Rel: September 30, 2022

SUPREME COURT OF ALABAMA

SPECIAL TERM, 2022

1210140

Mark Blackburn

v.

Shire U.S., Inc., and Shire, LLC

Certified Questions from the United States Court of Appeals for the Eleventh Circuit (Case No. 20-12258)

MENDHEIM, Justice.

Pursuant to Rule 18, Ala. R. App. P., the United States Court of Appeals for the Eleventh Circuit has certified to this Court the following questions:

> "1. 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?
>
> "2. May a plaintiff establish that a failure to warn caused his injuries by showing that his doctor would have adopted a different course of testing or mitigation, even though he would have prescribed the same drug?"

Blackburn v. Shire US Inc., 18 F.4th 1310, 1322 (11th Cir. 2021) ("Blackburn II"). This Court accepted and now answers those questions.

I. Facts

Dr. Dino Ferrante, a gastroenterologist, prescribed LIALDA, which is manufactured by Shire U.S., Inc., and Shire, LLC (referred to collectively as "Shire"), to help patient Mark Blackburn with his Crohn's disease. "LIALDA is the brand name for Shire's mesalamine drug, which is an anti-inflammatory drug specifically aimed at the gut. LIALDA is not approved by the FDA to treat Crohn's, but it is approved to treat ulcerative colitis, Crohn's 'sister' disease." Blackburn II, 18 F.4th at 1314. Thus, Dr. Ferrante prescribed LIALDA for an "off-label" purpose, but one that is common. After taking LIALDA for between 12 to 16 months,

Blackburn discovered that he had developed kidney disease, specifically advanced chronic interstitial nephritis, which had resulted in irreversible scarring and had diminished his kidney function to 20% of normal capacity. As a result, Blackburn is awaiting a kidney transplant.

In November 2013, when Blackburn began taking LIALDA, the "Warnings and Precautions" portion of its label included the following:

> "**5.1 Renal Impairment**
>
> > "Renal impairment, including minimal change nephropathy, acute and chronic interstitial nephritis, and, rarely, renal failure, has been reported in patients given products such as LIALDA that contain mesalamine or are converted to mesalamine.
> >
> > "It is recommended that patients have an evaluation of renal function prior to initiation of LIALDA therapy and periodically while on therapy. Exercise caution when using LIALDA in patients with renal dysfunction or a history of renal disease."

(Bold typeface in original; emphasis added.) The recommendation to "have an evaluation of renal function prior to initiation of LIALDA therapy and periodically while on therapy" was included in LIALDA's first label when it was approved for distribution in 2007, and it is that portion of the label which is the basis of Blackburn's failure-to-warn claim. See Shire's brief, p. 7.

In June 2016, Blackburn sued Shire in the United States District Court for the Northern District of Alabama, alleging strict liability for failure to warn under the Alabama Extended Manufacturer's Liability Doctrine ("the AEMLD"), breach of express warranty, and fraud. The breach-of-warranty and fraud claims were dismissed, and Shire sought summary judgment on the failure-to-warn claim.

> "Mr. Blackburn does not contend that Shire failed to warn of possible kidney injury when using LIALDA. Instead, Mr. Blackburn alleges that the recommended 'periodic' evaluation 'constitutes a defective and unsafe instruction for safe use of LIALDA.' [Quoting Blackburn's complaint.] He contends that the term 'periodic' as generally used in drug labels refers to either semi-annual or annual testing and that Shire's warning should have 'provide[d] for blood testing of renal function at intervals necessary to reasonably protect patients from LIALDA's potential renal toxicity.' [Quoting Blackburn's complaint.]
>
> "Mr. Blackburn contends that the language regarding testing for renal function in Shire's warning should resemble language used by other manufacturers of mesalamine-based drugs. PENTASA, like LIALDA, is a 5-aminosalicylic acid ('5-ASA') or mesalamine-based drug. In the United Kingdom, PENTASA is marketed with the warning that patients 'should have renal function monitored, with serum creatinine levels measured prior to treatment start, every 3 months for the first year, then [every 6 months] for the next 4 years and annually thereafter.' Similarly, OCTASA, another 5-ASA drug, is marketed in the United Kingdom with the following instruction:

> "'It is recommended that all patients have an evaluation of their renal function prior to initiation of Octasa therapy and repeatedly whilst on therapy. As a guideline, follow-up tests are recommended 14 days after commencement of treatment and then every 4 weeks for the following 12 weeks. Short monitoring intervals early after the start of Octasa therapy will discover rare acute renal reactions. In the absence of an acute renal reaction monitoring intervals can be extended to every 3 months and then annually after 5 years.'
>
> "Mr. Blackburn asserts that an appropriate label for LIALDA, a mesalamine-based drug, should include instructions recommending 'evaluation of renal function by a simple serum (blood) test of creatinine levels on a monthly basis for the first three months after initiation of therapy and then on a quarterly basis for at least one year.' [Quoting Blackburn's complaint.] Mr. Blackburn contends that Shire's failure to include this testing regimen in the LIALDA package warning in the fall of 2013 proximately caused his kidney injury."

Blackburn v. Shire U.S., Inc., No. 2:16-cv-00963-MHH, June 1, 2020 (N.D. Ala. 2020) ("Blackburn I") (not published in Federal Supplement) (citations to the record omitted).

> "[Dr. Agata] Przekwas[, a nephrologist,] and Dr. Jonathan Winston, a nephrology expert retained by Blackburn, concluded that Blackburn's injuries were preventable. Winston estimated that Blackburn's kidney disease was detectable at least six months before it was diagnosed, and possibly as early as August 2014. If Blackburn had stopped taking LIALDA at that time, Winston opined that his kidney function 'would be either normal or near normal.' And Winston attributed Blackburn's injury to the

> LIALDA label. Because of the amorphous 'periodic' instruction, Winston reasoned that a physician following the label's warning could fail to detect kidney disease before it 'worsen[ed] to a clinically significant level.'
>
> "Benjamin England, a regulatory expert retained by Blackburn, explained that Shire could have changed the label to include a stronger monitoring instruction. He concurred in Winston's assessment of the label's inadequacies and added that sufficient evidence, including … 'a growing body of medical literature,' supported a stronger monitoring instruction. England also identified reports of renal impairment that Shire received between the label's initial approval and Blackburn's injury. He concluded that sufficient evidence would have led to a label change, had Shire sought one."

