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Federal Circuit Clarifies Rules for Skinny Labeling for Generics and Biosimilar Companies

Last week, the Federal Circuit decided ***Amarin Pharma, Inc. v. Hikma Pharmaceuticals USA Inc***., 23-1169 (Fed. Cir. June 25, 2024), a case that spotlighted the issues of skinny labeling and induced infringement for generic pharmaceuticals and provided lessons for both innovator and generic companies. The core lesson is that generics and biosimilar companies must be extremely cautious in making statements about their generics when they are opting for a "skinny label" approach to avoid claims of infringement.

The Case

In 2012, the FDA approved Amarin's drug VASCEPA® (icosapent ethyl) for the treatment of severe hypertriglyceridemia ("the SH indication"). At that time, "Amarin included an express 'limitation of use,' disclosing that '[t]he effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.' ('the CV Limitation of Use')." [1] Amarin also had patents directed to the SH indication, but they were held invalid in a case involving Hikma.

In 2019, the FDA approved VASCEPA for a second indication: "a treatment to reduce cardiovascular risk (i.e., myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization) in patients having blood triglyceride levels of at least 150 mg/dL ('the CV indication')." [2] Given the new cardiovascular indication, VASCEPA's new label dropped the CV Limitation of Use. Amarin obtained two patents directed to methods of treating the CV indication, U.S. Patent 9,700,537 ("the '537 patent") and U.S. Patent 10,568,861 ("the '861 patent").[3]

In view of the invalidated patent protection for the SH indication but the existing protection for the CV indication, Hikma submitted a so-called "skinny label" for its generic icosapent ethyl directed only to the SH indication and not to the patent-protected CV indication. A skinny label, under 21 U.S.C. §355(j)(2)(A)(viii), includes a statement from the generic applicant that it is not seeking approval on its label for a particular patented method. A skinny label is typically used to avoid claims of infringement as to a particular indication or method of treatment, especially when the expiration dates of patent rights covering multiple indications are staggered. Hikma's label did not include the CV indication, but, like VASCEPA's new label, it also lacked the CV Limitation of Use that actively discouraged use of the CV indication.[4]

The FDA approved Hikma's skinny label for only the SH indication and Hikma issued a series of press releases.[5] None of the press releases stated that its product was approved for the CV

limitation and, indeed, its press release for the drug's launch stated, "Hikma's product is not approved for any other indication for the reference listed drug VASCEPA®." Hikma's website noted that its generic was AB-rated, including in small lettering, a disclaimer that reads: "Hikma's generic version is indicated for fewer than all approved indications of the Reference Listed Drug.'" [6] An "AB" rating reflects the FDA's determination that "a generic drug is therapeutically equivalent to a branded drug when the generic drug is used as labeled. It does not reflect a decision of therapeutic equivalence for off-label use." [7]

However, some of Hikma's press releases "referred to [its] product as 'Hikma's generic version of VASCEPA®' and 'generic VASCEPA®.'" Hikma's press releases also referenced VASCEPA's entire revenue for all uses, including the CV indication, which made up more than 75% of the drug's sales.[8] In addition, Hikma's AB rating did not appear in its press releases or all its public communications related to its generic icosapent ethyl.

Notwithstanding the disclaimers and the skinny label, Amarin filed suit for infringement of the '537 and '861 patents under an inducement theory, alleging that Hikma possessed "the specific intent to actively encourage physicians to directly infringe the asserted patents by prescribing its generic icosapent ethyl product for the off-label CV indication."[9] To support its inducement allegations, Amarin pointed to the label's warning and side effects sections, lacking the CV Limitation of Use. Amarin also alleged that statements in Hikma's press release like "Hikma's generic version of VASCEPA®," "generic version of VASCEPA®," and references to the entire revenue base of VASCEPA, inclusive of the CV indication were evidence of a specific intent to induce infringement of the CV indication patents.[10]

The Federal Circuit found that taken together, Hikma's label and press releases were sufficient to plausibly state a claim for infringement. The Federal Circuit was careful to note what the case was not: it is not a Hatch-Waxman case where the product is not yet on the market, it is not a section viii case where the inducement allegations rested solely on the label. Instead, it was a simple induced infringement case and, in particular, a case considered at the motion to dismiss stage, where the totality of the allegations plausibly stated a claim for induced infringement. The Federal Circuit implied that Hikma's label alone would not have supported an allegation of induced infringement. At the same time, the label's lack of the CV Limitation of Use was a factor favoring Amarin's claim.[11]

More significantly, the Federal Circuit agreed with Amarin that Hikma's press releases referring to a "generic version of VASCEPA," citing the entire revenue basis for the drug inclusive of both indications and remaining silent on the AB rating could plausibly be read to encourage a physician to prescribe Hikma's generic for the patented CV indication. In view of these facts, the Federal Circuit reversed the district court and held that Amarin's induced infringement complaint could proceed. Whether Amarin will be able to prove that Hikma's actions constituted induced infringement remains to be determined.

Practice Notes

In summarizing its opinion, the Federal Circuit stated that "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." [12]

For originators, the *Amarin* decision is good news. It provides a very clear deterrent to any statements that could create ambiguity about the scope of a generic's skinny label approval. Both the label and the generic's public statements about the originator's products can be grist for an inducement complaint.

For generic and biosimilar companies, the *Amarin* decision is a cautionary tale that underscores the extreme caution companies must take in their labeling and public statements to avoid being hauled into court on an induced infringement claim. Of course, surviving a motion to dismiss does not guarantee that Amarin will be able to successfully prove the required intent for inducement at the trial stage.

However, for generics and biosimilars, the entire point of Section viii statements and skinny labeling is to avoid the expense and uncertainty that accompany patent litigation. It seems now that seemingly basic information, such as including the branded name of the pharmaceutical product in the press release announcing the launch of a generic, can be a brick in the wall of pleading an induced infringement claim.

To reduce risk, biosimilar and generic companies should chart a conservative course with their IP counsel when labeling, launching, and marketing a skinny-labeled product, including:

- Over-communicating to the market about the indications that the product is approved for *and* the indications that the product is not approved for.
- Placing important information about the "skinny label" indications in prominent places on their websites and communications and avoiding footnotes or small print.
- Exercising care in calibrating the language on the label. Of course, conforming the generic label to the reference drug's label is an important part of the FDA approval process. However, the *Amarin* decision suggests that IP counsel should be in the loop to issue-spot and help balance induced infringement risk.
- Avoid referencing the originator's entire market or revenue—be it in indication or in dollars—when the generic or biosimilar will only be approved for an indication (or indications) that cover a fraction of that market or revenue. Clearly, Hikma's reference to the entire revenue base for VASCEPA was a significant part of the Federal Circuit's decision.

Congress created skinny labeling as a useful path to allow generics and biosimilars to come to market for fewer than all the approved indications. In view of the originator's intellectual property, that path has always been narrow and required generics and biosimilars to tread carefully. *Amarin* underscores the risks and provides guidelines for the types of communications that could land a generic in court defending against an induced infringement claim.

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1) Slip Op. at 3

2) *Id.* at 3

3) *Id.* at 8-9

4) Slip Op. at 5.

5) *Id.* at 5-6.

6) *Id.* at 7.

7) *Id.*

8) *Id.* at 6-7.

9) *Id.* at 9.

10) *Id.* at 17.

11) *Id.* at 17-18.

12) Slip Op. at 20.