Legal Backgrounder

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In re Fosamax Advances Trend Toward Broader Preemption of Pharmaceutical Failure-to-Warn Claims

by Daniel J. Feith

The Supreme Court's decision in *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668 (2019), represented a major victory for drug makers. By holding that judges, not juries, must decide whether prescription drug failure-to-warn claims are preempted, *Merck* enabled drug makers to obtain decisions on preemption defenses at an earlier stage of proceedings—summary judgment rather than trial—and from decision-makers better able to understand and apply relevant legal standards.

At the same time, *Merck* left open a variety of questions regarding what precisely a drug maker had to show to establish preemption. It described the preemption standard at a high level as requiring "clear evidence … that shows the court that the drug manufacturer fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." *Id.* at 1672. But *Merck* left unanswered such questions as whether FDA must have rejected the precise warning, with the precise wording, that a plaintiff claims was needed; what relevance, if any, informal communications from FDA and FDA inaction have; and whether FDA must have communicated its disapproval through final agency action.

These questions and others came to the fore when the case returned to the district court on remand. And in a recent decision, the district court answered all these questions in Merck's favor, holding that the plaintiffs' claims are preempted and granting summary judgment to Merck. *See In re Fosamax (Alendronate Sodium) Prods. Liability Litig.*, 2022 WL 855853 (D.N.J. Mar. 23, 2022). This decision builds on a growing body of case law taking a broader view of how drug makers can establish preemption and offers drug makers valuable insight into how effective FDA engagement can preempt liability down the road.

Background

In *In re Fosamax*, more than 500 plaintiffs who suffered atypical femoral fractures between 1999 and 2010 while taking Fosamax to treat and/or prevent osteoporosis brought claims alleging that Fosamax's manufacturer, Merck Sharp & Dohme, had failed to warn that use of Fosamax was associated with such fractures (which are essentially stress fractures in the thigh bone that develop into complete breaks). *See In re Fosamax*, 2022 WL 855853, at *8. After a bellwether trial in 2013, the district court granted summary judgment to Merck, holding that the plaintiffs' claims were preempted because Merck had shown by "clear evidence" that, prior to 2010, FDA would not have approved the warning plaintiffs claimed was necessary—the showing required by the Supreme Court's decision in *Wyeth v. Levine*, 555

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U.S. 555 (2009). *See In re Fosamax (Alendronate Sodium) Prods. Liability Litig.*, 2014 WL 1266994 (D.N.J. Mar. 26, 2014); *Glynn v. Merck Sharp & Dohme Corp.*, 951 F. Supp. 2d 695 (D.N.J. 2013).

Merck ultimately appealed that ruling to the Supreme Court, which in 2019 issued a decision clarifying that judges, not juries, must decide whether FDA would have rejected the proposed warning, and that "clear evidence" of FDA's disapproval entails showing that the manufacturer "fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve changing the drug's label to include that warning." *Albrecht*, 139 S. Ct. at 1678. The case was then remanded to the district court to determine whether preemption applied under the framework announced in *Albrecht*.

The District Court's Decision

In March, the district court held the claims preempted. *See In re Fosamax*, 2022 WL 855853. The court first found that Merck had fully informed FDA of the justifications for the warning plaintiffs sought. The court recounted that from 1995, when FDA first approved Fosamax, until 2010, when the agency finally agreed a warning related to atypical femoral fractures was warranted, Merck regularly and voluntarily notified FDA of scholarly articles and case studies documenting an association between Fosamax and such fractures. *See id.* at *13–17. In 2008, these efforts culminated in Merck's submission of a formal safety update comprising 30 pages surveying studies, articles, and internal data on atypical femoral fractures and, later that year, a Prior Approval Supplement (PAS) seeking to add warnings on atypical femoral fractures to the Precautions and Adverse Reactions sections of Fosamax's labeling. *See id.* at *14. The court concluded that "[b]etween its formal safety updates, periodic emails, and PAS, [Merck] clearly and fully informed the FDA of the panoply of risks with long-term Fosamax use and the justifications for its proposed label change." *Id.*

Next, the court found that FDA had informed Merck that it would not approve the proposed warning. In 2009, FDA issued a complete response letter (CRL) to Merck rejecting the addition of a warning to the Precautions section of Fosamax's label (but approving the addition to the Adverse Reactions section). Merck argued that the CRL established FDA's disapproval for preemption purposes, but the plaintiffs countered that the CRL did not carry preemptive effect because it is not a "final agency action" as the Supreme Court had defined that term. *See id.* at *17–18. The plaintiffs also argued that the CRL indicated that FDA had rejected only the specific wording Merck had proposed for the warning, but had not categorically rejected all atypical femoral fracture-related warnings. *See id.* at *19–23.

