Under the learned intermediary doctrine in effect in many jurisdictions, a manufacturer of a prescription drug has a duty to provide an adequate warning of the risks associated with that manufacturer’s drug to a prescribing physician. The learned intermediary doctrine is an exception to the general product liability rule that requires a manufacturer to warn the ultimate user directly.

Regardless of the learned intermediary doctrine’s focus on the warning provided to a physician, as a practical matter, the mantra, “I would never have taken this drug if I had known there was a risk,” can turn a case into an issue about whether a consumer was effectively warned. Whether a plaintiff received a warning may be legally irrelevant under the learned intermediary doctrine; however, ask yourself, how many jurors will likely ignore that plaintiff’s testimony?

As a practical matter, consumers of prescription medications receive myriad warnings from different sources regarding the risks associated with their medications. These sources could reasonably be expected to result in well-informed consumers who make considered decisions about the risks and benefits of the drugs that they take. As mentioned in a recent FDA report, “When a person decides to use a medication, he or she is agreeing to take certain risks.” See Safe Use Initiative, U.S. Food & Drug Admin., FDA’s Safe Use Initiative: Collaborating to Reduce Preventable Harm from Medications 4 (Nov. 4, 2009). In litigation, appropriately emphasizing the risk information provided to a patient may make jurors less willing to reward a plaintiff who claims that he or she had no idea that risks were associated with his or her medication. But even if a patient directly receives warning of the risks associated with a prescription medication, the legal effect of the warning remains unsettled in today’s product liability jurisprudence.

This article will address juridical attitudes toward consumer-directed pharmaceutical warnings in relation to the learned intermediary doctrine. It will then explore some of the current ways that patients receive information about the health risks associated with prescription medications.

Consumer-Directed Warnings in the Courts

Surprisingly few published opinions have addressed consumer-directed warnings in relation to the learned intermediary doctrine. There is no clear consensus among
courts that have taken up whether the doctrine insulates drug manufacturers from liability.

One school of thought considers the learned intermediary doctrine and warnings directed to consumers as inherently inimical and that the advent of consumer warnings on prescription medications as warranting abolishing the learned intermediary doctrine. The allegedly pervasive influence of direct-to-consumer advertising has undermined the doctrine in some states. See, e.g., Perez v. Wyeth, 734 A.2d 1245 (N.J. 1999); Centocor, Inc. v. Hamilton, 2010 Tex. App. LEXIS 1623 (Tex. App. Mar. 4, 2010). West Virginia has outright rejected it. State of West Virginia ex rel Johnson & Johnson Corp. v. Karl, 647 S.E.2d 899 (W.Va. 2007). Those in favor of abrogating the learned intermediary doctrine typically claim that the doctrine is an anachronism that reflects the paternalistic “doctor knows best” relationship that prevailed when the doctrine was first articulated. Similarly, they emphasize that patients have unprecedented access to medical information today and are now greatly empowered to make informed decisions about their own health care, which frees them from strict and unquestioning reliance on their physicians’ advice. In addition, they claim that cases holding the learned intermediary doctrine inapplicable to prescription oral contraceptives and mass vaccinations provide analogous precedent for the inapplicability of the doctrine in other instances if warnings have been provided directly to patients.

Relying on the underpinnings of oral contraceptive cases, the Oklahoma Supreme Court in Edwards v. Basel Pharmaceuticals, 933 P.2d 298 (Okla. 1997), held that the learned intermediary doctrine did not automatically protect a manufacturer from liability when the FDA required a manufacturer to provide a warning directly to patients. Note that in Edwards, the defendant smoked cigarettes while wearing two nicotine patches, the professional labeling stated that an overdose of the product could be lethal, but the patient insert stated that an “overdose might cause you to faint.” Id. at 299.

While there is some validity to observations regarding the evolving nature of the patient-physician relationship, it hardly compels the conclusion that we should discard the learned intermediary doctrine. Prescription pharmaceuticals are, after all, still available to patients only with prescriptions from licensed health care providers. Even Internet savvy medical mavens still lack the training, experience, and judgment to diagnose their own maladies and to identify appropriate treatment, risks, and benefits.

Even if an independent duty arises from FDA-mandated, direct-to-consumer warnings, the more reasoned conclusion is that the learned intermediary doctrine and consumer-directed warnings can peacefully coexist and provide independent defenses for pharmaceutical manufacturers defending failure-to-warn claims. When warnings are provided directly to consumers, why shouldn’t manufacturers have independent opportunities to avoid liability based on either of two or more warnings advising patients about drug risks?

