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RECENT CASE DEVELOPMENTS

How Much Information is Enough? Understanding the Alabama Supreme Court's Expansion of the Causation Standard in Failure to Warn Claims

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Abstract
This RCD analyzes the Alabama Supreme Court's recent answer to two certified questions sent to the court from the Eleventh Circuit. The questions involved whether a pharmaceutical company's duty to warn included a duty to provide instructions about how to properly mitigate for warned of risks, and if the pharmaceutical company had such a duty could a plaintiff recover if their physician would have prescribed the same drug but just changed their monitoring scheme. The Alabama Supreme Court answered both questions in the affirmative, expanding the causation standard in failure to warn claims.

Keywords: Preemption; Physician; Label; Pharmaceutical; FDA

Summary and legal background

On November 7, 2022, the United States Court of Appeals for the Eleventh Circuit reversed and remanded the Northern District of Alabama's grant of summary judgment to Shire U.S., Inc. ("Shire") in *Blackburn v. Shire U.S., Inc.*[1] The plaintiff, Mark Blackburn, initially brought suit in the District Court for the Northern District of Alabama seeking damages for the harm he suffered from taking LIALDA,[2] a drug manufactured by Shire and prescribed to Blackburn to treat his Crohn's disease.[3] As his theories of recovery, Blackburn claimed strict liability under Alabama's Extended Manufacturers Liability Doctrine, breach of express warranty, suppression and concealment and fraud.[4] On May 8, 2017, the District Court dismissed the breach of express warranty, concealment and fraud claims with prejudice on Shire's

[1]Blackburn v. Shire U.S., Inc., No. 20-12258, 2022 WL 16729466, at *1, *4 (11th Cir. Nov. 7, 2022).

[2]LIALDA is the brand name for the drug mesalamine. It is part of a class of drugs called aminosalicylates. *Lialda*, WebMD, https://www.webmd.com/drugs/2/drug-147055/lialda-oral/details#:~:text=Generic%20Name%3A%20mesalamine,decreasing%20swelling%20in%20the%20colon. (last visited Apr. 24, 2023). The FDA approves LIALDA to treat ulcerative colitis, the sister disease of Crohn's and is often used off-label to treat Crohn's disease. Alex Brewer, *Lialda Dosage*, Medical News Today, https://www.medicalnewstoday.com/articles/drugs-lialda-dosage (last updated Jan. 18, 2022); Blackburn v. Shire U.S., Inc., 18 F. 4th 1310, 1314 (11th Cir. 2021). The drug works by decreasing swelling in the colon. *Lialda*, WebMD, https://www.webmd.com/drugs/2/drug-147055/lialda-oral/details#:~:text=Generic%20Name%3A%20mesalamine,decreasing%20swelling%20in%20the%20colon. (last visited Apr. 24, 2023).

[3]Blackburn, 18 F. 4th at 1314-16.

[4]Blackburn v. Shire U.S., Inc., No. 2:16-CV-963-RDP, 2018 WL 2159927, at *1 (N.D. Ala. May 10, 2018).

motion to dismiss.[5] On June 1, 2020, the District Court granted Shire's motion for summary judgment, which Blackburn then appealed to the Eleventh Circuit.[6]

Upon first review on November 29, 2021, the Eleventh Circuit refused to affirm the District Court decision and held that there was a genuine issue of material fact in Blackburn's failure to warn claim.[7] To assess an alternative basis for affirming the District Court's grant of summary judgment to Shire, the Eleventh Circuit also certified[8] two state law questions to the Alabama Supreme Court dealing with failure to warn claims in the pharmaceutical context. After the Supreme Court of Alabama answered the two certified questions, the Eleventh Circuit again took up the case to determine if federal law preempted this state law claim.[9] Viewing the facts in Blackburn's favor, as the court must at the summary judgment phase, the Eleventh Circuit did not find that federal law preempted Blackburn's state law claim and reversed and remanded the case for further proceedings.[10]

Learned Intermediary Doctrine ("LID")

Alabama, like the majority of U.S. states, follows a version of the LID.[11] In Alabama, it is known as Alabama's Extended Manufacturers Liability Doctrine ("EMLD").[12] Under Alabama's EMLD, a drug manufacturers duty to warn is "filtered through the 'learned-intermediary doctrine.'"[13] Accordingly, the question of whether Shire had a duty to include more details in their monitoring instructions on LIALDA's label turns on whether Shire's information about monitoring had an adequate effect on the prescribing physician.[14] The LID provides that the 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 drug's use"[15] and serves as a total defense for drug manufacturers in failure to warn claims.[16]

The purpose of the LID is to ensure that information about complex goods, namely drugs, is given to the person best able to understand it and convey it to the patient.[17] Thus, physicians are tasked with relaying the risks to patients who can only obtain the prescription drugs through physicians.[18]

[5]Blackburn v. Shire U.S., Inc., No. 2:16-CV-963-RDP, 2017 WL 1833524, at *8-10 (N.D. Ala. May 8, 2017).