Blackburn II, 18 F.4th at 1315.

Dr. Ferrante testified that, to him, testing renal function "periodically" meant "once a year," though he "acknowledged that 'periodically' can mean other time periods as well and that there is no specific definition of 'periodically' in the medical profession." Blackburn I. He also stated that if the LIALDA label had contained language similar to the labels for PENTASA and OCTASA, mentioned in the initial quote from Blackburn I above, he "'would have followed those protocols.'" Id.

The federal district court granted Shire's summary-judgment motion, holding that there was an "absence of admissible evidence of a causal link between Shire's instructions for renal evaluations when

prescribing LIALDA and Mr. Blackburn's injury." Blackburn I. Blackburn appealed. The Eleventh Circuit Court of Appeals disagreed with the federal district court's application of the facts on summary judgment. It concluded that Dr. Ferrante's testimony that he did not read the LIALDA label should not have been interpreted as meaning that the label's contents did not matter to him but, rather, that "the existing label's warning was so well known to the physician that he did not read it before each new prescription." Blackburn II, 18 F.4th at 1319. Furthermore, the Eleventh Circuit Court of Appeals rejected the federal district court's conclusion that Dr. Ferrante's testimony that he would have altered his testing regimen for Blackburn if the LIALDA label had been different was "unsubstantiated speculation" and "self-interested" because such a conclusion "goes to credibility, not the usefulness of the testimony at summary judgment." Id. at 1320.

Even though the Eleventh Circuit Court of Appeals rejected the federal district court's basis for entering a summary judgment in favor of Shire, it acknowledged that Shire had presented an alternative basis for summary judgment.

> "As an alternative basis to affirm the district court's summary judgment, Shire argues that the district court erred

> in recognizing Blackburn's theory of liability as a matter of Alabama law. There are two parts to this argument, as we see it. First, citing the learned intermediary doctrine, Shire contends that it satisfied its duty as a matter of law by warning of the risk of renal impairment and that, once a drug manufacturer warns of a risk, it is up to the prescribing doctor to assess and mitigate that risk. Second, Shire argues that Blackburn's theory of proximate cause is 'not in accord with Alabama law.' Specifically, Shire argues that a failure-to-warn plaintiff may establish that his injury was caused by a prescription drug only by showing that the physician would not have prescribed the drug if the warning had been adequate."

Id. at 1321. That alternative legal basis for summary judgment prompted the certified questions submitted to this Court.

II. Analysis

We initially note that both sides, in one legal forum or another, have contended that federal preemption warrants a ruling as a matter of law in its favor. The Eleventh Circuit Court of Appeals observed in its opinion:

> "Shire also argues that federal law would preempt a state law cause of action if it existed. The district court rejected this preemption defense. See generally Wyeth v. Levine, 555 U.S. 555, 581, 129 S. Ct. 1187, 173 L. Ed. 2d 51 (2009). We will address it, if necessary, after we know the contours of state law. See Blue Cross & Blue Shield of Ala., Inc. v. Nielsen, 116 F.3d 1406, 1412 (11th Cir. 1997) (certifying a question because 'the state law issues must be decided before we can dispose of' the preemption question), certified question answered, 714 So. 2d 293 (Ala. 1998)."

Blackburn II, 18 F.4th at 1319 n.1. Before this Court, Blackburn argues that federal regulations mandate that prescription-drug labels have instructions regarding the required frequency of testing related to use of a prescription drug.

Regardless of whether either side is correct in its assertions, federal preemption is not an issue of Alabama law. To be answered by this Court, federal certified questions must be "questions or propositions of law of this State which are determinative of said cause and [for which] there are no clear controlling precedents in the decisions of the Supreme Court of this State ...." Rule 18(a), Ala. R. App. P. (emphasis added). Thus, unsurprisingly, certified questions concern Alabama law, not federal law. Federal preemption is an issue of federal law that the Eleventh Circuit Court of Appeals needs no assistance in evaluating. See, e.g., Glover v. Bausch & Lomb Inc., 6 F.4th 229, 241 n.9 (2d Cir. 2021) (noting that, "[b]ecause preemption is a question of federal law, ... we certify only the question of whether Connecticut law recognizes such a cause of action, and not whether that cause of action would be preempted under the [Food, Drug, and Cosmetic Act]"). Therefore, we decline to address the parties' arguments concerning federal preemption.

A. The First Certified Question

The first certified question probes the contours of a prescription-drug manufacturer's duty to warn under Alabama law. As the question indicates, in Alabama such a duty to warn is filtered through the "learned-intermediary doctrine," which essentially holds that the warning is directed toward the physician who prescribes a drug rather than the patient who takes the drug. This Court first adopted the learned-intermediary doctrine in Stone v. Smith, Kline & French Laboratories, 447 So. 2d 1301 (Ala. 1984), in which the Court explained:

> "Plaintiffs-appellants misconceive the physician's role in prescribing ethical drugs, and the significance of a drug manufacturer's warnings in undertaking that responsibility. A proper understanding of that role has been articulated by the United States Court of Appeals for the Fifth Circuit as follows:
>
> > "'We cannot quarrel with the general proposition that where prescription drugs are concerned, the manufacturer's duty to warn is limited to an obligation to advise the prescribing physician of any potential dangers that may result from the drug's use. This special standard for prescription drugs is an understandable exception to the Restatement's general rule that one who markets goods must warn for[e]seeable ultimate users of dangers inherent in his products. See Restatement (Second) of Torts, Section 388 (1965). Prescription drugs are likely to be complex medicines, esoteric in formula and varied in effect.

> As a medical expert, the prescribing physician can take into account the propensities of the drug as well as the susceptibilities of his patient. His is the task of weighing the benefits of any medication against its potential dangers. The choice he makes is an informed one, an individualized medical judgment bottomed on a knowledge of both patient and palliative. Pharmaceutical companies then, who must warn ultimate purchasers of dangers inherent in patent drugs sold over the counter, in selling prescription drugs are required to warn only the prescribing physician, who acts as a "learned intermediary" between manufacturer and consumer.'
>
> "Reyes v. Wyeth Laboratories, 498 F.2d [1264,] 1276 [(5th Cir. 1974)]."

