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PREEMPTION

Two Arnold & Porter attorneys examine the Supreme Court's jurisprudence on preemption in the prescription drug context and how that may play out in the *In re Fosamax* case.

INSIGHT: The Prospects for Pharmaceutical Preemption in the Supreme Court

BY ANAND AGNESHWAR AND PAIGE SHARPE

In an era of proliferating pharmaceutical litigation, preemption—which can put an early end to a case—is a key defense for drug manufacturers.

Yet preemption is an ''issue [that] has repeatedly vexed the [U.S. Supreme] Court—and produced widely divergent view—in recent years.'' *Mutual Pharm. Co. v. Bartlett*, 570 U.S. 472, 492-93 (2013) (citing *Wyeth v. Levine*, 555 U.S. 555 (2009) and *PLIVA, Inc. v. Mensing*, 564 U.S. 604 (2011)). Now, having granted certiorari in *Merck Sharp & Dohme Corp. v. Albrecht*, No. 17-290, the Court has another opportunity to provide clarity in a significant area of mass tort law.

Merck is the Court's docketed name for its review of *In re Fosamax (Alendronate Sodium) Products Liability Litigation*, 852 F.3d 268 (3d Cir. 2017), a decision that reversed summary judgment in thousands of consolidated cases on preemption grounds. In *In re Fosamax*, the Third Circuit:

(1) interpreted Supreme Court precedent as setting forth a ''high probability'' standard of proof for preemption in pharmaceutical cases, and

(2) found that these cases can raise a question of fact that a jury should decide. *Id.* at 284-86.

Both aspects of the decision are up for the Supreme Court's review.

In this article, we trace the Supreme Court's jurisprudence on preemption in the prescription drug context, review the issues at stake in *In re Fosamax*, and evaluate how the case might (and should) play out in a Court that has been in flux in the decade since it first spoke on preemption in pharmaceutical cases.

The Court's Record on Preemption in Pharmaceutical Cases

Wyeth v. Levine was the Supreme Court's opening salvo on preemption in prescription drug cases, and interpretation of the case has remained the subject of fierce debate. The central question in *Levine* was whether ''impossibility preemption''—a form of implied preemption that applies where it is impossible for a party to comply with both state and federal law—should shield brand-name drug manufacturers from liability for state law tort claims of failure to warn. *Id.* at 563.

In a 6-3 decision, the Court found that such claims are not preempted, ''absent 'clear evidence' that the [U.S. Food and Drug Administration (FDA)] would not have approved a change to [a drug's] label.'' 555 U.S. at 571. Preemption of state tort claims is thus possible, but requires a showing that the warning would not have passed muster with the FDA.

The FDA's drug labeling framework was pivotal to the Court's reasoning. Under the Federal Food, Drug, and Cosmetic Act (FDCA), before a brand-name manufacturer can market a new drug, it must obtain FDA approval of the drug, including its labeling. 21 U.S.C. § 355. The manufacturer has two avenues for updating risk information. First, under the ''Changes Being Effected'' (CBE) regulation, a manufacturer can unilaterally change a drug label to reflect ''newly required in-

formation,'' subject to later FDA review and approval. 21 C.F.R. § 314.70(c)(6)(iii).

Alternatively, a manufacturer can seek to change a label by filing a ''Prior Approval Supplement'' (PAS), which requires FDA approval before it can be implemented. *Id.* § 314.70(b). The FDA has the ultimate authority to reject either type of change. *See, e.g.*, 73 Fed. Reg. 2848, 2851 (Jan. 16, 2008).

The CBE process provided the hook for the rejection of preemption in *Levine*. The Court reasoned that the ''newly acquired information'' required for a CBE label change could include ''new analyses of previously submitted data,'' and Wyeth could have analyzed accumulating data of the adverse event and strengthened the label warning on that basis. 555 U.S. at 569-70. Wyeth had not shown by ''clear evidence'' that the FDA would have rejected the labeling change, so it had not established the ''demanding defense'' of impossibility preemption. *Id.* at 573.

The Court's next two pharmaceutical preemption decisions came in *PLIVA Inc. v. Mensing*, 564 U.S. 604 (2011), and *Mutual Pharmaceutical Co. v. Bartlett*, 570 U.S. 472 (2013). Both were 5-4 decisions that found preemption of claims against generic drug manufacturers.