[6]Blackburn v. Shire U.S., Inc., No.: 2:16-cv-00963-MHH, 2020 WL 2840089, at *1 (N.D. Ala. June 1, 2020)

[7]Blackburn, 18 F. 4th at 1319.

[8]Forty-nine states and Washington D.C. have adopted the Uniform Certification of Questions of Law Act of 1995 or 1967 or adopted their own procedures for certification using language very similar to the Uniform Certification of Questions of Law Act. Bennett Evan Cooper, *Certification of Questions of Law to State Supreme Courts*, Reuters (June 22, 2021, 3:46 PM), https://www.reuters.com/legal/legalindustry/certification-questions-law-state-supreme-courts-2021-06-22/ [https://perma.cc/ND3Z-2HCM]. The Uniform Certification of Questions of Law Act of 1995 states that a state's highest court "may answer a question of law certified to it by a court of the United States…. if the answer may determinative of an issue in pending litigation in the certifying court and there is no controlling appellate decision, constitutional provision, or statute of this State." Unif. Certification of Questions of Law Act § 3. Put simply, certification can be invoked so a federal court can avoid using an Erie guess and obtain an answer to a question of state law while still maintaining authority over the case and its outcome. *See* Fiat Motors of North America, Inc. v. Mayor and Council of City of Wilmington, 619 F. Supp. 29, 33 (D. Del. 1985). Once the state court has answered the federal court's certified questions, the federal court accepts their conclusions and decides any remaining issues necessary to resolve the case. Barbara J. Van Arsdale et al., 1A Federal Procedure, Lawyers Edition § 1:635 (2023); Bennett Evan Cooper, *Certification of Questions of Law to State Supreme Courts*, Reuters (June 22, 2021, 3:46 PM), https://www.reuters.com/legal/legalindustry/certification-questions-law-state-supreme-courts-2021-06-22/ [https://perma.cc/QU9J-H8WY].

[9]Blackburn v. Shire U.S., Inc., No. 20-12258, 2022 WL 16729466, at *1 (11th Cir. Nov. 7, 2022).

[10]*Id.* at *3-4.

[11]Kasey Adams, *50-State Survey: The Learned Intermediary Doctrine*, JD Supra (Nov. 16, 2020), https://www.jdsupra.com/legalnews/50-state-survey-the-learned-70847/ [https://perma.cc/27VS-TG93].

[12]Charles Bennett Long, *Products Liability and the Merger Doctrine: The Alabama Extended Manufacturers Liability Doctrine is No Longer the Sole Vehicle of Recourse for Plaintiffs in Alabama*, 35 Cumb. L. Rev. 671, 671 (2005).

[13]Blackburn v. Shire U.S., Inc., 2022 WL 4588887 at *4 (Ala. Sept. 30, 2022).

[14]*Id.* at *5.

[15]Reyes v. Wyeth Laboratories, 498 F.2d 1264, 1276 (5th Cir. 1974).

[16]Blackburn, 2022 WL 4588887, at *5.

[17]Watts v. Medicis, 365 P.3d 944, 949 (Ariz. 2016).

[18]Wyeth, Inc. v. Weeks, 159 So. 3d 649, 673 (Ala. 2014).

