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Prescription medications all carry potential risks—risks the prescriber must weigh against the benefits associated with the therapy as well as the risks associated with not prescribing it. Where there are no risk-free alternatives and leaving the disease untreated exposes the patient to substantial harm, prescribing the medication may be the lowest-risk option. Nonetheless, courts in several jurisdictions apply a presumption that if a pharmaceutical manufacturer had provided an "adequate" warning, the physician would not have prescribed the medication. Cases involving biologics, which have revolutionized the treatment of many serious diseases, offer a particularly compelling illustration of why there is no place for such a "heeding" presumption in prescription drug cases, and present significant opportunities to fight it.

Biologics and the Heeding Presumption

ABOUT THE AUTHORS

Mollie Benedict is Partner-in-Charge of the Tucker Ellis Los Angeles office and Chair of the firm's Medical & Pharmaceutical Liability Group. Mollie represents clients in federal and state courts across the United States, both as national counsel and as lead counsel in California Coordinated Proceedings. Mollie has garnered litigation experience in the areas of medical devices, pharmaceuticals, food and cosmetics, product liability, false advertising, and has tried several cases to verdict. She also handles class actions and complex business litigation. She can be reached at mollie.benedict@tuckerellis.com.

Traci Shafroth is counsel in the San Francisco office of Tucker Ellis LLP. Traci represents pharmaceutical and medical device manufacturers in product liability coordinated proceedings and litigation across the country. She has defended a global pharmaceutical company in litigation involving its flagship product, a biologic that revolutionized the treatment of rheumatoid arthritis and other autoimmune diseases, in state and federal litigation across the country. She can be reached at traci.shafroth@tuckerellis.com.

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Kara T. Stubbs
Vice Chair of Newsletters
Baker Sterchi Cowden & Rice, L.L.C.
stubbs@bscr-law.com

Prescription medications all carry potential risks—that is why they can only be acquired through a physician. A physician will prescribe a medication if, in the physician's medical judgment, the benefits associated with the therapy outweigh the potential risks from the medication and the risks to the patient without the therapy. In many cases, there are no risk-free alternatives and leaving the patient's condition untreated is not an option, so prescribing the medication is, on balance, the lowest-risk option despite the potential risks.

Nonetheless, in failure-to-warn cases, courts in several jurisdictions apply a presumption—known as the read-and-heed or heeding presumption—that if a pharmaceutical manufacturer had provided an adequate warning, the prescriber would have read and "heeded" it by failing to prescribe the medication. But these Courts typically fail to consider what heeding a warning means when there is no risk-free alternative available. Presuming that a risk would be avoided makes sense in the context of some risks—such as the risk of fire or explosion from leaving a pressurized can near a heat source—that can be avoided. But there is no reason to presume that "adequate" prescription medication warnings will cause a physician not to prescribe the medication: the potential risks warned of can only be avoided by foregoing the use of the product, an option that in many cases will increase the patient's overall risk of harm. Cases involving biologics, which have revolutionized the treatment of many serious diseases, offer a particularly compelling illustration of why there is no place for such a "heeding" presumption in prescription drug cases, and present significant opportunities to fight it.

I. The Heeding Presumption

The heeding presumption has been a fixture of product liability law since at least the 1970s, and has been adopted and rejected by jurisdictions across the country in roughly equal number. Some jurisdictions that have adopted the presumption rely on commentary to the rule of Restatement (Second) of Torts § 402A regarding strict liability for defective products. Comment j to Section 402A establishes a presumption in favor of the *seller* of a product—a seller may reasonably assume that an adequate warning will be read and heeded. Yet some courts, including the Ohio Supreme Court, have read in a corollary presumption favoring plaintiffs: where a plaintiff establishes that a warning is inadequate, a rebuttable presumption arises that the inadequate warning was a proximate cause of the plaintiff's ingestion of a medication. *See, e.g., Seley v. G. D. Searle & Co.*, 423 N.E.2d 831, 838 (Oh. 1981).

Courts holding that comment j suggests such a presumption ignore the scientific literature addressing the typical consumer's failure to heed warnings of every stripe. And as previous commentators have noted, the suggested symmetry in the presumptions is illusory. Plaintiffs are absolved of the burden of proving that the allegedly inadequate warning was the proximate cause of the plaintiff's ingestion of defendant's medication; instead, the burden shifts to the defendant to rebut the presumption (e.g., by showing that a different warning would not

have made a difference in the physician's decision to prescribe the medication). Defendants, meanwhile, gain nothing from the comment j presumption that an adequate warning will be read and heeded. If the warning was adequate, plaintiff's failure-to-warn claim cannot stand—there is no need to evaluate whether the warning was the proximate cause of the plaintiff's use of the medication. Accordingly, there is no justifiable basis in comment j for shifting plaintiffs' burden on this aspect of proximate causation to defendants.