447 So. 2d at 1304-05 (second emphasis added).

The Court last expounded on the learned-intermediary doctrine in Wyeth, Inc. v. Weeks, 159 So. 3d 649 (Ala. 2014), stating:

> "In Stone v. Smith, Kline & French Laboratories, 447 So. 2d 1301 (Ala. 1984), this Court adopted the learned-intermediary doctrine in a case addressing whether a manufacturer's duty to warn extends beyond the prescribing physician to the physician's patient who would ultimately use the drugs. The principle behind the learned-intermediary doctrine is that prescribing physicians act as learned intermediaries between a manufacturer of a drug and the consumer/patient and that, therefore, the physician stands in the best position to evaluate a patient's needs and to assess the risks and benefits of a particular course of treatment for the patient. A consumer can obtain a prescription drug only through a physician or other qualified health-care provider. 21 U.S.C. § 353(b)(1). Physicians are trained to understand

the highly technical warnings required by the FDA in drug labeling. 21 C.F.R. § 201.56. The learned-intermediary doctrine was established in Marcus v. Specific Pharmaceuticals, 191 Misc. 285, 77 N.Y.S.2d 508 (N.Y. Sup. Ct. 1948), as an absolute defense for 'failure to warn' cases. Mitesh Bansilal Shah, Commentary, As a Matter of Fact or a Matter of Law: The Learned Intermediary Doctrine in Alabama, 53 Ala. L. Rev. 1299, 1301 (2002). …

"The learned-intermediary doctrine recognizes the role of the physician as a learned intermediary between a drug manufacturer and a patient. As the United States Court of Appeals for the Eleventh Circuit has explained:

> "'In cases involving complex products, such as those in which pharmaceutical companies are selling prescription drugs, the learned intermediary doctrine applies. Under the learned intermediary doctrine, a manufacturer's duty to warn is limited to an obligation to advise the prescribing physician of any potential dangers that may result from the use of its product. This standard is "an understandable exception to the Restatement's general rule that one who markets goods must warn foreseeable ultimate users of dangers inherent in his products." As such, we rely on the expertise of the physician intermediary to bridge the gap in special cases where the product and related warning are sufficiently complex so as not to be fully appreciated by the consumer.... "[U]nder the 'learned intermediary doctrine' the adequacy of [the defendant's] warning is measured by its effect on the physician, ... to whom it owed a duty to warn, and not by its effect on [the consumer]."'

"Toole v. Baxter Healthcare Corp., 235 F.3d 1307, 1313-14 (11th Cir. 2000) (citations omitted).

> "A prescription-drug manufacturer fulfills its duty to warn the ultimate users of the risks of its product by providing adequate warnings to the learned intermediaries who prescribe the drug. Once that duty is fulfilled, the manufacturer has no further duty to warn the patient directly. However, if the warning to the learned intermediary is inadequate or misrepresents the risk, the manufacturer remains liable for the injuries sustained by the patient. The patient must show that the manufacturer failed to warn the physician of a risk not otherwise known to the physician and that the failure to warn was the actual and proximate cause of the patient's injury. In short, the patient must show that, but for the false representation made in the warning, the prescribing physician would not have prescribed the medication to his patient."

159 So. 3d at 672-74 (emphasis added).[1]

The parties bicker at length concerning the import of Stone and (especially) Weeks on the certified questions. Shire contends that Weeks definitively answers both certified questions in the negative and that there is no need to consider "expanding a prescription drug

[1]The Weeks Court concluded that a prescription-drug designer could be held liable for alleged injuries caused by a generic version of the drug that the designer did not manufacture. As this Court noted in Forest Laboratories, LLC v. Feheley, 296 So. 3d 302, 316 (Ala. 2019), the Alabama Legislature enacted § 6-5-530, Ala. Code 1975, in the year following the Weeks decision, which "abrogates this Court's prior decision in Weeks. … [U]nder the plain language of § 6-5-530, a pharmaceutical manufacturer cannot be held liable for injury caused by a product it did not manufacture."

manufacturer's duty to warn under the learned intermediary doctrine." Shire's brief, p. 18. As already noted, both Stone and Weeks acknowledged that a "'manufacturer's duty to warn is limited to an obligation to advise the prescribing physician of any potential dangers that may result from the use of its product.'" Weeks, 159 So. 2d at 673 (quoting Toole v. Baxter Healthcare Corp., 235 F.3d 1307, 1313 (11th Cir. 2000)); Stone, 447 So. 2d at 1304 (quoting Reyes v. Wyeth Lab'ys, 498 F.2d 1264, 1276 (5th Cir. 1974), for the same proposition). Weeks also stated that "[t]he patient must show that the manufacturer failed to warn the physician of a risk not otherwise known to the physician …." 159 So. 3d at 673. Shire interprets those statements as meaning that a prescription-drug manufacturer's duty to warn consists solely of listing a drug's known side effects.[2] Thus, Shire takes the position that Weeks forecloses any notion that the duty to warn could include instructions for safely monitoring a patient while taking a prescription drug.

[2]Shire drove home its position in oral argument when it asserted that if a prescription-drug manufacturer produces two drugs that have the same known side effect, but the side effect occurs quickly in one of the drugs and occurs very slowly in the other drug, the drug manufacturer's only responsibility for both drugs is to list the side effect.

