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Duty To Warn and the Learned Intermediary Doctrine in New York: Does the Duty Require Instructions About How To Mitigate Risk?

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The U.S. Court of Appeals for the Eleventh Circuit recently certified "unsettled questions of Alabama law" to the Alabama Supreme Court related to "failure-to-warn" claims. *Blackburn v. Shire US*, 18 F.4th 1310, 1321 (11th Cir. 2021). The fundamental question is: "Consistent with the learned intermediary doctrine, may a pharmaceutical company's duty to warn include a duty to provide instructions about how to mitigate warned-of risks?" Id. Although New York and Alabama may not have much else in common, it does seem that in this regard they are similar—New York courts have not yet answered this question directly. Still, there certainly are clues to suggest how the issue might be resolved in New York. In most instances, precise mitigation instructions likely go beyond the obligations imposed by the learned intermediary doctrine. An exception might be found if the mitigation strategy was unknown to the medical profession generally and the manufacturer had special knowledge that it did not communicate to the U.S. Food & Drug Administration (FDA). Absent these circumstances, however, the learned intermediary doctrine and federal preemption law would, in all probability, preclude a failure-to-warn claim based on a failure to provide mitigation instructions.

Learned Intermediary Doctrine and Mitigation Instructions. Under New York law, a failure-to-warn claimant must show "(1) that a manufacturer has a duty to warn; (2) against dangers resulting from foreseeable uses about which it knew or should have known; and (3) that failure to do so was the proximate cause of harm." *Bustamante v. Atrium Med.*, No. 18-CV-08395, 2020 WL 583745, *6 (S.D.N.Y. Feb. 6, 2020); see also *In re Fosamax Prods. Liab. Litig.*, 924 F. Supp. 2d 477, 486 (S.D.N.Y. 2013). Mitigation instructions may be appropriate with products sold directly to and for use by consumers. See,

e.g., *Alicea v. Gorilla Ladder Co.*, 181 A.D.3d 512, 512 (1st Dep't 2020). With regard to prescription products like pharmaceuticals or medical devices, New York has adopted the learned intermediary doctrine which requires, as part of the proximate cause, showing "that an *appropriate* warning would have affected the course of treatment of the plaintiff's physician." *In re Fosamax Prods. Liab. Litig.*, No. 06-MD-1789, 2010 WL 1257299, at *5 (S.D.N.Y. March 26, 2010) (emphasis added). Other cases indicate that the warning must be "adequate." *Bustamante*, 2020 WL 583745, at *6.

In New York, as in many states, the learned intermediary doctrine reflects the principle that it is the physician who bears the duty "to

balance the risks against the benefits of various drugs and treatments and to prescribe them and supervise their effects." *Martin v. Hacker*, 83 N.Y.2d 1, 9 (1993); see also *Wolfgruber v. Upjohn Co.,* 72 A.D.2d 59, 61 (4th Dep't 1979) (citing the Restatement (Second) of Torts §402A cmt. k (Am. L. Inst. 1965)), aff'd, 52 N.Y.2d 768 (1980). It is not for manufacturers to interfere with the care rendered by physicians nor to dictate the treatment choices made between physicians and patients. Thus, the manufacturer's duty "is fulfilled by giving adequate warning through the prescribing physician, not directly to the patient." *Martin*, 83 N.Y.2d at 9 (citations omitted); see also *Wolfgruber*, 72 A.D.2d at 61; *Glucksman v. Halsey Drug Co*., 160 A.D.2d 305, 307 (1st Dep't 1990).

The question posed in *Blackburn* and not squarely answered under New York law boils down to this: Does an "appropriate" or "adequate" warning require not only a description of the risks posed by the product but also advice on how to mitigate those risks?

The principle that the physician is best suited to advise a patient about the preferred course of treatment suggests that directions on how to mitigate risk might go beyond the duty owed by the manufacturer. On the other hand, the New York State Court of Appeals has indicated that "[t]he warning must provide sufficient information to that category of prescribing physicians who may be expected to have the least knowledge and experience with the drug." *Martin*, 83 N.Y. 2d at 9 (citations omitted). In some cases, this may set the bar so low as to require more than just a recitation of the risk.