II. Unavoidable vs. Preventable Risks

The Ohio Supreme Court adopted the heeding presumption in a case involving a prescription birth control medication. *See Seley*, 423 N.E.2d at 838. Absent from the Court's opinion is any consideration of the distinct difference between potential risks from the use of prescription medications and risks from other types of consumer products. This difference is explained in detail in the carefully reasoned *Thomas v. Hoffman-LaRoche, Inc*., 949 F.2d 806 (5th Cir. 1992), applying Mississippi law. After noting that no Mississippi court had adopted the heeding presumption, the *Thomas* court predicted that it was unlikely that those courts would do so in the future. *Id*. at 813. The court reasoned that the risks warned about in the prescription drug context are typically *unavoidable risks*, meaning they cannot be avoided if the product is used. *Id*. If the medication carries a risk that one in 400,000 patients will suffer an adverse reaction, nothing can be done to eliminate that risk—the treating physician either determines that the benefits of the medication outweigh the risk and prescribes the medication, or determines that they do not and prescribes an alternative or leaves the condition untreated.

Warnings of *preventable risks* are very different: for example, a pressurized can may warn the consumer of the dangers of puncturing the can or exposing it to extreme heat. *Id*. The consumer can avoid this risk entirely by heeding the warning. The *Thomas* court noted that, because the precautions associated with preventable risks are typically minimal (e.g., don't store the can next to a heat source), it might make sense to assume that a reasonable consumer would heed the written warning. *Id*. The court rejected the presumption in the context of prescription medications, however, because the choice

> is not between the safe use and the unsafe use of a product, but between using and not using the product. The consumer can choose to use the product and face its risks, or choose not to use the product and lose its potential benefits. ***Generally, using the product will present the less risky of these two alternatives***.

Id. In other words, a presumption that a physician confronted by an adequate warning would have declined to prescribe the medication to the plaintiff will often lead to a conclusion that the physician would have chosen the riskier of two alternative courses of treatment.

III. Case in Point: Biologics

Cases involving biologics, such as anti-TNF therapies, provide a particularly good illustration of why the presumption is ill fit to the pharmaceutical context. The anti-TNF class includes monoclonal antibodies such as Remicade (infliximab), introduced in 1998, and Humira (adalimumab), which entered the market a few years later. The FDA has approved these medications to treat serious autoimmune diseases, such as rheumatoid arthritis and inflammatory bowel disease. Rheumatoid arthritis ("RA") results from the overproduction of tumor necrosis factor, or "TNF," which leads to chronic inflammation and, in many cases, irreversible destruction of the joints. It is a systemic disease that causes crippling deformities. Before the advent of TNF inhibitors, there were no treatments that effectively controlled severe rheumatoid arthritis—multiple joint replacement surgeries and eventual wheelchair confinement were the all-too-common outcome for patients with severe disease. Moreover, the less-effective treatments of the pre-biologic era have their own attendant risks. Chronic steroid treatment, for instance, can have serious side effects, many of them common—gastrointestinal bleeding, osteoporosis, weight gain, insomnia, and blood sugar effects, to name a few. And failure to bring the patient's RA under control will expose the patient to the known risks of RA itself, which include, in addition to ongoing joint destruction, increased risk of lymphoma, heart disease, stroke, and a host of other ailments.

The anti-TNF therapies changed all that. But, like all prescription medications, they carry potential risks. Because they suppress part of the immune system, the FDA, manufacturers, and the medical community have focused from the beginning on the possibility that they might increase the risk of serious infections and malignancies. Lymphoma was a particular concern, given the higher rate of this type of cancer in patients with moderate to severe RA compared to the general population. Accordingly, the package inserts accompanying Remicade and Humira have always carried warnings and information about, among other potential risks, serious infections and lymphoma.