In *Mensing*, the question was whether federal law preempts failure-to-warn claims against generics. Generic drugs gain FDA approval simply by showing equivalence to an already approved brand-name drug. While a brand-name manufacturer is responsible for maintaining the adequacy and accuracy of its labels, a generic manufacturer has a duty of ''sameness''—that is, ensuring that its label is the same as that of the brand-name drug. 21 U.S.C. § 355(j)(2)(A)(v).

Unlike in *Levine*, where the CBE regulation offered an avenue for the manufacturer to strengthen the warning, the generic manufacturer in *Mensing* would have violated federal law if it made changes to the label unilaterally. 564 U.S. at 614-15. Because the manufacturer could not comply with both a state law duty to change the label and a federal duty to keep the label the same, the failure-to-warn claims were preempted. *Id.* at 618.

Bartlett expanded the reasoning and application of *Mensing* to design defect claims against generics. Under federal law, a generic drug must have the same active ingredients, route of administration, dosage form, and strength as its brand-name counterpart, so a generic manufacturer can no more redesign the drug unilaterally than it can change the label. 570 U.S. at 573-74.

In finding the claims preempted on that basis, the Court rejected the suggestion that the generic could have complied with both state and federal law simply by choosing not to make the drug at all. *Id.* at 488. This ''stop-selling'' rationale conflicts with the premise of the Court's preemption cases, which presumes that an actor can satisfy both federal and state law obligations, and would render impossibility preemption ''all but meaningless.'' *Id.* (citing *Mensing*, 564 U.S. at 621).

While *Mensing* and *Bartlett* involved generic drugs, they have become part of the framework for evaluating impossibility preemption in branded cases, where the alleged inadequacies are in the initial product labeling. As the First Circuit has held, claims alleging a labeling deficiency based on information ''plainly known to the FDA prior to approving the label,'' which is not subject to correction using the CBE regulation, are preempted. *In re Celexa & Lexapro Mktg. & Sales Practices Litig.*, 779 F.3d 34, 43 (1st Cir. 2015). ''[R]ead holistically,'' the trio of *Levine*, *Mensing*, and *Bartlett* ''indicate[] that federal law preempts all pre-FDA approval failure to warn and design defect claims for branded prescription medication.'' *Utts v. Bristol-Myers Squibb Co.*, 226 F. Supp. 3d 166, 178 (S.D.N.Y. 2016).

In re Fosamax in the Third Circuit

In re Fosamax raised the question of how to apply *Levine* when the questions were whether the FDA would have rejected the warning proposed by the plaintiffs, and whether the judge or the jury should decide the issue. 852 F.2d at 282.

Fosamax is an osteoporosis drug known as a bisphosphonate that allegedly causes atypical femur fractures. The Fosamax label did not warn of the risk of bone fractures when it was first approved in 1995, but studies over the following 15 years suggested a possible connection. *Id.* at 275. Merck kept the FDA informed of these studies and submitted additional information regarding the possible risk through periodic reporting. *Id.*

The record also showed the defendant proposed a label change that the FDA rejected. Merck submitted a warning about the risk of ''stress fractures,'' but the FDA found that it was ''not warranted'' and ''not adequately supported by the available literature and postmarketing adverse event reporting.'' *Id.* at 277. Two years later, after reviewing additional data, the agency announced it would require all bisphosphonate manufacturers to warn about atypical femoral fractures. *Id.* at 278.

While the lower court found that the FDA's rejection of the proposed label change resulted in preemption, the Third Circuit disagreed.

The court seized on the phrase ''clear evidence'' and held that, with those words, ''the Supreme Court intended to announce a standard of proof'' stronger than preponderance of the evidence. *Id.* at 284-85. The manufacturer must show that ''it is highly probable that the FDA would not have approved a change to the drug's label.'' *Id.* at 286. The court further decided that ''the question of whether the FDA would have rejected a proposed label change is a question of fact that must be determined by a jury.'' *Id.*

Applying this framework to the facts at hand, the Third Circuit determined that a reasonable jury could ''reconstruct a hypothetical event'' and find that Merck could have amended the Fosamax label through the CBE process. *Id.* at 297. A jury could also conclude that the FDA rejected Merck's proposed warning because it referred to ''stress fractures'' rather than atypical femoral fractures. *Id.* at 298. Accordingly, the court held, Merck was not entitled to summary judgment on preemption grounds. *Id.* at 300.