Blackburn, on the other hand, contends that a prescription-drug manufacturer's duty to warn is twofold: the manufacturer must warn of a drug's known side effects and it must warn about safe use of the drug. Blackburn argues that the formulations of the duty to warn expressed in Stone and Weeks were geared more toward the side-effect aspect of that duty because both of those cases ultimately concerned whether side-effect warnings had been adequate.[3] In Stone, the plaintiff contended that the prescription drug Thorazine had caused her to develop cholestatic jaundice. The plaintiff conceded that her "physician was adequately warned of the adverse side effects, including cholestatic jaundice," but she contended that "the warnings issued [were] of no consequence, because prescribing physicians cannot accurately predict which of their patients will develop jaundice as a result of treatment with Thorazine." Stone, 447 So. 2d at 1304. This Court rejected the plaintiff's contention because, it held, it was the physician's responsibility to "'take into

[3]In his brief to this Court, Blackburn also argued that the statements in Weeks concerning the duty to warn were not "good law" because the central holding in Weeks has been abrogated. Blackburn's brief, p. 25; see note 1, supra. Blackburn categorically abandoned that position in oral argument before this Court.

account the propensities of the drug as well as the susceptibilities of his patient'" and to weigh "'the benefits of any medication against its potential dangers.'" Id. at 1305 (quoting Reyes, 498 F.2d at 1276). In Weeks, the plaintiff contended that prescription-drug designers had "materially misinformed and misled [the plaintiff's physician] about the likelihood that the [prescription] drug [Reglan] would cause the movement disorder tardive dyskinesia and related movement disorders." 159 So. 3d at 655. Blackburn asserts that the context of the allegations in those cases must be borne in mind when considering the statements that a prescription-drug manufacturer must warn a prescribing physician of "any potential dangers that may result from the use of its product" and that a plaintiff must demonstrate that a drug manufacturer "failed to warn the physician of a risk not otherwise known to the physician." Weeks, 159 So. 3d at 673. In other words, Blackburn argues that the mere fact that "side-effects cases" such as Stone and Weeks state that the duty to warn includes warning about known dangers of a prescription drug does not mean that such a duty cannot include instructions for mitigating those side effects.

For several reasons, we agree with Blackburn. First, the Weeks decision was not primarily concerned with outlining all the contours of a prescription-drug manufacturer's duty to warn. The duty to warn was discussed simply because the drug-designer defendants had contended that they had no relationship with the plaintiff because the plaintiff had ingested a generic version of Reglan that they did not manufacture. This Court rejected that argument by observing that the learned-intermediary doctrine and the fact that "the FDA mandates that the warning on a generic-drug label be the same as the warning on the brand-name-drug label" rendered the plaintiff's lack of a relationship with the drug's designers irrelevant. Weeks, 159 So. 3d at 674. In other words, the duty to warn was only an issue in Weeks because, according to the Court, what mattered was the drug label's communication to the plaintiff's physician, and the labeling on the generic version of Reglan was controlled by the drug's designers. Because Weeks concerned retail-drug-designer liability for alleged harms caused by a generic version of a drug, the decision did not settle whether a prescription-drug manufacturer's duty to warn only includes listing known side effects of a drug.

In fact, after the Weeks Court made the statements we quoted above, the Court more generally described the learned-intermediary doctrine as providing "that a prescription-drug manufacturer fulfills its duty to warn users of the risk associated with its product by providing adequate warnings to the learned intermediaries who prescribe the drug and that, once that duty is fulfilled, the manufacturer owes no further duty to the ultimate consumer." 159 So. 3d at 674 (emphasis added). Whether a warning "adequate[ly]" warns users of a drug's risks certainly involves listing a drug's known side effects, but it also may include instructions for mitigating those side effects. This is so because merely listing a prescription drug's side effects may not sufficiently alert a physician to the nature of the danger of the drug's side effects. More specific to this case, it is one thing to state that LIALDA can cause kidney damage; it is another thing if the potential for such damage is so likely that frequent monitoring of renal function, rather than "periodic" monitoring, is advisable. In other words, recommendations about monitoring represent one method of informing a physician about the degree of danger associated with a particular side effect. If a prescription-drug manufacturer knows the extent of a side effect's danger, then

instructions about monitoring certainly could be part of warning about the drug's dangers. From that perspective, Blackburn is simply questioning whether LIALDA's instruction about "periodic" testing was sufficient to alert his physician as to the danger posed by LIALDA's side effect of kidney damage. Cf. Stahl v. Novartis Pharms. Corp., 283 F.3d 254, 270 (5th Cir. 2002) (stating that "[t]here appears to be no compelling reason to exempt recommended medical monitoring schemes -- which are, in essence, instructions for safe use of prescription drugs -- from a drug manufacturer's duty to warn" and observing that "many courts applying the law of other states have implicitly assumed that medical monitoring recommendations contained in package inserts are 'warnings' by evaluating such recommendations (or the absence of such recommendations) in determining whether a drug manufacturer has fulfilled its duty to warn").

That an adequate warning might have to include instructions for mitigating side effects becomes even more apparent through a closer examination of Stone. As Blackburn notes, in the course of adopting the learned-intermediary doctrine, the Stone Court also adopted Comment k to § 402A of the Restatement (Second) of Torts (Am. L. Inst. 1965) ("the

Restatement"). See Stone, 447 So. 3d at 1303 (stating that "[t]he [federal] district court rightly recognized the applicability of Comment k to Section 402A of the Restatement (Second) of Torts (1965) … to the facts of this case"). In Purvis v. PPG Industries, Inc., 502 So. 2d 714, 718 (Ala. 1987), this Court explained:

> "In Stone v. Smith, Kline & French Laboratories, 447 So. 2d 1301 (Ala. 1984), this Court, adopting comment k to Section 402A of the Restatement (Second) of Torts[] (1965)[, concluded that] an unavoidably unsafe product, when properly prepared and accompanied by proper directions and warnings, is not 'defective' or 'unreasonably dangerous' under Alabama's Extended Manufacturer's Liability Doctrine."

(Footnote omitted.) Comment k to § 402A of the Restatement provides:

> "k. Unavoidably unsafe products. There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs. An outstanding example is the vaccine for the Pasteur treatment of rabies, which not uncommonly leads to very serious and damaging consequences when it is injected. Since the disease itself invariably leads to a dreadful death, both the marketing and the use of the vaccine are fully justified, notwithstanding the unavoidable high degree of risk which they involve. Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it unreasonably dangerous. The same is true of many other drugs, vaccines, and the like, many of which for this very reason cannot legally be sold except to physicians, or under the prescription of a physician. ... The seller of such products, again with the qualification that they are properly prepared and marketed, and proper warning is given, where

> the situation calls for it, is not to be held to strict liability for unfortunate consequences attending their use, merely because he has undertaken to supply the public with an apparently useful and desirable product, attended with a known but apparently reasonable risk."

