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Stage-Setting For Circ Split: Generic Drug Preemption?

Law360, New York (March 25, 2010) -- Two separate United States Courts of Appeal recently rejected arguments by generic drug manufacturers that they should be treated differently from name-brand manufacturers under the Food, Drug and Cosmetic Act by ruling that the FDCA does not preempt plaintiffs' state law failure-to-warn claims against generic manufacturers based on the alleged inadequacy of generic drug labels.

The decisions by the Fifth Circuit in Demahy v. Actavis Inc. and the Eighth Circuit in Mensing v. Wyeth Inc., et al., were issued in the wake of, and were informed by, the United States Supreme Court's decision last year in Wyeth v. Levine ("Levine"), which held such state law claims against name brand drug manufacturers are also not preempted by the FDCA.

However, decisions on this issue are pending in two other cases before the United States Courts of Appeal for the Sixth and the Ninth Circuits, potentially setting the stage for a split among the federal circuits on this important issue for the pharmaceutical industry.

The plaintiffs in Demahy and Mensing both alleged that they developed tardive dyskinesia, a neurological movement disorder, as a result of their four-year use of metoclopramide, the generic form of Wyeth's name brand medication, Reglan, which is used to treat certain gastric disorders.

Plaintiffs alleged that the warnings contained in the generic labels were insufficient to warn them of the risks of developing tardive dyskinesia after long-term use of the drug.

Plaintiffs asserted state law failure-to-warn claims against the generic manufacturers arguing that the generic manufacturers ignored mounting evidence, including scientific and medical literature, that long-term metoclopramide use carries a higher risk of developing tardive dyskinesia.

Plaintiffs also argued that the generic manufacturers failed to take any steps to change the warnings in the label even though no prior FDA approval was required to effect such changes.

In both cases, the generic manufacturers responded that plaintiffs' state law failure-to-warn claims were preempted because it was impossible for the generic manufacturers to comply with both the federal regulatory regime governing generic drugs and an obligation under state law to strengthen warning labels.

Specifically, the generic manufacturers argued that federal regulations, including the 1984 Hatch-Waxman Amendments to the FDCA, require generic manufacturers to use the same label as the name-brand manufacturer and that the regulatory regime does not allow a generic manufacturer to alter its drug label without prior FDA approval through the changes being effected ("CBE") procedure or otherwise.

Without the ability to unilaterally change their drug labeling, the generic manufacturers argued that it is impossible for them to comply with state law that would require additional warnings for tardive dyskinesia.

Plaintiffs countered that the CBE procedure is applicable to generic drugs and allows generic manufacturers to make changes to the label without waiting for FDA approval.

In response to the parties' arguments, both the Demahy and Mensing courts reiterated the Supreme Court's pronouncement in Levine that the central premise of federal drug regulation is that drug manufacturers, not the FDA, bear ultimate responsibility for the content of drug labels at all times.

In addition, both courts pointed to FDA commentary that support the requirement that "at a minimum a generic manufacturer should alert the agency to any new safety hazard associated with its product."

Although stopping short of addressing the issue of whether generic manufacturers could unilaterally enhance a warning label through the CBE procedure, the Eighth Circuit in Mensing, specifically stated that generic manufacturers "could have at least proposed a label change that the FDA could receive and impose uniformly on all metoclopramide manufacturers if approved."

The court's comment suggests that making such a proposal would have gone a long way to fulfilling the generic manufacturer's duty to plaintiff, although the court also noted that "[t]o support preemption the generic [manufacturers] must show the likelihood of FDA inaction" in response to such proposals.

The Mensing court also suggested that, in addition to proposing a label change, the generic manufacturers could have suggested that the FDA send out a warning letter to health care professionals.

In Demahy, the Fifth Circuit took the extra step that the Mensing court declined to take and specifically held that the FDCA does not bar generics from unilaterally changing drug labeling through the use of the CBE procedure.

The Demahy court also echoed the Mensing court's conclusions that the prior approval process and the sending of "Dear Doctor" letters were additional avenues for generic manufacturers to comply with their state law duties.

In both Demahy and Mensing, the generic manufacturers also argued that even if compliance with state and federal laws were not impossible, state claims could nevertheless be preempted where they obstruct the purposes and objectives of federal law.

