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Brand's Off-Label Promotion: Valuable Tool For Generics

Law360, New York (December 08, 2011, 1:07 PM ET) -- On Nov. 3, GlaxoSmithKline PLC announced that it will pay $3 billion to settle civil and criminal allegations that it promoted the drug Avandia for off-label uses.[1] This is only the latest in a long list of such settlements. Since 2004, pharmaceutical companies have paid a combined $13 billion to settle charges of off-label promotion of numerous brand-name drugs.

A little-appreciated consequence of this promotional activity is its potential impact on patent infringement claims brought by brand companies against generics. Experience from the recently settled multibillion-dollar patent litigation involving gabapentin (Neurontin) demonstrates that evidence of off-label promotion can be admissible at trial and effective in both weakening the brand company's defense of the validity of its patent and in reducing its infringement damages. Furthermore, and perhaps of equal importance, the ability to present evidence of off-label promotion at trial can be a significant advantage in the contest for the jury's hearts and minds.

Background

In order to market a new drug in the United States, a manufacturer must first obtain approval from the U.S. Food and Drug Administration. To obtain approval, the manufacturer must submit an application to the FDA containing, among other things, a proposed label specifying the intended uses for the drug and data demonstrating the drug's safety and efficacy for each of those uses. The FDA approves the drug only for the uses with demonstrated safety and efficacy.

Once on the market, however, physicians may prescribe a drug for uses that are not approved and listed on the label, i.e., "off-label" uses. Even so, the manufacturer may not promote the drug for off-label uses. The FDA deems that doing so demonstrates that the manufacturer intends the drug to be used for purposes other than it listed in its drug application and for which the drug is approved, thereby violating the statutory prohibitions against introducing unapproved and misbranded drugs into interstate commerce.[2]

Despite the FDA's position on off-label promotion, the incentive to promote for off-label uses can be substantial, potentially lifting a run-of-the-mill drug to blockbuster status. Neurontin, for example, was a $2 billion drug for Pfizer Inc. in the year prior to generic entry and approximately 90 percent of those sales were for off-label uses.

Since Pfizer's admission of off-label promotion of Neurontin in 2004, settlements by other brand companies have reportedly spanned an impressive list of drugs, including Abilify, Actiq, Gabatril, Provigil, Zyprexa, Bextra, Geodon, Zyvox, Lyrica, Seroquel, Topomax, Botox, Celexa, Lexapro, Zonegran, Advicor, Natrecor, Detrol and Avandia.

Admissibility of Evidence of Off-Label Promotion in a Patent Litigation

Prior to the gabapentin patent litigation, it was unclear whether evidence of a brand company's off-label promotion would be admissible at trial in a patent infringement case. In the gabapentin litigation, for example, Pfizer contended that such evidence was irrelevant to any claim or defense and should in any case be excluded because any probative value would be substantially outweighed by the danger of unfair prejudice.

Shortly before trial, U.S. District Judge Faith S. Hochberg issued a ruling on the parties' in limine motions that might serve as a road map for future generic defendants seeking to introduce evidence of off-label promotion.[3] The ruling provides three independent paths to the conclusion that evidence of off-label promotion is relevant and admissible:

1) Obviousness

Invalidity based on obviousness is a common defense to patent infringement and the legal framework is familiar: The alleged infringer first attempts to establish prima facie obviousness based on a comparison of the prior art to the claimed invention. If successful, the patent holder may then attempt to rebut the prima facie case by presenting so-called secondary considerations of nonobviousness, including the invention's commercial success, long-felt but unmet need, the failure of others, skepticism by experts, copying of the invention by competitors, and others.

Pfizer asserted two of the most common secondary considerations — commercial success and long-felt but unmet need. These are closely related, and their animating idea is essentially that if the patented product had substantial sales and/or met a need that other products did not satisfy, the claimed invention could not have been obvious because normal market forces would then have produced the solution earlier.

It is not sufficient to merely demonstrate substantial sales or long-felt need, however. The patent holder must also demonstrate a "nexus" between the sales or need and the invention claimed in the patent. If, for example, the sales are not attributable to the claimed invention but to other factors such as promotional activity, they are not probative of nonobviousness.