(First and third emphasis added.) The adoption of Comment k in Stone provided a strong indication that a prescription-drug manufacturer's duty to warn is not necessarily limited to listing a drug's known side effects but also may include directions for mitigating those side effects.[4]

The definition of a "product liability action" in § 6-5-501(2), Ala. Code 1975, provides further support for the fact that a failure-to-warn claim against a prescription-drug manufacturer may include a failure to provide adequate directions for using the drug. Section 6-5-501(2) provides:

> "(2) Product liability action. Any action brought by a natural person for personal injury, death, or property damage caused by the manufacture, construction, design, formula, preparation, assembly, installation, testing, warnings, instructions, marketing, packaging, or labeling of a manufactured product when such action is based upon (a) negligence, (b) innocent or negligent misrepresentation, (c) the manufacturer's liability doctrine, (d) the Alabama extended manufacturer's liability doctrine, as it exists or is

[4]We note that Shire was conspicuously silent in its brief and at oral argument with respect to Blackburn's observations about Comment k to § 402A of the Restatement.

> hereafter construed or modified, (e) breach of any implied warranty, or (f) breach of any oral express warranty and no other. A product liability action does not include an action for contribution or indemnity."[5]

(Emphasis added.)

Shire discounts the foregoing legal definition as too generic to be of any use to our analysis of the issue at hand. But it is telling that "warnings" and "instructions" are listed together and that they are mentioned along with a product's "labeling." What this definition shows is that inadequate instructions on a label for a product are not outside the bounds of an AEMLD product-liability action. Shire has pointed us to nothing beyond its cramped readings of Stone and Weeks to demonstrate that Alabama law specially limits this aspect of the duty to warn for prescription-drug manufacturers in a way it does not for the manufacturer of any other product.

In place of an argument supported by Alabama law, Shire substitutes a policy argument: Shire insists that allowing instructions for mitigating warned-of risks to be part of a drug manufacturer's duty

[5]Blackburn correctly notes that § 6-5-521(a), Ala. Code 1975, contains an identical definition of a "product liability action."

to warn intrudes upon a physician's practice of medicine. According to Shire, "once a physician is advised of the risks of a drug, he or she will use that information, together with her or his medical training and knowledge of a particular patient, to determine if the drug should be prescribed, and how the patient should be followed and monitored." Shire's brief, p. 15. Further, Shire argues that its view of "[a] prescription drug manufacturer's duty under the learned intermediary doctrine is consistent with the one-on-one relationship a patient has with his or her physician, as compared to the non-existent relationship between a patient and a prescription drug manufacturer." Id., p.17.

Shire's contention is undermined by the fact that LIALDA's current label already includes instructions for monitoring: "It is recommended that patients have an evaluation of renal function prior to initiation of LIALDA therapy and periodically while on therapy." If that instruction does not interfere with a physician's practice of medicine, it is difficult to see why Blackburn's desired instruction of monitoring a patient's renal function "on a monthly basis for the first three months after initiation of therapy and then on a quarterly basis for at least one year" represents the drastic intrusion upon the physician-patient relationship that Shire

claims it to be. It cannot be because Blackburn's desired instruction is more specific. After all, as this Court has said, the goal of requiring a prescription-drug manufacturer to provide a warning is to enable a physician to be able to make an "informed" decision, i.e., "'an individualized medical judgment bottomed on a knowledge of both patient and palliative.'" Weeks, 159 So. 3d at 673 (quoting Reyes, 498 F.2d at 1276). Providing a physician more information presumably improves the physician's treatment of a patient. Indeed, a duty to warn that includes adequate instructions for mitigating warned-of risks does not interfere with the doctor-patient relationship any more than the presence of a drug label does in the first place. For example, in this case, LIALDA's label expressly states that it is approved for the treatment of ulcerative colitis, but that instruction obviously did not deter Dr. Ferrante from making his own medical judgment of prescribing it for Blackburn's Crohn's disease. Prescription drugs ordinarily include dosage recommendations for how often a patient should take a particular drug, but physicians freely modify those recommendations based on a patient's needs and tolerance of the medication in question. The same would be true of an instruction for monitoring: even if LIALDA's label

recommended testing a patient's renal function at certain specific intervals, rather than recommending "periodic" testing, a physician could deviate from the recommended course of monitoring based on his or her own medical judgment of what would be prudent for a particular patient.

The real issue is not whether instructions for monitoring would interfere with physician responsibility, but whether warnings about side effects of a prescription drug are sufficient in themselves to apprise physicians of a prescription drug's dangers. The ostensible answer would seem to be that it depends upon the drug in question. But nothing in Alabama's learned-intermediary doctrine prevents Blackburn from asserting a claim alleging that a failure to provide adequate monitoring instructions violates Shire's duty to warn. And that is the issue posed by the first certified question: Has Blackburn stated a viable cause of action under Alabama law with respect to Shire's duty to warn physicians about LIALDA? The answer is yes.

The parties have mentioned several facts in their briefs and at oral argument that are not within the purview of our assessment. For example, Shire's assertion that Dr. Ferrante failed to follow the LIALDA label as written and would not have followed Blackburn's desired

warning has nothing to do with the aspect of a failure-to-warn claim we have been tasked with explicating. Likewise, whether there is a medical consensus about the frequency of monitoring that is necessary when taking a mesalamine drug is a fact question that is not properly before us. In answering the first question presented, we are strictly concerned with the scope of a prescription-drug manufacturer's duty to warn physicians. Blackburn's claim does not exceed the boundaries of that duty. Accordingly, we answer the first certified question in the affirmative.