In re Fosamax in the Supreme Court

On the last day of its 2018 term and a day after Justice Anthony Kennedy announced his retirement, the Supreme Court granted cert in *In re Fosamax*. The timing of the Court's review of the case is worth noting.

In the nine years since *Levine*, the Court has undergone significant change. Four of the five justices who decided *Levine* are now gone: Justice John Paul Stevens, who authored the opinion; Justices David Souter and Kennedy, who joined the majority; and Justice An-

tonin Scalia, who joined the dissent. Justice Samuel Alito, moreover, who penned the dissent in *Levine* and the opinion finding preemption in *Bartlett*, has recused himself from review of *In re Fosamax*.

We're not professional Court watchers, but the fact that eight justices will likely decide the case (assuming Senate confirmation of the new justice before then) raises the prospect for a tied decision that would leave the Third Circuit's opinion standing.

Four justices are likely to favor a narrower reading of preemption: Justices Stephen Breyer and Ruth Bader Ginsburg, who went with the majority in *Levine* and the dissent in *Mensing* and *Bartlett*, and Justices Elena Kagan and Sonia Sotamayor, who also dissented in *Mensing* and *Bartlett*. Whether the remaining four will align will be interesting to see.

Chief Justice John Roberts dissented in *Levine* but joined the majority in finding preemption in *Mensing* and *Bartlett*. Justice Clarence Thomas concurred in *Levine* because of concern with the majority's ''implicit endorsement of far-reaching implied preemption doctrines,'' 555 U.S. at 583, but he authored *Mensing* and joined the majority in *Bartlett*.

Justice Neil Gorsuch has not ruled on these issues, nor, should he be confirmed, has Judge Brett Kavanaugh.

But multiple other scenarios are also in play.

The Court could uphold the Third Circuit in its entirety—though this result seems unlikely. The Court granted cert in the absence of a circuit split on the jury issue and in a case takes *Levine* to a new extreme, suggesting that the Court believes a course correction is in order.

The Court could simply reverse the Third Circuit's conclusion that preemption is a jury question and remand for further review of the trial court's finding of preemption as a matter of law.

The Court could also reverse on the jury question and itself decide whether Merck met the standard for preemption, even if the justices do not agree on the parameters of that standard. Or the Court could deliver a majority view that breathes new life into a preemption analysis that is currently considered ''cryptic and open-ended.'' *In re Fosamax*, 852 F.3d at 282.

In our view, *In re Fosamax* illustrates the need for the Supreme Court to pick up where the *Levine*, *Mensing*, and *Bartlett* trilogy left off.

Several issues merit attention.

First, the Supreme Court never suggested in its earlier preemption decisions that it meant to impose the sort of ''high probability'' standard of proof that the Third Circuit applied in *In re Fosamax*. To the contrary, the Third Circuit ignored a ''wall of countervailing authority'' in which the Supreme Court has embraced a ''preponderance of the evidence'' standard as the one generally applicable in civil actions. Petition for Writ of Certiorari, *Albrecht* (No. 17-290), at 25-26 (citing cases).

Second, the Supreme Court's repeated invocation of the regulatory framework that applies to prescription drugs demonstrates that, for purposes of uniformity and consistency, judges are better suited to this type of analysis. In any event, an agency action such as the FDA's decision on a proposed warning ''is a legal question within the exclusive province of a court.'' Brief for the United States as Amicus Curiae, *Albrecht* (No. 17-290), at 13.

Finally, as it has said repeatedly, the Court does not condone a reading of impossibility preemption that would render the doctrine ''all but meaningless.'' *Mensing*, 564 U.S. at 620; *Bartlett*, 570 U.S. at 488. Under the Third Circuit's reasoning, there could always be some ''hypothetical event'' in which a branded manufacturer could have proposed a different warning that the FDA might have rejected. But this invites the very sort of game of ''possibles'' that the Supreme Court has rejected. *See Mensing*, 564 U.S. at 620 (''If these conjectures suffice to prevent federal and state law from conflicting for Supremacy Clause purposes, it is unclear when, outside of express pre-emption, the Supremacy Clause would have any force.'').

Where the record shows that a branded manufacturer submitted not only a proposed label change but also the underlying data and analysis to the FDA, and the agency rejected that proposal, the manufacturer has satisfied its preemption burden.

With these issues teed up, *In re Fosamax* offers the Court an opportunity to dispel the confusion around impossibility preemption in branded pharmaceutical cases and make clear that the doctrine still has teeth.

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