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Because the pharmaceutical company has a duty to warn the physician, not the patient, the adequacy of a pharmaceutical company's warning is determined by its effectiveness of relaying risks to physicians, not consumers.[19] When the warning conveyed to the physician is deficient, the drug manufacturer is liable for injuries sustained by patients.[20] To make out a claim under the LID a 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."[21]

Issues one and two: The supreme court of Alabama's evaluation of the certified questions

In *Blackburn*, the plaintiff developed advanced chronic interstitial nephritis fourteen months after being prescribed LIALDA, a drug Shire manufactured.[22] The label on LIALDA noted chronic interstitial nephritis as a potential risk for patients taking LIALDA and consequently recommended that the doctor evaluate the patient's renal function before starting the drug and "periodically" while on the drug.[23] However, the plaintiff argued that the label warning was deficient because it should have provided more detailed recommendations on the frequency of testing and that if the label had included this, he would have received testing more frequently,[24] and his doctor would have diagnosed him up to six months earlier.[25] And if he had ceased taking LIADLA six months earlier, he would have normal to near-normal kidney function compared to his present twenty-percent functionality.[26]

Throughout the litigation, Shire argued that it had satisfied its duties under the LID because it warned of the risk of renal impairment, and "once a drug manufacturer warns of a risk, it is up to the prescribing doctor to assess and mitigate that risk."[27] Shire also argued that Alabama law did not support Blackburn's theory of proximate cause; to recover under a failure to warn claim the plaintiff must show that if the warning were adequate, then the physician would not have prescribed the drug.[28] In response to these arguments the Eleventh Circuit certified two questions to the Alabama Supreme Court.[29] These questions were:

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?
1. 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?[30]

The Alabama Supreme Court answered both questions affirmatively.[31] In answering the first certified question, the Alabama Supreme Court relied heavily on Stone v. Smith, Kline & French Laboratories, 447 So. 2d 1301 (Ala. 1984) and its adoption of Section 402A comment k in the Second Restatement of Torts.[32] Both state that a drug manufacturer's duty to warn is equally comprised of providing directions

[19] *Id.*
[20] *Id.* at 673–74.
[21] *Id.*
[22] Blackburn, 2022 WL 4588887, at *1.
[23] *Id.*
[24] Blackburn's doctor in a deposition stated that he complied with what he believed the instructions on the label meant, which was testing much less frequent than the plaintiff alleges is adequate. *See* Blackburn v. Shire U.S., Inc., 18 F. 4th 1310, 1320 (11th Cir. 2021).
[25] Blackburn, 2022 WL 4588887, at *2.
[26] *Id.*, at *1-2.
[27] Blackburn, 18 F. 4th at 1321.
[28] *Id.*
[29] *Id.*
[30] *Id.*
[31] Blackburn v. Shire U.S., Inc., 2022 WL 4588887 at *13 (Ala. Sept. 30, 2022).
[32] Restatement (Second) of Torts § 402A comment k (1965).

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on naming the potential side effects and explaining how to mitigate said side effects.[33] The Supreme Court of Alabama's answer to this certified question broadened the causation standard for failure to warn claims that apply to Alabama's LID by recognizing claims that allege a failure to provide adequate monitoring instructions.[34]

In answering the second certified question, the Supreme Court of Alabama held that Alabama precedent did not foreclose a plaintiff from showing causation by presenting evidence that their physician would have changed the course of treatment or monitoring while still prescribing the same drug.[35] The court further stated that this conclusion flows logically from the conclusion that drug manufacturer warnings can be deficient if they lack adequate instructions on the mitigation of informed risks.[36]

Issue three: Preemption

Next, the Eleventh Circuit analyzed whether federal law preempted Blackburn's state law claim.[37] Federal law preempts state law when there is a direct conflict between state and federal law, and it is "impossible for a private party to comply with both state and federal requirements."[38]

The Food and Drug Administration ("FDA") must approve all prescription drug labels before the drug manufacturer distributes the medication.[39] After the label is approved, drug manufacturers are only allowed to alter it with the FDA's approval or under the changes-being-effected regulation.[40] To make a change without prior approval under the FDA's changes-being-effected regulation, a manufacturer can file a supplemental application in response to newly acquired information[41] to "add or strengthen a contraindication, warning, precaution," or "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product."[42]

Because the changes-being-effected regulation allows changes to a drug's label without FDA approval, drug manufacturers are typically unable to show that there was a conflict between state and federal law that made it impossible for them to obey both laws.[43] Drug manufacturers can only show federal preemption of the state law when a judge decides as a matter of law that there is clear evidence that the FDA would not have approved a change of the label.[44]

In reviewing the case under the summary judgment standards, the Eleventh Circuit viewed the facts in Blackburn's favor and found that federal law did not preempt Blackburn's state law claim.[45] The Eleventh Circuit found that Blackburn's expert's testimony about a "growing body of medical literature" that supported a more defined monitoring instruction was enough to beat preemption because the definition of "newly acquired information" must be construed broadly.[46] Further, the Eleventh Circuit held that