The court rejected both of the plaintiffs' arguments. First, it explained that the Supreme Court in *Merck* had explicitly cited the regulation authorizing FDA to issue CRLs as an example of FDA action carrying preemptive effect, and observed that, in any event, the relevant question is whether the agency acted within the scope of its delegated authority, not whether its action is "final." *See id.* at *18. Then, to shed light on the CRL's meaning, the court looked to informal communications between Merck and FDA and to the broader regulatory scheme. The court found that informal correspondence around the time of the CRL demonstrated that, as Merck argued, FDA at that time in fact did not believe there was a sufficient scientific basis for the proposed warning. *See id.* at *24–26. (FDA changed its view only in late 2010, after a task force further studied the issue, at which point FDA directed Merck to add a warning regarding atypical femoral fractures. *See id.* at *7.)

The court also found that the plaintiffs' interpretation of the CRL was inconsistent with the applicable regulatory regime. The court explained that to accept the notion that FDA would think a warning was warranted but reject Merck's PAS based on a quibble with specific wording "would

effectively overlook the FDA's *raison d'etre* to regulate drug safety, its independent legal duty to notify a manufacturer as soon as it 'becomes aware of new safety information that [it] believes should be included in the labeling of a drug and 'initiate discussions to reach an agreement … on labeling,' 21 U.S.C. § 355(*o*)(4)(A), and the 'presumption of regulatory' accompanying its actions." *Id.* at *27. The court also noted that FDA's own regulations require that a CRL reflect the agency's "complete review of the data submitted," not merely the particular labeling language proposed. *Id.* Based on these statutory and regulatory provisions, the court construed the CRL to mean that FDA did not think there was a sufficient scientific basis to add a warning regarding atypical femoral fractures, even one involving different wording from what Merck had proposed. *See id.* at *27–29. Moreover, the court held that given FDA's view that there was an inadequate basis for such a warning, Merck was not required to attempt to add the warning to its label unliterally, via a changes-being-effected amendment, simply to preserve its preemption defense. *See id.* at *32.

Significance

The *In re Fosamax* decision is significant in several respects. First, it highlights the importance for manufacturers of diligent engagement with FDA regarding risk-related information. Courts closely scrutinize whether manufacturers "fully informed" FDA of the justifications for a proposed warning, evaluating whether the information they provided omitted any relevant information or studies identified by the plaintiffs. A clear record that a manufacturer was thorough and proactive in sharing risk-related information with FDA is critical to making this showing. This decision also illustrates how closely courts examine whether FDA has conveyed disapproval of the proposed labeling change, and here too, a clear, well-developed administrative record is key. Without Merck's informal correspondence with FDA, the preemption analysis might have come out differently.

Second, *In re Fosamax* is the latest in a series of post-*Albrecht* cases taking a broader view of what evidence can establish preemption. *See also In re: Zofran (Ondansetron) Prods. Liability Litig.*, 541 F. Supp. 3d 164 (D. Mass. 2021); *In re Incretin-Based Therapies Prods. Liability Litig.*, 524 F. Supp. 3d 1007 (S.D. Cal. 2021). In dicta, *Albrecht* "noted" that only agency action carrying the force of law can have a preemptive effect, *Albrecht*, 139 S. Ct. at 1679, but Justice Alito observed in a concurrence that FDA's decision "not to act" on new information is also relevant to preemption, given FDA's duty under 21 U.S.C. § 355(*o*)(4) to initiate a labeling change if it becomes aware of safety information that should be included in the labeling, *id.* at 1684 (Alito, J., concurring in the judgment). *In re Fosamax* adopts Justice Alito's approach, relying both on FDA's inaction and on informal correspondence to construe the CRL and find preemption. This broader view reinforces the value of putting all relevant information before FDA, as courts will presume, based on FDA's statutory and regulatory obligations, that FDA considered whatever information was before it, even if it did not expressly act on or discuss that information.

Finally, *In re Fosamax* helpfully holds that a manufacturer need not submit a changes-being-effected (CBE) supplement simply to preserve a preemption defense. *Wyeth* held that the option to file a CBE supplement can preclude preemption, but *In re Fosamax* builds on an emerging consensus of courts in holding that the rule applies only when a manufacturer truly has "newly acquired information" providing "reasonable evidence of a causal association of a clinically significant adverse reaction linked to a drug," 21 C.F.R. §§ 314.70(c)(6)(i), 201.57(c)(6)(i), and that fully informing FDA of risk-related information via a PAS and having FDA reject that information as insufficient by definition means no CBE option was available.