The Fed. Circ. In June: More Liability For Generic-Drug Makers

By **Jeremiah Helm and Sean Murray** (August 2, 2024)

This article is part of a monthly column that highlights an important patent appeal from the previous month. In this installment, we examine Amarin v. Hikma and what it means for how generic drugs are marketed.

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The U.S. Court of Appeals for the Federal Circuit recently decided a case with potentially important consequences for how generic drugs are marketed, and induced infringement in general.

In Amarin Pharma Inc. v. Hikma Pharmaceuticals USA Inc., Amarin marked a drug called Vascepa that the U.S. Food and Drug Administration approved for the treatment of severe hypertriglyceridemia.

Hikma submitted an abbreviated new drug application, or ANDA, to the FDA. An ANDA is a way for a generic-drug manufacturer to bring a drug equivalent to a branded drug to market but avoid much of the regulatory cost of other approval pathways.

As part of an ANDA approval, the generic drug product copies, in relevant part, the label used by the branded drug, including the indications for the product.

When Hikma submitted its ANDA seeking approval of a generic version of Vascepa, Vascepa was only approved for the severe hypertriglyceridemia indication. While Hikma's ANDA was pending, Amarin obtained FDA approval for an additional indication for Vascepa as a treatment to reduce cardiovascular risk.

Amarin added the cardiovascular indication to its label and, at the same time, removed a warning that indicated that the effect of Vascepa on cardiovascular mortality had not been determined.

After Amarin added the cardiovascular indication, Hikma had a choice. Hikma could either modify its own label to add the cardiovascular indication, or Hikma could carve out the cardiovascular indication, and only seek approval for the original severe hypertriglyceridemia indication. This latter approach is colloquially called a "skinny label" because the generic label includes less than all of the indications for the approved drug.

A generic-drug manufacturer might choose the skinny label approach to simplify the ANDA approval process. Because one ANDA approval pathway involves the generic certifying that the patents covering the branded drug are invalid, unenforceable or will not be infringed by the generic product, a skinny label lets the generic company avoid infringing patents that only cover certain indications.

In this case, Amarin had two patents that covered the cardiovascular indication. To avoid those patents, Hikma chose to carve out the cardiovascular indication using a skinny label that sought approval to market generic Vascepa indicated for the treatment of only severe hypertriglyceridemia.

Hikma's label, however, was not an exact copy of the original Vascepa label because the Hikma label did not include the warning that the effect of Vascepa on cardiovascular mortality had not been determined.

The FDA eventually approved Hikma's generic product for treatment of severe hypertriglyceridemia. During and after the approval, Hikma issued a series of press releases related to its generic product. In these releases, Hikma referred to its generic version of Vascepa.

The releases also referred to the sales data for Vascepa, which accounted for all uses of Vascepa and not just the severe hypertriglyceridemia indication. Hikma also marketed its product on its website, with the statement, in small type, that its generic version is indicated for fewer than all approved indications of Vascepa.

After FDA approval, Hikma launched its generic product. A month later, Amarin sued, alleging that Hikma induced infringement Amarin's cardiovascular-related patents.

Amarin's complaint alleged Hikma's press releases, website, and product label — by removing the warning that the effect on cardiovascular mortality had not been determined — demonstrated that Hikma had a specific intent to encourage physicians to directly infringe the cardiovascular patents by prescribing Hikma's generic product for cardiovascular indications.

The U.S. District Court for the District of Delaware granted Hikma's motion to dismiss, holding Amarin's complaint did not sufficiently state a claim for induced inducement.

On appeal, the Federal Circuit reversed the dismissal and remanded for the case to go forward on Amarin's induced infringement theory because, in the court's view, Hikma pled sufficient factual support to plausibly support a finding of induced infringement.

The Federal Circuit drew a clear distinction between the ANDA approval process, which involves questions of infringement resolved by the skinny label, and infringement after the ANDA approval involving marketing.

The court explained that during the ANDA approval process, the generic product is merely hypothetical. The court distinguished this process from the postlaunch situation, where the generic drug is sold and marketed.

The court also distinguished Hikma's actions from situations where infringement is based solely on the scope of the skinny label. The court found that Amarin's allegations transformed the case into a different question than asked during the ANDA approval process because Amarin alleged both Hikma's label and Hikma's postapproval statements and marketing actions combined to induce infringement.