Rush v. Wyeth, 514 F.3d 825 (8th Cir. 2008), represents a step in the right direction. In Rush, the plaintiff admittedly receiving patient package inserts with her medication, but she testified that she did not read them. The Eighth Circuit agreed that, under Arkansas law, the defendant, the manufacturer, was entitled to assume that the plaintiff would exercise ordinary care and, therefore, that she would read the insert’s warnings. The Eighth Circuit then held that although an adequate warning to a patient’s physician can suffice to defeat a failure-to-warn claim, the doctrine does not preclude informing a patient directly. In other words, if a patient is independently aware of a drug’s risk, then the drug manufacturer’s failure to warn adequately of the danger is irrelevant. The Eighth Circuit in Rush concluded that the trial court properly instructed the jury to find for the defendant if the plaintiff was aware of the drug’s risks before the diagnosis of her injury. Rush recognized that warning consumers directly, in addition physicians, is consistent with underlying principles of tort law and not antithetical to the learned intermediary doctrine.

Sources of Direct-to-Consumer Warnings

Begin planning your trial cross-examination of a plaintiff and identifying the evidence that you will need to demonstrate that he or she received an effective warning of the risks associated with a drug early in your case. Generally speaking, aside from the risk information provided by a prescribing healthcare professional, warnings about the risks associated with a prescription drug potentially may reach a patient through four broad categories of patient-directed information.

Patient Package Inserts

Patient package inserts, sometimes abbreviated as “PPIs,” are FDA-approved, consumer friendly adjuncts to the approved professional labeling for certain prescription drugs. The FDA requires patient package inserts only for a few drugs. For instance, 21 C.F.R. §310.501 sets forth the requirements for patient package inserts accompanying oral contraceptives, as does 21 C.F.R. §310.515 for estrogen-containing medications. Among other things, a patient package insert for an oral contraceptive must contain a boxed warning, a discussion of the drug’s contraindications, a statement of the risks and benefits associated with the drug, and a list of potential adverse reactions. For other drugs, the content of a patient package insert varies according to the drug and its risks. But patient package inserts commonly discuss what the drug is, how it works, who should not take the drug, and possibly or reasonably anticipated side effects.

Although patient package inserts are rarely required, a manufacturer may voluntarily submit one for FDA approval. Several drugs currently reach consumers accompanied by FDA-approved patient package inserts, including, for example, certain antibiotics, retinoids, and chemotherapeutic agents.

As the name implies, a patient package insert is usually included in the actual packaging intended for the consumer. This literally puts risk information and warnings in a patient’s hands every time a patient fills a prescription. If a patient opens a drug package to take the drug, the patient can in no way avoid the insert. The more a patient refills a prescription, the more times he or she will receive a warning!

Although they cover some of the same topics, a patient package insert tends to
be shorter and use less complex language than a drug’s professional labeling. Patient package inserts are intended for a different audience. If you question a plaintiff about a patient package insert during a deposition, ask the plaintiff specifically to identify anything he or she claims that he or she did not understand about the risks discussed in the insert or the particular words that he or she found confusing. Ask the plaintiff if he or she called his or her doctor or pharmacist for clarification.

Once approved, a patient package insert may be used with printed advertisements for the drug. See Ctr. for Drug Evaluation & Research, U.S. Food & Drug Admin., Consumer Medication Information (CMI): Expert and Consumer Evaluation of Consumer Medication Information 2008: Questions and Answers, http://www.fda.gov/AboutFDA/CentersOffices/CDER/ReportsBudgets/jcm163786.htm. When a plaintiff claims that a drug advertisement in a magazine either convinced him or her to start taking a drug or offered “reassurance” that continuing to take the drug was a good idea, ask if he or she read the entire advertisement. At trial, be prepared to introduce an authenticated copy of the entire document, which should include the patient package insert.

Medication Guides

Plaintiffs often admit that they received “printouts” or “flyers” from pharmacies with their prescriptions. In many cases, they are describing a FDA-approved “medication guide” created by the manufacturer. The FDA may determine that certain prescription drugs and biological products “pose a serious and significant public health concern” that makes a written, patient-oriented medication guide “necessary to patients’ safe and effective use” of the product. 21 C.F.R. §208.1(a)–(b). The FDA can require a medication guide in one of three circumstances: (1) patient labeling may help prevent serious adverse effects, (2) a drug has serious risks that patients should weigh against its benefits in deciding to use the drug, or (3) a drug is considered “important to health” and patient adherence to directions for use is critical to the drug’s effectiveness. 21 C.F.R. §208(1)(c).

Among other things, a medication guide is

- Written in “non-technical, understandable” English;
- Legible and clearly presented;
- Not promotional in tone or content;
- Scientifically accurate and consistent with the professional labeling; and
- Specific and comprehensive.