B. The Second Certified Question

Our answer to the second question flows naturally from our conclusion concerning the first question. Given that we have concluded that a failure-to-warn claim may include allegations of inadequate instructions about how to mitigate warned-of risks, it follows that a plaintiff may establish causation by showing that his or her physician would have adopted a different course of testing or mitigation, even though the physician would have prescribed the same drug. As Blackburn observes: "Instructions for safe use ... generally provide direction on how to minimize risk while using this product." Blackburn's

reply brief, p. 31. Indeed, "mitigation" implies lessening risk during use of the product. It defies logic to require a plaintiff to demonstrate that his or her physician would not have prescribed a subject drug with respect to an allegation that the drug's warnings provide insufficient instruction for monitoring a patient while taking the drug.

Shire's arguments asserting otherwise rely almost entirely upon the statement from Weeks that "the patient must show that, but for the false representation made in the warning, the prescribing physician would not have prescribed the medication to his patient." 159 So. 3d at 673-74. But as we observed in Part A of our analysis, the Weeks Court was not attempting to encapsulate the entirety of duty-to-warn law with respect to prescription-drug manufacturers; it was simply providing a summary in the context of a case alleging misinformation about the side effects of a drug. As Blackburn notes, several federal-court decisions applying Alabama law have intimated that a plaintiff may demonstrate causation by showing that a different warning from a prescription-drug manufacturer would have caused the plaintiff's physician to act differently, even if the physician still would have recommended the drug or procedure in question.

In Barnhill v. Teva Pharmaceuticals, USA, Inc., 819 F. Supp. 2d 1254, 1261 (S.D. Ala. 2011), the United States District Court for the Southern District of Alabama explained:

> "Theoretically, proof of proximate cause could take one of two forms: (1) evidence that Dr. Jaalouk would not have prescribed cephalexin at all if the warning had been stronger or (2) evidence that, though she still would have prescribed cephalexin, Dr. Jaalouk would have changed her behavior or treatment in some way that would have resulted in a different outcome for the Plaintiff. As to the latter argument, the record is devoid of any evidence that the outcome would have been better or different … if the cephalexin had been prescribed or administered in a different manner.[6]
>
> "_____
>
> "[6]For example, there is no reason to believe that Plaintiff's SJS [Stevens-Johnson syndrome] would have been diagnosed earlier or treated differently if Dr. Jaalouk had taken different precautions when she prescribed the drug, such as warning Plaintiff or her mother of the potential for SJS."

819 F. Supp. 2d at 1261 (emphasis added). In Fields v. Eli Lilly & Co., 116 F. Supp. 3d 1295 (M.D. Ala. 2015), the United States District Court for the Middle District of Alabama discussed the Eleventh Circuit Court of Appeals' decision in Toole v. McClintock, 999 F.2d 1430 (11th Cir. 1993) ("Toole").

> "In Toole, the plaintiff developed scar tissue around her silicone breast implants and underwent a closed capsulotomy,

> a procedure where a surgeon manually compresses the affected breast to rupture the scar tissue. This procedure ruptured her breast implants, causing serious injuries. The plaintiff sued the manufacturer of her breast implants, alleging that it had failed to warn her doctor of the risk of ruptures during a closed capsulotomy. 999 F.2d at 1431. The jury returned a verdict in the plaintiff's favor, and the Eleventh Circuit affirmed the district court's denial of the manufacturer's motion for a directed verdict, rejecting the manufacturer's argument that there was 'no evidence that a different warning from [the manufacturer] would have caused [the plaintiff's physician] to behave differently.' Id. at 1433.
>
> "Applying Alabama's learned-intermediary doctrine, the Eleventh Circuit held that a reasonable jury could have found that the manufacturer's warning 'understated the risks of implant rupture from closed capsulotomies' and that the jury heard evidence that 'a different warning would have caused [the physician] to warn [the plaintiff] before her augmentation surgery.' Id. (emphasis added). Hence, the physician would have behaved differently had the manufacturer issued a stronger warning because he testified that he would have warned the plaintiff of the risk of implant rupture prior to performing the augmentation surgery."

116 F. Supp. 3d at 1306-07 (second emphasis added). In Cooper v. Bristol-Myers Squibb Co., Civil Action No. 07-885 (FLW), Jan. 7, 2013 (D. N.J. 2013) (not published in Federal Supplement), applying Alabama law and relying on both Barnhill and Toole, the federal district court in New Jersey stated:

> "Conversely, a plaintiff may demonstrate proximate cause by showing that the new warning would have changed the physician's calculation of the risks and benefits of the drug

> and caused the physician not to prescribe the drug. See Brasher [v. Sandoz Pharms. Corp., No. CV-98-TMP-2648-S, Sept. 21, 2001 (N.D. Ala. 2001) (not published in Federal Supplement)]. Alternatively, where the new warning would not have caused the physician to alter his prescribing habits, a plaintiff may demonstrate proximate cause by showing that the new warning would have at least 'changed [the physician's] ... treatment in some way that would have resulted in a different outcome for [the] Plaintiff.' Barnhill, 819 F. Supp. 2d at 1261; see also Toole, 999 F.2d at 1433 (denying summary judgment on proximate cause grounds where physician testified that had he known 'in 1981 that there was a -- even a slightly significant instance of rupture of the implants, then I would have ... warned my patient.') (emphasis added)."

(First emphasis added; footnote omitted.)

Shire ineffectively attempts to distinguish the foregoing authorities. Regarding Barnhill, Shire states that "Barnhill was referenced in Weeks, but the proximate cause theory was not mentioned and the express language of Weeks is contrary to the theory." Shire's brief, p. 58. But Barnhill was cited only in passing in the Weeks opinion's rendition of the facts that quoted from the federal district court's opinion posing the certified questions. See Weeks, 159 So. 3d at 654. The Weeks Court said nothing -- positive or negative -- about the Barnhill Court's understanding of the causation element of a prescription-drug duty-to-warn claim.

Shire argues that in Fields the court "relied on a misreading of Toole" and "completely ignor[ed] the differences between the practice of medicine and the role of pharmaceutical manufacturers." Shire's brief, p. 59. But that latter point amounts to disagreeing with the Fields court's conclusion, not distinguishing it, and it is Shire that misreads Toole, not the Fields court. Shire contends that the Toole court adopted "the defendant's causation argument in that case based on patient choice" when it considered the fact that the plaintiff's doctor would have provided a different warning to the plaintiff about the procedure if he had known about the true danger of the implants rupturing. Id., p. 58 (emphasis omitted). Shire argues that the Toole defendant's selection of a defense strategy "does not change the standard for proximate cause." Id., p. 59. However, Shire confuses "patient choice" and what effect a warning may have on a physician. The Toole court explained that defendant Baxter Healthcare Corporation ("Baxter") made three arguments against the jury's conclusion that Baxter had provided an inadequate warning with respect to the risk of rupture for its implants.