New York courts have specified a number of criteria by which to measure the adequacy of a warning. Basic to the analysis is the idea that the warning "must be commensurate with the risk involved in the ordinary use of the product." *Cooley v. Carter-Wallace*, 102 A.D.2d 642, 645 (4th Dep't 1984). Against that backdrop, the warning must be evaluated for its "accuracy, clarity and relative consistency. For a warning to be accurate it must be correct, fully descriptive and complete, and it must convey updated information as to all of the drug's known side effects." *Martin*, 83 N.Y.2d at 11 (citations omitted). None of these criteria, however, suggest that mitigation strategies must be included to render a warning legally adequate. Indeed, the very concept of a strategy to mitigate the risk of any particular therapeutic treatment would seem to implicate the doctor-patient relationship, a relationship in which a drug company should not interfere.

Nonetheless, some drug labels do contain specific instructions on risk mitigation. For example, the label for Plaquenil, a drug prescribed for the treatment of arthritis, contains the following recommendation:

Within the first year of starting PLAQUENIL, a baseline ocular examination is recommended including best corrected distance visual acuity (BCVA), an automated threshold visual field (VF) of the central 10 degrees (with retesting if an abnormality is noted), and spectral domain ocular coherence tomography (SD-OCT). For patients at higher risk of retinal damage, monitoring should include annual examinations which include BCVA, VF and SD-OCT. For patients without significant risk factors, annual retinal exams can usually be deferred until five years of treatment.

Plaquenil Labeling-Package Insert, Drugs@FDA: FDA-Approved Drugs (revised May 2021).

The drug Clozaril, a drug used to treat schizophrenia, is available only through a restricted program under a Risk Evaluation Mitigation Strategy because of the significant risk of neutropenia. Clozaril's FDA-approved label indicates:

Prior to initiating treatment with CLOZARIL a baseline ANC [absolute neutrophil count] must be at least 1500/μL for the general population; and must be at least 1000/

μL for patients with documented Benign Ethnic Neutropenia (BEN). During treatment, patients must have regular ANC monitoring.

Clozaril Labeling-Package Insert, Drugs@FDA: FDA-Approved Drugs (revised Feb. 2021).

These examples, among many others, suggest that the FDA is more than capable of requiring a label that includes mitigation advice in those rare instances when the agency finds such labeling necessary.

Interplay Between the Learned Intermediary Doctrine and Preemption. The FDA's labeling requirements implicate a second doctrine that would likely impact the potential need for mitigation advice in a given case. Lurking behind the issue whether a drug's label should contain specific instructions about risk mitigation is the concept of preemption. In the context of pharmaceutical product liability litigation, preemption refers to the defense often asserted by pharmaceutical defendants that, subject to certain conditions and exceptions, they are protected from failure-to-warn claims as long as their product label has been approved by the FDA. See *Wyeth v. Levine*, 555 U.S. 555 (2009).

Of course, FDA approval is not an absolute shield from liability. In *Wyeth*, the court determined that preemption is not a defense if a pharmaceutical company knows of certain risks and could have modified its label through the "Changes Being Effected" (CBE) mechanism set forth in the Federal Food, Drug, and Cosmetic Act. See 21 C.F.R. §314.70(c)(6)(iii). As described in *Utts v. Bristol-Myers Squibb Co.*, 226 F. Supp. 3d 166 (S.D.N.Y. 2016), the *Wyeth* court "focused exclusively on how the CBE regulation permits—and even requires—drug manufacturers to maintain and update their labeling with new safety information as it becomes available." Id. at 179 (citation omitted). "According to the [*Wyeth*] court, 'the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market.'" Id. (quoting *Wyeth*, 555 U.S. at 570-71).

Thus, if a risk is discovered long after a label was approved by the FDA, preemption may not provide a defense. Similarly, if a means of mitigating risk is discovered after the FDA approved a label, a court could find that the manufacturer had an obligation to change its label via the CBE mechanism. However, such a finding would implicate only the question of preemption; it would not answer the antecedent question of whether state law requires mitigation information on the label under learned intermediary doctrine.

Conclusion

The question posed by the Eleventh Circuit in *Blackburn* does not appear to have been answered directly in New York any more than it has in Alabama. But the existing jurisprudence suggests that in considering a claim based on the failure to include mitigation instructions in a drug warning, New York courts would likely confront two issues: First, whether the various risk-mitigation options were unknown to the medical profession generally or to the medical specialists involved in the care and treatment of the plaintiff; Second, whether the manufacturer had special knowledge about risk mitigation that was not communicated to the FDA. Absent both conditions, the learned intermediary doctrine and federal preemption would likely protect manufacturers.

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