21 C.F.R. §208.20(a). The regulations further specify the formatting and required content of a medication guide. 21 C.F.R. §208.20(b).

Because the primary objective of a medication guide is to ensure that a patient is well-advised of the risks associated with the medication, risks are discussed in several different sections and subheadings of a medication guide. See 21 C.F.R. §208.20(b)(2) (“What is the most important information I should know about the drug”); 21 C.F.R. §208.20(b)(4) (“Who should take” the drug); 21 C.F.R. §208.20(b)(6) (“What should I avoid while taking” the drug); 21 C.F.R. §208.20(b)(7) (“What are the possible or reasonably likely side effects of” the drug). Note that, in terms of the section describing likely side effects, a medication guide must describe adverse “reactions that are likely to be caused” by the drug product that are serious or occur frequently.” 21 C.F.R. §208.20(b)(7)(i) (emphasis added).

While a drug manufacturer is responsible for preparing and obtaining FDA approval of a medication guide before distribution, medication guides are distributed to consumers by pharmacies, or “dispensers” or “distributors.” See 21 C.F.R. §208.24. A patient should receive a medication guide with a new prescription and with each refill.

Medication guides were not intended to be ubiquitous. When the final rule establishing medication guides went into effect in 1998, the FDA expected that “no more than 5 to 10 products per year would require such information.” Prescription Drug Product Labeling: Medication Guide Requirements; Final Rule, 63 Fed. Reg. 66479 (Dec. 1, 1998). However, in 2005, the FDA began approving classwide medication guides. As a result, medication guides are currently available for more than 200 prescription medications and over the counter drugs, including antidepressants, nonsteroidal anti-inflammatory drugs (NSAIDs), narcotic pain relievers, attention deficit hyperactivity disorder (ADHD) medications, and certain antibiotics. See U.S. Food & Drug Admin., Medication Guides, http://www.fda.gov/Drugs/DrugSafety/ucm085729.htm (listing currently available medication guides, including .pdf images) (last visited Sept. 2, 2010).

Risk Evaluation and Mitigation Strategies


The draft guidance provides a blueprint for developing and implementing REMS. Although the REMS provisions took effect only recently, the FDA’s website currently lists over 100 pharmaceutical products that have been subject to and for which it has approved REMS.

The FDA may require REMS for any drug or biological product subject to a new drug application (NDA), abbreviated new drug application (ANDA), or therapeutic biologic application (BLA) at any time if it determines that (1) “new safety information” comes to light, and (2) it is necessary to make certain that the benefits of
the drug continue to outweigh the risks. “New safety information” may develop from adverse event reports, clinical trials, post-marketing monitoring systems, medical literature, or other appropriate scientific data about a serious risk, whether previously known or unknown.

As with a patient package insert, the holder of a drug application may voluntarily propose REMS and submit them to the FDA. If the FDA approves the REMS, the manufacturer will have the same obligations that it would have had if the FDA had initiated the REMS. If the FDA rejects the REMS, which essentially means that the drug does not require heightened safeguards, the manufacturer may still pursue the strategies but without the formal obligations of a FDA-mandated REMS. The manufacturer may propose modifications to approved REMS at any time.

REMS include patient package inserts and medication guides. Among the currently approved REMS, medication guides and preferred package inserts are the predominant components. Sometimes, a drug’s REMS may require both a patient package insert and a medication guide, although the FDA expects that rarely. The FDA will regulate products with formerly approved patient package inserts or medication guides that meet the REMS program standards under the REMS provisions and requirements from this point forward. And the FDA may require a manufacturer to develop a communication plan as part of a drug’s REMS, which can include a Dear Healthcare Professional letter, web-based product support, and educational materials that it will provide to prescribers through professional associations and meetings, or the FDA can require the communications plan instead of something else.

The FDA may also require additional measures or interventions, termed “elements to ensure safe use,” abbreviated as “ETASU” in the REMS draft guidance, for drugs with demonstrated efficacy, albeit “with known serious risks that would otherwise be unavailable.” The draft guidance mentions that these elements to ensure safe use may include one or more of the following: requiring prescribers to have special certification, training, or experience; requiring drug dispensers, such as pharmacies or hospitals, to have special certification and training to dispense the drug; restricting the locations where a drug may be dispensed, such restricting dispensing privileges to hospitals; requiring laboratory testing to confirm that the patients’ condition will allow them to use the drug safely; asking patients sign acknowledgements of understanding concerning the drug’s risks; requiring periodic testing of patients to mitigate serious risk; and enrolling patients in a drug-use registry.