[33]Blackburn, 2022 WL 4588887 at *8.
[34]*Id.* at 10.
[35]*Id.* at *13.
[36]*Id.*
[37]Blackburn v. Shire U.S., Inc., No. 20-12258, 2022 WL 16729466, at *1 (11th Cir. Nov. 7, 2022).
[38]Merck Sharp & Dohme Corp. v. Albrecht, 139 S. Ct. 1668, 1672 (2019).
[39]Blackburn, 2022 WL 16729466, at *2.
[40]*Id.* The changes-being-effected regulation is a way for a drug manufacturer to make certain changes to a drug's label without getting prior approval from the FDA.
[41]Examples of newly acquired information are "data, analyses, or other information not previously submitted to the agency, which may include (but is not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data." 21 C.F.R. § 314.3(b) (2016).
[42]Blackburn, 2022 WL 16729466, at *2.
[43]Merck Sharp & Dohme Corp., 139 S. Ct. at 1679.
[44]*Id.*
[45]Blackburn, 2022 WL 16729466, at *2.
[46]*Id.*

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Shire provided no persuasive argument that the FDA would have rejected Blackburn's proposed label change.[47]

Finding that Blackburn's state law claim was not preempted by federal law, the Eleventh Circuit reversed and remanded the case for further proceedings. The case is currently pending in the United States District Court for the Northern District of Alabama.[48] The most recent action in the case occurred on April 6, 2023, when plaintiff Blackburn filed a renewed and amended motion for leave requesting to file a motion for partial summary judgment on Shire's preemption defense.[49]

Discussion

Failure to adequately monitor individuals on prescription drugs is a big problem in the United States.[50] This failure increases adverse drug events among older adults than errors in prescribing.[51] This problem will only increase in coming decades; increasingly more Americans take prescription drugs.[52] Clinical laboratories offer the potential to address this problem by providing ongoing monitoring laboratory work for individuals on long term prescription drugs.[53] However, despite the convenience afforded by increasing densities of clinical labs, many patients on long-term prescription drugs are not receiving adequate testing to detect adverse health outcomes until it is too late.[54]

One potential reason for inadequate testing and monitoring of patients on prescription drugs is the lack of adequate information to inform the doctor on the frequency of and type of monitoring on drug labels. *Blackburn* was not the first case where courts have taken up the issue of specificity in drug manufacturers' monitoring recommendations on drug labels. In *Stahl v. Novartis Pharma Corp*, the Fifth Circuit held that medical monitoring schemes are essentially instructions for the safe use of prescription drugs, and that a manufacturer's duty to warn includes a duty to provide adequate instructions for the safe use of the product, including adequate monitoring information.[55] Further, in *Formella v. Ciba-Geigy Corp*, the Michigan appeals court found a warning label to be adequate, based on the information in a label specifying blood testing frequency.[56]

Drug labels that recommend testing "periodically" or at a different unspecific and ambiguous intervals undermine the purpose of the LID. There is no standardized definition of what "periodically" means in the medical profession.[57] While some physicians may say periodically means once a year, or twice a year, other physicians could believe that periodically means a much shorter or longer duration.[58] The fundamental purpose of the LID is to ensure that information about complex goods, including drugs, is given to the person best able to pass that information on to the patient, the physician. The lack of consensus in the meaning of "periodically" here shows the potential for vastly different care on a patient-

[47] *Id.*

[48] Plaintiff's Renewed and Amended Motion for Leave to File a Motion for Partial Summary Judgment on Shire's Preemption Defense, Blackburn v. Shire, No. 2:16-CV-00963 (N.D. Ala. Apr. 6, 2023).

[49] *Id.*

[50] Michael A. Steinman et al., Beyond the Prescription: Medication Monitoring and Adverse Drug Events in Older Adults, 59 J. Am. Geriatr. Soc. 1513 (2011).

[51] Inadequate monitoring and ignoring a clinical or laboratory result were 1.4x more likely to cause an adverse drug event than prescription of an improper drug, drug dose, or dose frequency. Michael A. Steinman et al., Beyond the Prescription: Medication Monitoring and Adverse Drug Events in Older Adults, 59 J. Am. Geriatr. Soc. 1513 (2011).