The court explained that even though the case had its genesis in the ANDA approval process, postapproval "it is nothing more than a run-of-the-mill induced infringement case." For such an inducement case, the court held, the proper analysis is to consider whether the totality of the allegations, when taken as true, plausibly plead Hikma induced infringement.

Because the case came to the Federal Circuit as an appeal of the grant of a Rule 12(b)(6) motion to dismiss, the review is only of the allegations accepted as true, and only for plausibility, not probability.

The court focused narrowly on the question of whether Hikma actively induced direct infringement by healthcare workers prescribing Hikma's generic product for cardiovascular indications. The court rejected the idea that the indications listed in Hikma's label alone controlled the infringement analysis.

Instead, the court held that other parts of the label might still support inducement, including the fact that Hikma did not include the warning from the original severe hypertriglyceridemia label that indicated a lack of testing for cardiovascular-related indications. More importantly, the court emphasized that the combination of the label and Hikma's public statements and marketing materials provided a basis for induced infringement.

Among other things, the court pointed to the fact that Hikma referred to its drug as a "generic equivalent to Vascepa" or "generic Vascepa," and Hikma's statement in a press release that Vascepa is indicated in part for the severe hypertriglyceridemia indication.

The court also noted that Hikma's releases pointed to the total Vascepa market, and not just the market for the severe hypertriglyceridemia indication — the cardiovascular indication makes up at least 75% of total Vascepa sales. The court concluded that these allegations, in combination with the label, plausibly stated a claim for induced infringement.

The court also held that Amarin's allegations presented a factual issue of what Hikma's label and public statements conveyed to the marketplaces. At the motion to dismiss stage, the court explained, any such factual disputes must be presumed in Amarin's favor.

Thus, the court held it was at least plausible that a physician could read press releases "touting sales figures attributable largely to an infringing use" and Hikma's reference to its "generic version" of a drug indicated "in part" for the severe hypertriglyceridemia indication as an instruction to prescribe Hikma's generic drug for any approved indication of Vascepa.

The Federal Circuit also addressed the issue of whether identifying the generic drug as AB-rated could avoid allegations of inducement. An AB-rated drug means there is generic equivalence for only the labeled uses, and no others. The court seemingly left open the possibility that identifying a generic drug as AB-rated might avoid induced infringement.

But the court disagreed that the allegations in this case required that result at the motion to dismiss stage because at least some of Hikma's statements did not include the disclaimer that its generic drug was AB-rated.

The court also rejected the idea that reversing the motion to dismiss would effectively eviscerate the skinny label carveouts used by generic companies to receive FDA approval. Instead, the court indicated, "clarity and consistency in a generic manufacturer's communications regarding a drug marketed under a skinny label may be essential in avoiding liability for induced infringement."

The court concluded that, at the motion to dismiss stage, Hikma's alleged actions did not achieve such clarity and consistency.

Amarin creates uncertainty in the sale and marketing of generic drugs postapproval. Under Amarin, it appears that a generic drug company may not always be able to avoid inducement just because the FDA-approved label does not include the infringing indication.

The court provided little guidance about what a generic label should include to help avoid inducement, and generally left that question unresolved. Hikma's allegedly inducing actions were also relatively general, for example stating that the drug was a generic equivalent of Vascepa. That statement accurately reflects the FDA approval, but Amarin suggests that such accurate statements regarding regulatory approval may constitute inducement.

The court's opinion may also suggest that additional context, for example clear statements in every single communication about the drug explaining the AB-rating or the approved indications, might have justified the dismissal. But, again, the exact steps that might have allowed dismissal under 12(b)(6) are not articulated.

The ultimate result from Amarin is a very permissive pleading standard for induced infringement. While Amarin was decided in the context of FDA-approved drugs and generic equivalents, the court expressly noted its decision applied a run-of-the-mill inducement analysis not limited to the specific pharmaceutical regulatory situation.

Moving forward, Amarin may allow for creative inducement pleadings outside of just the pharmaceutical context. For example, Amarin suggests that citing sales data related to a patented method might be enough to support allegations of induced infringement.

Ultimately, Amarin will likely result in more allegations of induced infringement by generic drugs postapproval, with more of those cases proceeding to at least the summary judgment stage instead of being cut off at the outset.

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