptions, "the same as" the branded drug's labeling. Pliva Brief at 6-14; Actavis Brief at 3-7.

The petitioners further assert that generic-drug labeling must remain the same as the branded drug's labeling after approval and that generic companies cannot change their labeling through the "changes being effected" or prior approval processes or by sending a Dear Doctor letter communicating additional warnings. Pliva Brief at 32-47; Actavis Brief at 18-26. They also argue that the ability to "take steps" to suggest to the FDA a labeling change or Dear Doctor letter does not avoid pre-emption because the inevitable uncertainty as to how the FDA would have responded would preclude plaintiffs from establishing that such "steps" would have prevented injury, at least absent an intrusive and speculative judicial inquiry into FDA's likely labeling policy. Pliva Brief at 47-61; Actavis Brief at 26-33. The respondents reply that they need only establish that inadequate warnings caused their injuries, not that the FDA would have approved a stronger warning, which they assert is an essential element of a pre-emption defense – not their affirmative case. Resp. Brief at 42-47.

The Supreme Court will face a difficult choice in deciding these cases, which, like *Wyeth*, highlight the tension between the national policy of maintaining a single, comprehensive source of prescription-drug risk information and state-law-based policies permitting injured persons to sue manufacturers on claims that FDA-

approved labeling was inadequate. In *Wyeth*, the Court sidestepped that tension by holding that conflict pre-emption attaches only when a manufacturer clearly establishes that the FDA would have barred it from honoring state-law duties by making labeling modifications to cure the defect claimed by the injured party. 129 S. Ct. at 1196-97. In the metoclopramide cases, the generic manufacturers argue that they meet this standard because federal law forbids them from deviating from the innovator drug's labeling.

The Supreme Court could side with the respondents and hold that claims based on the failure of generic manufacturers to request enhanced labeling warnings are not pre-empted. That result would read *Wyeth* to make the interests of the injured paramount; however, it could well prove chaotic, as multiple generic manufacturers, potentially operating in different jurisdictions, seek to protect themselves by launching inevitably inconsistent notice initiatives. It also could threaten the viability of generic manufacturers that operate on thin margins and could be bankrupted by liability claims, an interest that the Court seemed to recognize in shielding vaccine manufacturers from state-law-based design defect claims in its recent decision in *Bruesewitz v. Wyeth LLC*.

Conversely, the Court could hold that the curative actions allegedly available to generic manufacturers are too amorphous to avoid a pre-emption conclusion that generic-manufacturer compliance with state-law duties to warn was impossible. As respondents argued, however, that result would create an anomalous and unstable situation in which state courts could enforce duties on pioneer, but not generic, manufacturers, and relief would be available only to those injured persons who happened fortuitously to receive the branded drug when generic substitution is permissible or compelled under most state laws. Respondents' Brief at 26-27. Cases in which an injured patient received both the branded drug and one or more generic versions over time would be even more difficult to unravel.

Either scenario could induce courts to find unconventional ways to resolve this tension. For example, one outlier state-court decision found that a plaintiff injured by a generic drug could sue the pioneer company on the theory that the pioneer company has a continuing duty to maintain an adequate label and the power under federal law to force labeling changes on generic manufacturers. *Conte v. Wyeth Inc.*, 85 Cal. Rptr. 3d 299 (Calif. Ct. App. 2008). That decision, however, would leave no incentive for generic companies to monitor and warn about new safety information concerning drugs that they sell, and could create difficulties when relevant safety information is available only to generic manufacturers rather than the pioneer company. It also would contradict the products liability premise that legal responsibility attaches only to the manufacturer and seller of the injurious goods. Moreover, information-based tort claims against nonsellers could raise difficult questions when plaintiffs claim to rely on safety information generated by Web sites or other publications.

Alternatively, to avoid the unpalatable choices that are now exposed by the metoclopramide cases, the Supreme Court could decide to rethink and narrow *Wyeth* by expanding the circumstances under which preemptive conflicts between federal and state law will be found. This approach could bring greater consistency to the nation's drug labeling policy and result in labeling that better reflects FDA's comprehensive risk-benefit assessment regarding appropriate warnings. It also would reduce the public health risks of over-warning about rare or uncertain side effects, which even FDA recognizes can dilute the impact of more important warnings and lead to under-treatment of serious medical conditions.

Moreover, the resolution of pharmaceutical liability cases under *Wyeth* is difficult because it requires manufacturers and the courts to try to answer the speculative question of what the FDA would have done in connection with hypothetical new label warnings advocated after the fact by plaintiffs' counsel, an exercise that *Buckman Co. v. Plaintiffs' Legal Committee*, 531 U.S. 341 (2000), seems to preclude in any event. Thus, the pre-emption standard established by Wyeth may in practice not be administrable.

Regardless of the outcome, these cases offer the Supreme Court (and its two new post-*Wyeth* members) a golden opportunity to clarify the scope of *Wyeth* and to provide important and much-needed guidance concerning the operation of impossibility conflict pre-emption principles in cases involving prescription drug injuries.