What does the presumption that a physician would have read and "heeded" a warning mean in this context? The rheumatologist, confronted by a severe case of rheumatoid arthritis that has proven refractory to traditional treatments, will no doubt consider anti-TNF therapy for her patient. That these medications have become the standard of care for the treatment of moderate to severe cases of RA despite their warnings of life-threatening potential risks is ample illustration that heeding the warning does not equate to a decision not to prescribe the medication. In many such cases, the physician concludes that the substantial benefits from anti-TNF therapy, unattainable from traditional alternatives, outweigh the remote risk that the therapy might further increase the patient's risk of lymphoma—especially in light of widely-cited studies showing that the inflammation from uncontrolled severe RA

itself dramatically increases lymphoma risk.[1] When faced with a choice between an effective medication that carries a remote potential risk, less-effective medications that carry their own potential risks, and leaving the disease untreated—an option that in severe cases has been shown to *increase* the risk in question—it is unsurprising that rheumatologists the world over have opted to prescribe anti-TNF therapies for their patients despite warnings of serious potential adverse events.

Yet in a jurisdiction that applies the presumption as the *Seley* Court did, if a plaintiff persuades the fact-finder that the warnings accompanying an anti-TNF therapy are inadequate, a rebuttable presumption will arise that, had the plaintiff's preferred warning been given, the plaintiff's physician would have declined to prescribe the TNF inhibitor. This might be the end of the story, given the difficulties in rebutting the presumption under *Seley*. Defendant Searle succeeded in doing so in that case, but only because of its peculiar facts: Mrs. Seley failed to disclose to her prescribing physician significant facts about her medical history which, if known, may have led him to relate the potential risk to her case. *Id*. Given that Searle successfully rebutted the presumption, the Court need not have reached Searle's argument that Mrs. Seley could not establish proximate cause because her physician was already aware of the risk in question—i.e., that no additional warning would have changed his prescription decision because he was already aware of the risk. Nonetheless, the Court stated in dicta that even *unrebutted testimony by the prescribing physician that he was fully aware of the risk* would be insufficient to rebut the presumption, based on its supposition that "one may benefit from being warned or reminded of what he already knows." *Id*. at 839. According to the Court, "only speculation can support the assumption that an adequate warning, properly communicated, would not have influenced the course of conduct adopted by a physician, even where the physician had previously received the information contained therein." *Id*.

Yet the *Seley* Court's concern is not borne out in the context of unavoidable risks, as *Thomas* makes clear. Applying *Thomas*, a defendant can show that where a risk is unavoidable, whether a stronger warning would make a difference is not a matter of speculation. It should instead be the result of a careful balancing of the evidence of the potential risks from using the medication against the potential risks of not using it. A presumption shifting plaintiff's burden of showing that the proposed warning would have made a difference has no place in this context. The *Thomas* court rejected the heeding presumption, but concluded that, even if the presumption applied, to "'heed' in this context means only that the learned intermediary would have incorporated the 'additional' risk into his decisional calculus."

[1] *See, e.g.*, Baecklund E, et al., Disease Activity and Risk of Lymphoma in Patients With Rheumatoid Arthritis: Nested Case-Control Study, *BMJ* 1998;317:180-181; Baecklund E, et al., Association of chronic inflammation, not its treatment, with increased lymphoma risk in rheumatoid arthritis, *Arthritis Rheum* 2006; 54(3):692-701.

Thomas, 949 F.2d at 814. "The burden remains on the plaintiff to demonstrate that the additional non-disclosed risk was sufficiently high that it would have changed the treating physician's decision to prescribe the product for the plaintiff." *Id*. In the example of a rheumatologist who prescribed an anti-TNF therapy for a patient with severe RA, a plaintiff would have to show that the remote potential increase in lymphoma risk that might accompany anti-TNF therapy outweighed not only the potential benefits—often dramatic—from the therapy, but the risks from alternative medications, not to mention the risks from failing to effectively control the patient's RA, including the increased risk of lymphoma from the disease itself.

IV. Opportunities to Limit *Seley*

In light of the Ohio legislature's determined efforts to enact comprehensive tort reform—despite repeated attempts to limit the effect of the legislation—the status of *Seley* as controlling law in Ohio is unclear at best. The legislature enacted the Ohio Product Liability Act ("OPLA") in 1988, amending it repeatedly after successful constitutional challenges. *See, e.g.*, *State ex rel. Ohio Academy of Trial Lawyers v. Sheward*, 715 N.E.2d 1062, 1111 (Oh. 1999). It amended OPLA further in 2005 to expressly refute the determination of the Supreme Court of Ohio that the legislature, in enacting OPLA, did not intend to abolish all common-law product liability actions. *See Carrel v. Allied Products Corp*., 677 N.E.2d 795, 799 (Oh. 1997). As amended, the statute explicitly states that OPLA is "intended to abrogate all common law product liability claims or causes of action." Ohio R.C. §2307.71(B); *see also Doty v. Fellhauer Elec., Inc.*, 888 N.E.2d 1138, 1142 (2008) ("the General Assembly stated that [R.C. 2307.71] is 'intended to supersede the holding of the Ohio Supreme Court in *Carrel v. Allied Products Corp*. (1997), 78 Ohio St.3d 284 [677 N.E.2d 795]").