[52] CDC, Health Trend Tables, Table 39: Prescription Drug Use in the Past 30 days by sex, race and Hispanic Origin, and Age: United States, Selected Years 1988-1994 through 2015-2018, (2019) https://www.cdc.gov/nchs/data/hus/2019/039-508.pdf.

[53] *LabCorp Strengthens Leadership Position in Precision Medicine with Expansion of Therapeutic Drug Monitoring Portfolio*, LabCorp, Feb. 19, 2019.

[54] Marsha A. Raebel et al., *Laboratory Monitoring of Drugs at Initiation of Therapy in Ambulatory Care*, 20 J. Gen. Intern. Med. 1120, 1120 (2005).

[55] Stahl v. Novartis Pharma Corp, 283 F.3d 254, 270 (5th Cir. 2002).

[56] Formella v. Ciba-Geigy Corp, 100 Mich. App. 649 (1980).

[57] Blackburn v. Shire U.S., Inc., No. 2:16-cv-00963-MHH, 2020 WL 2840089 at *4 (N.D. Ala. June 6, 2020).

[58] Blackburn v. Shire U.S., Inc., 2022 WL 4588887, at *3 (Ala. Sept. 30, 2022).

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by-patient basis and a high chance that no little to no patients will receive the monitoring and testing at optimal intervals. If the label of a drug uses "periodically" without a consensus definition amongst the medical community, it undermines the purpose of the LID because it provides unclear information to the physicians.[59]

Providing unclear information precludes physicians from relying on their advanced training to adequately reduce the risks of harm to consumers, thereby insufficiently protecting them.[60] Specific information on how and when to test will likely increase physicians' compliance with these monitoring protocols. Further, these ambiguous monitoring standards could lead to sub-optimal monitoring. Unclear monitoring standards are most problematic when pertaining to a hazardous but asymptotic condition, or when the condition has symptoms that mirror other minor medical concerns because testing and monitoring are the only ways the condition will be discovered and subsequently treated.[61]

Some proponents of more minimalist drug label instructions will argue that requiring pharmaceutical companies to include detailed monitoring instructions will undermine the physician-patient relationship and physician autonomy.[62] But requiring pharmaceutical companies to be more precise in their instructions for monitoring patients and mitigating risks will not undermine the physician-patient relationship. Just as doctors are free to prescribe off-label, they are free to depart from the recommended testing methods or monitoring intervals if they believe it is in their patient's best interests. On a practical level, many drug labels already include specific instructions on the frequency of patient monitoring.[63] There has been no evidence of any pushback from physicians claiming that these specific drug labels breach the physician-patient relationship or reduce their autonomy.[64]

Ultimately, providing physicians with more information about methods and frequency of monitoring and testing recommendations allows them more information to make a better determination for the individualized care of their patient.[65] For example, if one drug label recommended testing a patient periodically for kidney function, and the doctor was using the drug on a patient predisposed to risk of kidney disease, the physician would likely try and test this patient more frequently than a patient without the risk given his personalized understanding of the word periodically. However, if a different label recommended testing every four to six weeks, the doctor would likely recommend testing at four weeks, if not more frequently, for patients predisposed to kidney disease or even consider alternative treatment given the risks and demanding testing needs. Requiring drug manufacturers to define recommended testing and monitoring intervals will help ensure that patients on prescription drugs with potential silent and adverse effects receive proper monitoring and get the care they need in a timely manner.

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[59]Marsha A. Raebel et al., *Laboratory Monitoring of Drugs at Initiation of Therapy in Ambulatory Care*, 20 J. Gen. Intern. Med. 1120, 1120 (2005).

[60]*Id.*

[61]*Id.*

[62]Steven Boranian, *An Unwelcome Twist on the Learned Intermediate Rule in Alabama*, Drug & Device L. (Oct. 21, 2022), https://www.druganddevicelawblog.com/2022/10/an-unwelcome-twist-on-the-learned-intermediate-rule-in-alabama.html [https://perma.cc/LMV6-52PT].

[63]Vijay U. Rao et al., *Clinical Approach to Cardiovascular Toxicity of Oral Antineoplastic Agents: JACC State-of-the-Art Review*, 77 J. of the Am. Coll. of Cardiology 2693, 2699-2703 (2021).

[64]*Id.*

[65]Blackburn v. Shire U.S., Inc., 2022 WL 4588887 (Ala. Sept. 30, 2022).

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