> "Baxter contends that the district court erred in denying its motions for directed verdict and JNOV for three reasons. Baxter argues that its warning was clear that a closed capsulotomy could rupture the implant, that Ms. Toole

> admitted that, had the manufacturer's warnings been conveyed to her, she would not have consented to implant surgery, and that there is no evidence that a different warning from Baxter would have caused Dr. McClintock to behave differently. These arguments have insufficient merit."

Toole, 999 F.2d at 1433 (second emphasis added). The Toole court expressly rejected Baxter's "patient choice" argument because, "[u]nder the 'learned intermediary doctrine,' the adequacy of Baxter's warning is measured by its effect on the physician, Dr. McClintock, to whom it owed a duty to warn, and not by its effect on Ms. Toole." Id. The Toole court then concluded that "[t]he jury heard evidence from which it could reasonably conclude that a different warning would have caused Dr. McClintock to warn Ms. Toole before her augmentation surgery." Id. Thus, the Toole court plainly concluded that causation based on the allegedly inadequate warning could be established by showing the difference in behavior an adequate warning would have produced upon Dr. McClintock, not just by showing whether Dr. McClintock would have recommended not doing the surgery at all.

Decisions applying the law of other jurisdictions also support this view. For example, Bee v. Novartis Pharmaceuticals Corp., 18 F. Supp. 3d 268 (E.D. N.Y. 2014), applying New York law, clearly explained the

view that "even where a physician admits to continued recommendation of a drug, despite knowing of its ... risk, changes to that doctor's prescription or treatment procedures will generate triable questions of fact on the question of causation," and Bee cited cases from several jurisdictions, including multi-district litigation against prescription-drug manufacturers, reaching the same conclusion. 18 F. Supp. 3d at 294-95. Other such cases include: Knight v. Boehringer Ingelheim Pharms., Inc., 323 F. Supp. 3d 809, 831-33 (S.D. W. Va. 2018) (applying West Virginia law); In re Xarelto (Rivaroxaban) Prod. Liab. Litig., MDL No. 2592, Apr. 17, 2017 (E.D. La. 2017) (unpublished order) (applying Louisiana law); and Holley v. Gilead Scis., Inc., 379 F. Supp. 3d 809, 831-32 (N.D. Cal. 2019) (citing cases from several jurisdictions). See also Schrecengost v. Coloplast Corp., 425 F. Supp. 3d 448, 463 (W.D. Pa. 2019) (involving a medical device and applying Pennsylvania law).

The plethora of authorities running in the same direction undercuts Shire's assertion that limiting causation to whether a physician would have prescribed a drug at all comports with drawing clear lines between a prescription-drug manufacturer's responsibility and a physician's practice of medicine with a patient.

> "The Court's holding in Weeks that prescription drug manufacturers should be held liable only for not disclosing risks of their drugs of which a physician is not aware and which would cause the physician to not prescribe the drug, reflects legal policy that manufacturers should not be liable for the outcome of physician/patient discussions and the decisions arising from those discussions. That legal policy judgment is consistent with the separateness of the physician/patient relationship underlying the learned intermediary doctrine the Court has cited. It is a policy that recognizes pharmaceutical manufacturers have no control over what is or what is not discussed between physicians and patients or the decisions resulting from those discussions, including patient choice decisions."

Shire's brief, pp. 52-53. That argument is a red herring. The issue at the heart of the second certified question is whether information provided by a prescription-drug manufacturer would have changed how a physician chose to monitor a patient and whether such a change would have prevented the alleged harm suffered by the patient. More broadly, the learned-intermediary doctrine focuses on a prescription-drug manufacturer's communication to the physician, not to the patient, and the communication's effect on the physician's prescription and treatment of the patient with the subject drug. Obviously, if a physician changes a course of monitoring or treatment because of discussions the physician had with the patient, not because of information that should have been

provided on the drug's label, then any causal link between the drug manufacturer's warnings and the patient's injuries is severed.

Allowing a plaintiff to demonstrate causation by presenting evidence indicating that the physician would have changed his or her course of treatment or monitoring of the plaintiff when a failure-to-warn claim concerns allegedly inadequate instructions for mitigating warned-of risks makes logical sense, and it is not foreclosed by Alabama precedent. Accordingly, we answer the second certified question in the affirmative.

III. Conclusion

For the foregoing reasons, we answer the questions certified to this Court in the affirmative.

QUESTIONS ANSWERED.

Parker, C.J., and Bolin, Wise, Bryan, Stewart, and Mitchell, JJ., concur.

Shaw, J., dissents.

Sellers, J., dissents, with opinion.

SELLERS, Justice (dissenting).

I respectfully dissent. In 1984, this Court adopted the learned-intermediary doctrine and held that prescription-drug manufacturers have a duty to warn prescribing physicians of the known risks of prescription drugs:

> "'[W]here prescription drugs are concerned, the manufacturer's duty to warn is limited to an obligation to advise the prescribing physician of any potential dangers that may result from the drug's use. This special standard for prescription drugs is an understandable exception to the Restatement's general rule that one who markets goods must warn foreseeable ultimate users of dangers inherent in his products. See Restatement (Second) of Torts, Section 388 (1965). Prescription drugs are likely to be complex medicines, esoteric in formula and varied in effect. As a medical expert, the prescribing physician can take into account the propensities of the drug as well as the susceptibilities of his patient. His is the task of weighing the benefits of any medication against its potential dangers. The choice he makes is an informed one, an individualized medical judgment bottomed on a knowledge of both patient and palliative. Pharmaceutical companies then, who must warn ultimate purchasers of dangers inherent in patent drugs sold over the counter, in selling prescription drugs are required to warn only the prescribing physician, who acts as a "learned intermediary" between manufacturer and consumer.'"