For example, the FDA recently approved REMS for Onsolis, an opioid indicated for breakthrough cancer pain, under which Onsolis can be distributed only through pharmacies participating in a specific registry. Verification of an Onsolis prescription from a registered provider is required and checked against a database, and the drug is delivered to a patient via courier only after the patient participates in a telephonic counseling session. See Questions and Answers About Onsolis (fentanyl buccal soluble film) (July 16, 2009), http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm172039.htm; see also Ned Milenkovich, FDA-Mandated REMS Now In Force In Pharmaceutical Industry, Drug Topics, Oct. 8, 2009.

As a practical matter, a drug’s REMS may have a two-edged blade. Requiring specialized training, certification, or participation in registry programs may deter some physicians from prescribing medications that would otherwise significantly benefit certain patients. On the other hand, consider the undeniable value of a plaintiff’s signed acknowledgement of a drug’s risks in front of a jury or in support of a dispositive motion. Moreover, a physician who participated in special training or held a certification would likely provide valuable testimony concerning his or her awareness of a drug’s risk profile, the compelling reasons for prescribing it to a plaintiff, and the counseling that a patient received about the drug’s risks consistent with obtaining informed consent.

Consumer Medication Information
Consumer medication information, sometimes abbreviated “CMI,” is another potential consumer source of risk and warnings information. As with a medication guide, consumer medication information is typically provided to a consumer attached to the bag containing a new prescription. Consumer medication information is usually prepared by an outside vendor rather than a pharmacy or a drug’s manufacturer. Although it is typically based on the FDA-approved labeling, consumer medication information is not approved or regulated by the FDA.

In 1996, Congress enacted Effective Medication Guides, Public Law 104-180, Title VI, Sec. 601, 110 Stat. 1593 (1996). Public Law 104-180 established a series of staggered benchmarks for patients so that they would receive “useful written patient information” with their prescriptions: 75 percent were to receive this useful information by 2000 and 95 percent by 2006. The statute took the additional and unusual step of prohibiting the FDA from regulating the format and content of consumer medication information while a committee consisting of consumer organizations, pharmaceutical manufacturers, health care professionals, consumer medical information developers, and others developed recommendations. The committee issued a report in 1996, “Action Plan for the Provision of Useful Prescription Medicine Information,” delineating criteria for consumer medical information to meet the law’s goals. Studies conducted by the National Association of Boards of Pharmacy evaluated progress toward the target goals. The studies released in 2002 found that while consumer medication information generally reached the target proportion of the consuming public, the “usefulness” of that information lagged. In 2006, the FDA was asked to take a more active role in meeting the law’s objectives. Consequently, in July 2006, the FDA published a guidance, “Useful Written Consumer Medication Information (CMI),” which is available at the FDA’s website. Ctr. for Drug Evaluation and Research, U.S. Food & Drug Admin., http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm080602.pdf.

The guidance considers written information accompanying a prescription “useful” when it reflects the components and formatting elements of the 1996 action plan and its content is consistent with the most recent version of the manufacturer’s labeling. Specifically, “useful” consumer medication information should be scientifically accurate, unbiased, specific, com-
prehensive, understandable to consumers, and current.

A follow-up study released in 2008 found that 94 percent of consumers received consumer medication information with new prescriptions, but only 75 percent of the CMI “met the minimum criteria for usefulness.” Thus, while these results fall short of the 2006 target, the study did show that the vast majority of consumers do receive useful written information with their prescriptions.

For your discovery planning, note that many retail pharmacies can reproduce the particular consumer medication information or medication guide that accompanied a particular prescription at a particular time. Consider serving discovery to the vendor that produced a pharmacy’s consumer medication information if necessary to obtain copies of the information that a plaintiff would have received.

**Conclusion**

Today there is an unprecedented amount of information available to a consumer regarding prescription pharmaceuticals. Not surprisingly, much of the available information concerns the drug risks. Through patient package inserts, medication guides, consumer medication information, and some of the REMS procedures, consumers are receiving user-friendly, patient-oriented information about the risks and benefits associated with prescription medications. Effective marshalling and presenting the warnings that were provided directly to a plaintiff, perhaps many times, in many different forms, over many months or years, may make the difference in a pharmaceutical product liability case. Ironically, in 2006, the American Pharmacy Association published *Patient Safety Implications on Implementation of the Current FDA-Mandated Medication Guide Program*, which raised the concerns that consumers may be overloaded with too much information from medication guides, patient package inserts, and consumer medical information, and that the direct-to-consumer information tended to place too much emphasis on risk. *Id.* at 7–11. What a wonderful problem for a defense lawyer to have.