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Secondary Considerations For Pharma Patents Get 2nd Look

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In the years since the U.S. Supreme Court's landmark KSR decision redefining the standard for invalidating a patent on obviousness grounds, life sciences companies have become accustomed to fighting an uphill battle in defending the validity of their so-called "secondary" or "follow on" patents in Hatch-Waxman litigation. These patents typically are not directed to an original drug compound but instead to new formulations, dose regimens or, in some cases, new indications for a known drug.

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Typically, the case for novelty in the face of prior art disclosing the active ingredient is premised on evidence of some surprising and unexpected result achieved by using the new formulation, dose or method of treatment. Since unexpected results are a well-recognized factor for overcoming an obviousness challenge, such a showing often is enough to convince patent office examiners to issue claims.

However, in a number of cases decided in the past several years since KSR, the Federal Circuit has invalidated such patents notwithstanding evidence of traditional secondary considerations of nonobviousness like "unexpected results," "industry praise" or "commercial success." A more recent case, Ferring v. Watson, decided in the Federal Circuit in August 2014 may signal a return to some balance on this issue. At minimum, it demonstrates the court's continued struggles with how to handle obviousness challenges to pharmaceutical patents.

Some Background

Indeed, despite the "presumption of validity" and higher bar imposed by the "clear and convincing evidence" standard required to invalidate a patent, the Federal Circuit in a series of cases has invalidated formulation and dosage regimen patents under 35 U.S.C. § 103 as being obvious. These cases include Bayer Healthcare Pharms. Inc. v. Watson Pharms. Inc., 713 F.3d 1369 (Fed. Cir. April 16, 2013), where the Federal Circuit rejected Bayer's arguments regarding secondary considerations of nonobviousness in reversing the district court's decision and invalidating the asserted patent claims directed to formulations and dosing regimens for combined oral contraceptive products.

In particular, the court rejected Bayer's reliance on the FDA's request for additional safety information, dismissing the U.S. Food and Drug Administration's request as merely part of the FDA's "normal duties."

The court also appeared to place a great deal of weight on what was actually disclosed in the art, stating that even "industry praise of what was clearly rendered obvious by published references is not a persuasive secondary consideration."

One year later, in Hoffmann-La Roche Inc. v. Apotex Inc., 748 F.3d 1326 (Fed. Cir. April 11, 2014), the Federal Circuit again gave little weight to secondary considerations in invalidating formulation and dosing claims directed to a method of treating osteoporosis consisting of orally administering 150 mg of ibandronic acid, a bisphosphonate, once monthly on a single day.

In affirming the district court's finding of invalidity, the court first pointed to prior art that (1) identified a monthly dosing regimen as a possible means of delivering bisphosphonates generally, and that listed ibandronic acid as one of the many known bisphosphonic acids, (2) established that doses in the amount of 2.5 mg/day, 5 mg/day or even 35 mg/week were shown to be effective, and thus it would have been "obvious to try" to scale up those amounts to the claimed invention of 150 mg/month.

The court rejected Roche's argument that the prior art taught away from a 5 mg/day dosage because a higher frequency of gastrointestinal side effects was associated with that dosage, specifically holding that "a higher frequency of diarrhea does not necessarily teach away from the 5 mg daily dose or its equivalents, however, as the prior art indicated that modest gastrointestinal side effects must be weighed in light of the benefits of the drug."

Second, the Apotex court also rejected Roche's arguments regarding secondary considerations, essentially ignoring evidence that increased dosages created nonlinear and unexpected effects with respect to how much of the active ingredient was absorbed by the blood and the overall success of the drug. As Judge Newman noted in her dissent, "[t]he unexpected results of the patented method are conceded by the panel majority. ... Nonetheless, this court now holds that it was obvious to do what no one did or even suggested."