Far from codifying the *Seley* presumption, the legislature expressly placed the burden of proving proximate causation on plaintiffs: a plaintiff may only prevail on a product liability claim "if the claimant establishes, by a preponderance of the evidence," that "[a] defective aspect of the manufacturer's product in question . . . was a proximate cause of harm for which the claimant seeks to recover compensatory damages." Ohio R.C. § 2307.73(A). Nowhere does the Act reference the plaintiff-friendly *Seley* presumption. Nor can such a presumption justifiably be read into the statute, as it would directly contradict the express language of Section 2307.73(A). Had the legislature desired to incorporate the common-law presumption into OPLA, it could have done so—the same way it incorporated the learned intermediary doctrine. *See, e.g.*, *Wimbush v. Wyeth*, 619 F.3d 632, 637 (6th Cir. 2010) ("the common law 'learned intermediary doctrine" is codified in the Act" at § 2307.76(C)).

No Ohio court has directly decided the question of whether the legislature's omission of the *Seley* presumption from OPLA renders it inapplicable, although defendants in at least one non-Ohio case made this argument. *See In re Nuvaring Lit.*, 2013 WL 1874321 at *38 (N.J.Super.L. Apr. 18, 2013). The *Nuvaring*

court declined to hold that the presumption no longer applied, noting that defendants could not point to any Ohio cases reaching that conclusion, while the court found several that continued to apply the *Seley* presumption. *Id*. Yet two of the Ohio opinions cited by the New Jersey *Nuvaring* court were decided before the Ohio legislature enacted the 2005 amendment explicitly abrogating common law product liability claims. *See*, *Kennedy v. Streibel*, 2003 WL 23175489 (Oh. Ct. App., Dec. 31, 2003); *Hisrich v. Volvo Cars of N. Am., Inc.*, 226 F.3d 445, 451 (6th Cir. 2000). The third, *Boyd v. Lincoln Elec. Co.*, 902 N.E.2d 1023 (2008), relied on *Carrel*, which was abrogated by the 2005 amendment. And while the federal district court for the Southern District of Ohio has since applied the presumption in a group of cases remanded from the Aredia and Zometa MDL, *see, e.g.*, *Monroe v. Novartis Pharm. Corp*., 1:12-CV-00746 (WOB-KLL), 2014 WL 3378345, at *8 (S.D. Ohio July 10, 2014), there is no indication in any of the opinions that the defendants in those cases argued that the presumption no longer applies. Accordingly, the argument remains viable, and should be considered by defendants facing the presumption in cases applying Ohio law.

Even where the presumption currently applies, defendant pharmaceutical manufacturers can use the *Thomas* court's framework to help rebut the presumption or, in appropriately postured cases, perhaps persuade the court to either reject the presumption or to limit its application. *Thomas* fits the realities of cases involving unavoidable risks much better than the limited analysis of *Seley* and its progeny. A physician might decline to prescribe a medication where a milder product might adequately treat the condition, or where the condition might resolve on its own; in such cases, the risk is effectively a preventable one. But where a patient's condition should not be left untreated and there are no risk-free alternatives, the potential risks associated with prescription therapies are unavoidable. Defense experts can establish the benefits of defendant's therapy, as well as the risks associated with available alternatives and with leaving plaintiff's disease untreated—points that plaintiffs' experts can often be forced to admit. This evidence can help rebut the presumption by showing that the benefits of the therapy outweighed the risks in plaintiff's case. And every time a court reaches such a conclusion—or even hears the detailed argument supporting it—the court will come face-to-face with significant, logical reasons why the presumption should not be applied in the first instance. Eventually, courts may carve prescription medication cases out of the presumption entirely. Defense of biologics presents an opportunity for defendants to make the most of the *Thomas* analysis and, where the opportunity arises, attempt to limit the *Seley* presumption to cases involving preventable risks. Applying the *Thomas* framework, defendants can educate the courts on the difference between preventable and unavoidable risks—especially in cases involving medications used to treat serious diseases where no risk-free alternatives are available.

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