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Induced Infringement of Method of Treatment Claims: Looking to the Label and Beyond

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Reference product sponsors often obtain patents claiming methods of using a known drug to treat a condition or disease. Because generic and biosimilar developers typically do not treat patients, and thus do not directly infringe the claims, plaintiffs must sue under a theory of induced infringement—i.e., that the generic or biosimilar developer recommended, encouraged, or promoted a patented use for the drug. Demonstrating induced infringement most often involves the label of the defendant's product, but increasingly may involve non-label evidence such as the defendant's press releases, brochures, product catalogs, advertisements, and statements to the FDA, doctors, and investors. This non-label evidence is likely to be especially significant in the biologic context.

Using a Drug Label to Prove Induced Infringement of Pharmaceutical Method Claims

The label of the accused infringing product is most often used to show specific intent to encourage physicians to practice a patented method of treatment. Showing specific intent to induce infringement is relatively straightforward if a patented use directly matches an indication on an accused product label. However, a generic drug label may describe an infringing mode without recommending, encouraging, or promoting an infringing use, or suggesting that an infringing use should be performed. In *Bayer Schering v. Lupin*, the Federal Circuit addressed induced infringement of claims for "simultaneously achieving . . . a contraceptive effect, an anti-androgenic effect, and an antialdosterone effect." Bayer argued that Lupin's accused product was indicated for "oral contraception," and the Clinical Pharmacodynamics section mentions the potential for antimineralocorticoid activity and anti–androgenic activity. *Id*. at 1319–20. The Court explained that although Lupin's label mentioned the potential for the claimed effects, "it does not do so in any way that recommends or suggests to physicians that the drug is safe and effective . . . for the purposes of inducing these effects." *Id*. at 1322. Rather, the information only makes physicians aware of the full range of the drug's pharmacological effects when prescribing the drug. Likewise, in *Grunenthal v. Alkem*, the Federal Circuit found no induced infringement of a method of treating polyneuropathic pain when the generic label was indicated only for treating moderate to severe chronic pain. According to the Court, because severe chronic pain also includes mononeuropathic pain and nociceptive pain, the Court found that the proposed label did not specifically encourage use of the drug for treatment of polyneuropathic pain. *Id.*

A plaintiff may attempt to argue that any part of the label may show specific intent to induce infringement if the language recommends or encourages one to perform a patented method, or points to other information that would. For example, in *Vanda v. West-Ward*, the Federal Circuit found that a "recommendation" in the Pharmacokinetics section of the label to perform laboratory testing to identify poor CYP2D6 metabolizers was sufficient to induce infringement of a patented method for genotyping patients for poor CYP2D6 metabolism and adjusting drug dosage. In *Sanofi v. Watson Laboratories, Inc.*, the Federal Circuit affirmed the district court's finding of induced infringement based on statements made in the Clinical Studies section of the proposed generic label. The asserted patent claimed a method of reducing hospitalization by administering dronedarone to patients having specific characteristics and risk factors. *Id*. at 642. The Clinical Studies section included the class of patients for whom the drug achieved reduced hospitalization, and a reference to a clinical study setting forth positive results relating to reduced hospitalization for patients having the claimed risk factors. *Id*. at 640-42. The Court found that there was "considerable" evidence that the proposed label encouraged administration to the patients for whom the drug achieves reduced hospitalizations—including expert testimony from both sides that prescribing physicians would look to the drug label for information on use in specific populations. *Id*. at 645-46.

Using Evidence Besides the Label to Prove Induced Infringement

Non-label evidence may become more prevalent, especially in biosimilar cases. Biosimilar developers may choose to actively market their products (because, at least as of the date of this post, they are not automatically substituted), and will likely need to submit more data to the FDA than generic developers (who need only establish bioequivalence)—all of which may be used to show specific intent to induce infringement.

GlaxoSmithKline v. Teva, a rare post-launch generic case, illustrates the use of non-label evidence to show induced infringement. The asserted patent claimed a method of decreasing mortality caused by congestive heart failure (CHF) by administering carvedilol. For several years post-launch, Teva's label omitted the CHF indication. But the FDA later required Teva's label to be identical to that of the reference listed drug, Coreg, which included CHF. After a trial before Judge Stark in the District of Delaware, the jury found Teva induced infringement during both the time when its label included CHF and when it did not. Judge Stark granted Teva's motion for JMOL, holding the plaintiff must prove that the defendant's alleged inducement—as opposed to other factors—actually caused physicians to prescribe Teva's product in an infringing manner. Judge Stark found there was ample post-launch evidence of activities not involving Teva that might have influenced physicians, such as treatment guidelines, GSK's label and advertising, and expert testimony regarding prescribing decisions.

GSK appealed, arguing the district court failed to properly consider Teva's press releases and promotional materials—which touted the drug as "equivalent" to Coreg. On October 2, 2020, the Federal Circuit sided with GSK in a 2-1 decision, holding that "when the provider of an identical product knows of and markets the same product for intended direct infringing activity, the criteria of induced infringement are met." *Id.* at 1355. The majority found that Teva's press releases and marketing communications provided sufficient circumstantial evidence to show that Teva took active steps to encourage the infringing use even during the carve out period.

The holding indicates that marketing of a generic drug as "AB-rated" or "equivalent" to a reference listed drug may lead to a finding of inducement, even where the patented use has been carved out of the generic label. And, although this was a small molecule drug case, reference product sponsors may make similar arguments in BPCIA cases, particularly when interchangeable biosimilar products are involved.

Practice Points

Any part of the label may be used to prove inducement. If the approved indication does not quite match the asserted method of treatment, there may be other sections of the label—such as Clinical Studies or Pharmacodynamics—indicating to physicians that the drug is nevertheless safe and effective for the patented use.

Plaintiffs may also attempt to use non-label evidence to show specific intent to induce infringement, and this will likely figure heavily in the biosimilar context. The Federal Circuit's holding in *GSK v. Teva* may signal to plaintiffs that even when a patented indication is omitted, touting the generic (or biosimilar) product's equivalence to the reference product may show intent to induce infringement. Plaintiffs may also attempt to use promotional or marketing materials generated by the defendant, or data submitted to the FDA showing equivalence to the reference product, to show induced infringement. Accordingly, minimizing risk of induced infringement will require extensive planning and coordination between patent counsel, regulatory counsel and research, development, and marketing groups.

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