The generic manufacturers noted that forcing them to comply with state failure-to-warn law would require that they undertake expensive clinical studies, trials and other data-gathering exercises.

They contended that such requirements would necessarily increase the costs of developing and marketing generic medications, which would thwart one of the primary goals of the Hatch-Waxman amendments to the FDCA — to make more lower-cost generic drugs available.

However, both the Fifth and Eighth Circuits rejected the notion that generic manufacturers' compliance with state law would inevitably lead to increased costs.

As an initial matter, the courts noted that there were no statutory or regulatory provisions that obligated manufacturers to conduct their own clinical trials in order to justify labeling changes.

As the Fifth Circuit stated in Demahy, although requests to the FDA for label changes must be supported by scientific evidence, "nothing indicates that the evidence must be ... acquired through the manufacturer's own clinical tests."

The Fifth Circuit explained that FDCA regulations make clear that drug companies can make labeling changes without conducting new trials given the requirement that labeling be revised to include a warning "as soon as there is reasonable evidence of a serious hazard with a drug; a causal relationship need not have been proved."

The court went on to suggest that such "reasonable evidence" may be derived from new clinical studies, but may also come from reports of adverse events or new analyses of previously submitted data.

Indeed, the Demahy court noted that when the FDA itself mandated an enhanced warning for metoclopramide in early 2009, it did not conduct its own independent studies, but instead relied on previously conducted studies.

The issue of whether state law failure-to-warn claims against generic companies are preempted by the FDCA has previously been considered by numerous federal district courts (both pre and post Levine), with most, but not all, courts concluding, like Demahy and Mensing, that such state law claims are not preempted.

However, a number of district courts, two with pending appeals before two other federal appellate courts, have held that the FDCA does indeed preempt state law failure-to-warn claims against generic manufacturers.

In one such case, Morris v. Wyeth Inc., a pre-Levine decision, the Western District of Kentucky specifically declined to follow the reasoning of the trial court in Demahy and instead was persuaded by a footnote in a proposed rule issued by the FDA in which it stated, "CBE changes are not available for generic drugs approved under an abbreviated new drug application under 21 U.S.C. 355(j). To the contrary, a generic drug manufacturer is required to conform to the approved labeling for the listed drug."

The decision in Morris is currently on appeal before the United States Court of Appeal for the Sixth Circuit.

In a decision issued after Levine, the Northern District of California, in Gaeta v. Perrigo, denied plaintiffs' motion for reconsideration of the court's prior order granting summary judgment to defendants on the ground that FDA regulations completely preempted plaintiffs' state law failure-to-warn claims.

In reaching its decision, the Gaeta court held that Levine did not specifically address the issue of whether generic manufacturers may use the CBE process to unilaterally change a warning label and thus did not govern the court's prior decision to grant summary judgment on preemption grounds.

The decision in Gaeta is currently on appeal before the United States Court of Appeal for the Ninth Circuit.

Whether the decisions of the Fifth and Eighth Circuit Courts of Appeal in Demahy and Mensing portend a trend of holdings that state law failure-to-warn claims involving generic drugs are not preempted by the FDCA remains to be seen in light of the pending appeals before the Sixth and Ninth Circuits in Morris and Gaeta.

Even the decisions in Demahy and Mensing differ in their view of whether the CBE process is applicable to generic drugs, with the Court in Mensing declining to address the issue.

If either the Sixth or Ninth Circuits in Morris and Gaeta decide to affirm their respective district court's decision, there will be a split of authority among the federal appellate courts making the generic drug preemption issue potentially ripe for determination by the United States Supreme Court.

The cases in this article are Demahy v. Actavis Inc., No. 08-31204, 2010 WL 46513 (5th Cir. Jan. 8, 2010); Mensing v. Wyeth Inc. et al., 588 F.3d 603 (8th Cir. 2009); Wyeth v. Levine, 129 S.Ct. 1187 (2009); Morris v. Wyeth Inc., 642 F. Supp. 2d 677 (W.D. Ky. 2009), appeal docketed, No. 09-5509 (6th Cir. April 27, 2009); Gaeta v. Perrigo Pharm. Co., No. C05-04115JW, 2009 WL 4250690 (N.D. Cal. Nov. 24, 2009), appeal docketed, No. 09-15001 (9th Cir. Jan. 6, 2009).

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