Judge Hochberg focused on the nexus requirement and held that "Plaintiffs' off-label marketing of Neurontin is relevant to these claims insofar as the jury may infer that the marketing of the product was part of the cause of this commercial success and undermines the idea that there was a long felt need for Neurontin."[4]

It is worth noting that a different plaintiff brand company might close this door to the admissibility of evidence of off-label promotion by electing to not assert commercial success or long-felt but unmet need. However, foreclosing the brand company from asserting these common secondary considerations of nonobviousness might still be a significant pretrial achievement, even if the evidence of off-label promotion is ultimately not admitted.

2) Damages

The majority of pharmaceutical patent litigations are brought under the Hatch-Waxman Act. As such, they do not involve damages because they are filed on the basis of the generic defendant's drug application to the FDA and are typically resolved prior to the FDA's approval of the application and the launch of the generic product.

In cases where the generic defendant receives final approval and launches its product prior to the resolution of the litigation, however, the two alternative types of patent infringement damages — lost profits and reasonable royalties — may be asserted by the patent holder. This was the case in the gabapentin patent litigation, and Judge Hochberg ruled that evidence of off-label promotion is relevant to both types of damages.

With respect to lost profits, cases arising out of early 20th-century state law hold that lost profits cannot be recovered if they are predicated on the completion of illegal activity.[5] Whereas most of these cases involves facts patterns where the economic activity itself is unlawful, however, here only the promotional activity is deemed unlawful while the sales and prescriptions themselves are lawful.

Judge Hochberg held that this was a distinction without a difference and ruled that "if Defendants can prove that some portion of Neurontin sales are attributable to illegal promotion, then the jury may consider that evidence as one of the many complex factors it will weigh in calculating the appropriate damages in this case."[6] In cases where a large portion of sales of the branded drug are for off-label uses, this has the potential to dramatically reduce any lost profits award.

With respect to reasonable royalty, one of the Georgia-Pacific factors that are typically used to arrive at the royalty is "[t]he portion of the realizable profit that should be credited to the invention as distinguished from non-patented elements, the manufacturing process, business risks, or significant features or improvements added by the infringer."[7] Judge Hochberg held that off-label promotion was "just such a 'non-patented element'" and could be relevant to the jury's royalty calculation.[8]

3) Equitable Relief

In pharmaceutical patent litigations, the brand company will typically ask for a permanent injunction as part of the relief for the alleged infringement. Courts consider four factors when determining whether an injunction is warranted: (1) irreparable injury; (2) remedies available at law; (3) the balance of hardships between the plaintiff and defendant; and (4) the public interest. The last two are equitable considerations where evidence of unlawful promotional activities on the part of the brand company might be relevant. This was confirmed by Judge Hochberg, albeit in dicta.[9]

Judge Hochberg also emphasized that there would not be a separate fact hearing and that evidence of off-label promotion, along with all other evidence relevant to any equitable relief sought, had to be introduced at trial.[10] This position might be a dual-edged sword in future litigations as it suggests that brand companies might seek just such a separate fact hearing to avoid exposing the jury to evidence of off-label promotion.

In sum, generic drug companies that are involved in a patent litigation with a brand company, or that are contemplating filing a drug application with the FDA that might lead to a patent litigation, should investigate whether evidence of off-label promotion by the brand company is available or is likely to be obtained in discovery. While it is far from certain that such evidence will ultimately be deemed admissible, Judge Hochberg's in limine ruling should be a helpful roadmap.

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[1] http://www.gsk.com/media/pressreleases/2011/2011-pressrelease-710182.htm

[2] Par Pharmaceuticals is currently challenging the FDA's position that off-label promotion violates the statutory prohibitions on introducing unapproved and misbranded drugs. Par Pharmaceutical Inc. v. United States of America et al., No. 11-cv-1820 (D.D.C).

[3] In re Gabapentin Patent Litigation, No. 00-cv-2931 (D.N.J.), Doc. No. 1154 ("in limine ruling").

[4] Id. at 4.

[5] See, e.g., Gillmor v. Wright, 850 P.2d 431 (Utah 1993) (citing older cases).

[6] In Limine Ruling at 6.

[7] Georgia-Pacific Corporation v. U.S. Plywood Corporation, 318 F. Supp. 1116, 1120 (S.D.N.Y. 1970).

[8] In limine ruling at 5.

[9] Id. at 2-3.

[10] Id. at 3 n.5.