Stone v. Smith, Kline & French Lab'ys, 447 So. 2d 1301, 1304-05 (Ala. 1984) (quoting Reyes v. Wyeth Lab'ys, 498 F.2d 1264, 1276 (5th Cir. 1974)) (emphasis omitted).

"[T]he learned-intermediary doctrine addresses the question of liability in light of the relationships between the parties involved in the prescribing, distribution, and use of prescription drugs." Nail v. Publix Super Mkts., Inc., 72 So. 3d 608, 614 (Ala. 2011). In the nearly 40 years since Stone was decided, this Court has interpreted the learned-intermediary doctrine as requiring a prescription-drug manufacturer to warn prescribing physicians of the known risks of drugs. Stone, supra; Walls v. Alpharma USPD, Inc., 887 So. 2d 881, 884 (Ala. 2004); Wyeth, Inc. v. Weeks, 159 So. 3d 649, 673 (Ala. 2014). I would not expand that duty to mandate that prescription-drug manufacturers must also instruct physicians on how to specifically monitor or mitigate those risks.

Physicians, not drug manufacturers, are in the best position to evaluate patients to determine, based on a particular patient's unique medical history, personal features, and individual characteristics, whether to prescribe medication in the first place and how each patient should be monitored thereafter. See Weeks, 159 So. 3d at 673 ("[T]he

physician stands in the best position to evaluate a patient's needs and to assess the risks and benefits of a particular course of treatment for the patient."), superseded by statute on other grounds, as recognized in Forest Lab'ys, LLC v. Feheley, 296 So. 3d 302, 315 (Ala. 2019); Walls, 887 So. 2d at 886 ("'Neither [drug] manufacturer nor pharmacist has the medical education or knowledge of the medical history of the patient which would justify a judicial imposition of a duty to intrude into the physician-patient relationship.'" (quoting McKee v. American Home Prods. Corp., 113 Wash. 2d 701, 711, 782 P.2d 1045, 1051 (1989))); In re Chantix (Varenicline) Prod. Liab. Litig., 881 F. Supp. 2d 1333, 1342 (N.D. Ala. 2012) (indicating that a drug manufacturer did not have a duty to instruct prescribing physicians not to use a particular drug as a first line treatment for smoking addiction and noting that, "as other courts have recognized, it is the responsibility of the physician as a learned intermediary to assess the risks and benefits of a particular course of treatment"). As Shire U.S., Inc., and Shire, LLC (referred to collectively as "Shire"), state in their brief to this Court, "physicians routinely make decisions about following patients and deciding what monitoring will be done over a wide range of conditions and factors" and, "[i]n making those

decisions, physicians factor in avoidance of unnecessary testing because of concerns about inconvenience and expense for patient[s]." Shire's brief at 22-23. Imposing a duty on a prescription-drug manufacturer to instruct physicians on how patients should be monitored while on prescription medication could very well interfere with the physician-patient relationship by forcing physicians to choose whether to follow the drug manufacturer's instructions or to instead rely on their own education and experience with each individual patient, with whom the drug manufacturer has had no contact. Evaluating the efficacy of any drug regimen and its impact on a patient is best left to the physician, who is best able to fully interpret any risks and the suitability for continued treatment. Imposing the duty Mark Blackburn urges essentially forces prescription-drug manufacturers into the role of medical providers.

The Alabama statutory authority upon which Blackburn relies does not establish that prescription-drug manufacturers have a duty to instruct physicians on how to mitigate risks. Section 6-5-501(2), Ala. Code 1975, defines "product liability action" broadly for purposes of determining what actions are subject to the statute of limitations applicable to product-liability actions. Section 6-5-521(a), Ala. Code

1975, part of what has been commonly referred to as Alabama's "innocent-seller act," see Lang v. Cabela's Wholesale, LLC, [Ms. 1200851, June 24, 2022] ___ So. 3d ___, ___ n.1 (Ala. 2022), defines "product liability action" in the same manner as § 6-5-501(2), but for purposes of determining what actions are subject to the innocent-seller act. Although this definition of "product liability action" includes actions seeking damages for injuries caused by "instructions" accompanying a product, it in no way defines the scope of a prescription-drug manufacturer's duty. The word "instructions" is simply part of a long list of things related to a product that can form the basis of a product-liability action for purposes of the statutes at issue. Other things listed in the definition include, for example, "installation" and "construction," terms that hardly apply to prescription drugs. Product-liability actions commonly involve products like unavoidably dangerous tools, which necessarily must be accompanied by sufficient instructions for their use. Obviously, the term "instructions" would apply to those types of actions. But nothing indicates that the legislature intended that each thing listed in the definition of "product liability action" applies to every type of product-liability action or that, by defining "product liability action," the

legislature intended to delineate a prescription-drug manufacturer's duties.

The Alabama precedent upon which Blackburn relies, which involved actions based on allegedly insufficient instructions, are not prescription-drug cases. Rather, those cases involved medical devices or nonmedical products that necessarily required instructions for their use. Accordingly, the opinions in those cases do not establish that prescription-drug manufacturers must instruct physicians on how to mitigate risks in evaluating a patient after medication is prescribed.

As this Court reiterated in 2014, "'a [prescription-drug] manufacturer's duty to warn is limited to an obligation to advise the prescribing physician of any potential dangers that may result from the use of its product.'" Weeks, 159 So. 3d at 673 (quoting Toole v. Baxter Healthcare Corp., 235 F.3d 1307, 1313 (11th Cir. 2000)). Consistent with our precedent, I would hold that, once a prescription-drug manufacturer complies with its duty to warn of the known risks associated with a particular prescription drug, it is incumbent upon the learned intermediaries, not the drug manufacturer, to decide how to monitor patient compliance, the effectiveness of the drug, and the side effects

incident to the drug's use that should be mitigated. Thus, I would answer the first certified question in the negative.[6]

[6]Because Blackburn's only theory of liability is that Shire violated what I consider to be a nonexistent duty to provide different instructions to Blackburn's prescribing physician, the second certified question is, in my view, moot for purposes of this case. Thus, I would decline to answer it.