These outcomes were not unusual. See also Allergan Inc. v. Sandoz Inc., 726 F.3d 1286 (Fed. Cir. May 1, 2013) (reversing the district court in finding claims directed to drug combinations and methods of treating glaucoma obvious and rejecting proffered secondary considerations, including evidence of some unexpected results from the claimed drug combinations); Galderma Labs. LP v. Tolmar Inc., 737 F.3d 731 (Fed. Cir. Dec. 11, 2013) (rejecting evidence of unexpected results as sufficient indicia of nonobviousness, describing the alleged unexpected result — the lack of a percent increase in the prevalence of side effects — as constituting "only a difference in degree from the prior art results" and not a probative "difference in kind").

Secondary Considerations Get a Another Look

However, a recent decision suggests that the Federal Circuit has not given up on crediting secondary considerations to overcome an obviousness challenge. In Ferring BV v. Watson Labs. Inc., 2014 U.S. App. LEXIS 16178 (Fed. Cir. Aug. 22, 2014), the Federal Circuit held that Ferring's claims, directed towards modified release formulations of tranexamic acid (the active ingredient in the drug Lysteda), were not invalid under Section 103.

Ferring's claims were drawn to oral dosage forms or formulations for treating menorrhagia and required three elements: (1) 650 mg of the active ingredient tranexamic acid, (2) a modified release material comprising of a specified percentage of the formulation, and (3) a specified dissolution release rate of the tranexamic acid in water. Watson argued that the relevant prior art disclosed both the safety and

efficacy of a 500 mg tranexamic acid product comprising of a sustained release material called hydroxypropylcellulose for the treatment of menorrhagia, and that tranexamic acid was suitable for use with sustained release preparations such as hydroxypropylcellulose.

The Federal Circuit rejected Watson's arguments for several reasons. First, the court held that the prior art's disclosure of a 500 mg formulation was not sufficient to make obvious the claimed 650 mg formulation. Notably, the court relied on a single note from the prior art suggesting that an increased dosage would lead to increased gastrointestinal side effects as evidence that persons in the art would be motivated against creating an increased 650 mg formulation.

This is nearly the opposite approach taken by the Hoffmann-La Roche court, just four months earlier, when it invalidated claims based on a similar side effects argument. Second, the court rejected Watson's attempt to link hydroxypropylcellulose as a sustained release material with tranexamic acid, citing the failure of the prior art to specify the amount required of the release material as the reason for finding the disclosure inadequate. Finally, the court noted briefly that there was no specific evidence offered that the third limitation of the claims involving a specified dissolution release rate was disclosed.

What is most notable about the Ferring decision, however, is that in addition to its analysis of prior art, the Federal Circuit gave considerable weight to secondary considerations of nonobviousness in upholding the district court's finding. The court repeatedly referenced the fact that the FDA had granted Lysteda's new drug application "fast track" status for expedited review. In support of its point that this "fast track" status was a secondary consideration, the court quoted language from the expedited review statute, 21 U.S.C. § 356(b)(1), for the proposition that, by granting "fast track" status, the FDA had not merely performed its "normal duties" but actually "recognized that the drug was intended for the treatment of a serious or life-threatening disease or condition that demonstrated the potential to address unmet medical needs." The court thus concluded that "there was a long-felt and unmet need for a treatment for menorrhagia that avoided adverse events," and thus the patented dosage forms and formulations were not obvious.

Uncertainty Remains

While some of the issues surrounding the validity and enforceability of "follow on" patents remain muddled, the Federal Circuit's citation in Ferring to the FDA's "fast track" statute as a secondary consideration of nonobviousness presents a creative and noteworthy approach. At the very least, the Ferring opinion cuts against the trend of finding formulation and dosage regimen cases obvious, and it rebalances the weight given in the analysis to the disclosures of the prior art and secondary considerations of nonobviousness.

Still, as these cases make clear, particularly post-KSR, the demonstration of real surprising and unexpected results remains critical to defeating obviousness. It likely is not enough just to show "better" results or a "difference in degree." Rather, the validity case is strongest where success was achieved in the face of clear teaching away in the art.

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