IP Alert: Allergan v. Teva Pharmaceuticals USA: Will the Recognized Commercial Success of Restasis® Demonstrate Non-Obviousness?

Allergan v. Teva Pharmaceuticals USA: Will the Recognized Commercial Success of Restasis® Demonstrate Non-Obviousness?

By Sarah A. Kagan

At the November 6, 2018, oral arguments at the U.S. Court of Appeals for the Federal Circuit, Allergan and the St. Regis Mohawk Tribe faced off against four generic drug makers[1] who had filed Abbreviated New Drug Applications (ANDAs) at the U.S. Food and Drug Administration (FDA). Chief Judge Prost, and Circuit Judges Reyna and Hughes formed the appellate panel. The subject matter at issue relates to Restasis®, eye drops for increasing tear production. The appeal arose from a trial in the U.S. District Court for the Eastern District of Texas. The patents in suit are also involved in multiple inter partes review procedures at the Patent Trial and Appeal Board and in a separate lawsuit in the Eastern District of Texas.

Restasis® is an emulsion formulation of cyclosporin in castor oil. Allergan's U.S. Patent 5,474,979 (Ding I) describes emulsion formulations of cyclosporin in castor oil and its claims require an emulsifying system comprised of polysorbate 80 and a carbomer copolymer. U.S. Patent 5,981,607 (Ding II) describes the same emulsion system without cyclosporin. The four patents at issue in the appeal[2] are directed to the specific formulation in Restasis®.

The district court found all four patents obvious over prior art, which included the two Ding patents as well as published results from the Phase 2 and the Phase 3 clinical trials for Restasis®.

At the oral arguments, Allergan argued that the district court had improperly required statistical significance in assessing whether Allergan had shown unexpected results.[3] It also argued that the district court erroneously disregarded the evidence of commercial success and long-felt need based on the Ding I patent and a Kaswan patent; the district court viewed these patents as "blocking patents." Allergan had in-licensed the Kaswan patent and owned the Ding I patent prior to the effective filing dates of the four patents at issue in the appeal. The Kaswan patent covered use of cyclosporin to treat dry eye, while the Ding I patent covered cyclosporin emulsion formulations containing castor oil, polysorbate 80, and Pemulen®.

The district court explained the relevance of a blocking patent:

> [C]ommercial success is relevant "because the law presumes an idea would successfully have been brought to market sooner, in response to market forces, had the idea been obvious to persons skilled in the art." However, where market entry by others was precluded due to blocking patents, the inference of non-obviousness from evidence of commercial success is weak.

Findings of Fact and Conclusions of Law, page 103 (citations omitted).

Allergan characterized the district court's application of a putative blocking patent as an unwarranted extension of the holdings in Merck (2005)[4] and Galderma (2013)[5]. Allergan distinguished those cases as ones in which a drug was already enjoying FDA exclusivity and the blocking patents blocked all ways of treating a condition comparable to the claimed method. Allergan urged that there was no prior approved drug to treat dry eye, and no evidence was produced to show that the putative blocking patents actually blocked options for treatment. Allergan characterized the district court as assuming blocking without supportive evidence of any party who was actually precluded from bringing a competing product to market.

Allergan urged with respect to long-felt need that the district court focused too narrowly on castor oil/cyclosporin emulsions, rather than on any drug formulation that would solve the dry eye condition. It pointed to other companies' failed attempts to develop a dry eye treatment.

At the oral arguments, Teva pointed out the irony in Allergan's assertion that the Kaswan and Ding I patents were not blocking patents when Allergan had listed these very patents in the FDA's Orange Book as covering Restasis®. While that comment makes it sound like Allergan took inconsistent positions, listing in the Orange Book and the Blocking Patent Doctrine arguably address different questions. Listing in the Orange Book indicates that a patent encompasses a particular FDA-approved product. The application of a blocking patent indicates that potential competitors were prevented from bringing a competing, but not necessarily identical, product to market.

Chief Judge Prost raised the Federal Circuit's recent Acorda decision,[6] which held that "the magnitude of the diminution in incentive in any context—in particular, whether it was great enough to have actually deterred activity that otherwise would have occurred—is a 'fact-specific inquiry.'" The majority opinion of the Federal Circuit panel in Acorda gave a

detailed list of possible factors that could affect the weight given to a blocking patent. Chief Judge Prost asked Teva's counsel what facts should be investigated to inform this question. Teva answered that a court should look to the availability of licenses to the putative blocking patent. When Allergan took its opportunity to provide its answer to that question, it asserted that the district court should have assessed (a) the scope of the putative blocking patent, and (2) whether others could have easily designed around it, for example, by using other formulations.

Allergan asserted that the district court's failure to find non-obviousness based on secondary considerations was due to an assumption that the putative blocking patent actually blocked relevant activity. Teva, in contrast, urged that the district court carefully considered and weighed the evidence to arrive at its conclusion.

The Pharmaceutical Research and Manufacturers of America (PhRMA) filed an amicus brief in support of Allergan. PhRMA's brief pointed out that a blocking patent for a therapeutic agent does not prevent pre-FDA approval research due to a statutory exemption to infringement for such research (the safe harbor). Competitors could have done research and published their results without risk of infringing the putative blocking patents, PhRMA urged. Moreover, a competitor with a successful result could have offered to license its technology to Allergan, as a means of profiting from its research. PhRMA also asserted that a patent challenger bears the burden of proving that any potential competitors were actually blocked.

Despite labeling the blocking patent inquiry as fact-specific, the Acorda panel recognized that evidence of such factors would be both difficult to obtain and ambiguous. In a thoughtful conclusion to its discussion of the fact-specific inquiry, Judge Taranto wrote:

> In a particular case, a court may ultimately be left, for its evaluation, with the solid premise of diminished incentives, plus some evidence (possibly weak or ambiguous) about the significance of the deterrence, together with a background sense of the general realities in the area at issue that can affect the weight to be given to the evidence in the specific case.

Thus, although the Acorda decision voiced a need for a factual inquiry, at the same time it recognized the difficulty in presenting evidence of "negative acts," i.e., acts not taken. The only solid fact that a court may have to rely on is the existence of a putative blocking patent and its theoretical ability to diminish incentives to compete in its space. The Federal Circuit has the opportunity to apply its growing blocking patent guidance in this appeal. If the determination is fact-specific, as the Acorda panel held, which side bears the burden of proving the effect of the putative blocking patent? The Acorda panel stated that "the challengers always retain the burden of persuasion on obviousness." How much must the challenger prove to meet that burden? And what is the quantum of proof that must be shown to overcome the "solid premise of diminished incentives" when a blocking patent is invoked? So far, the Federal Circuit seems to have cloaked the doctrine in an aura of fact-finding, without really showing a concrete way of avoiding the presumption of blocking.

Click here to listen to oral arguments in Allergan, Inc. v. Teva Pharmaceuticals USA, Inc.

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[1] Teva Pharmaceuticals USA, Inc., Akorn, Inc., Mylan Pharmaceuticals Inc., and Mylan, Inc.

[2] U.S. Patents 8,629,111, 8,648,048, 8,685,930, and 9,248,191

[3] Teva denied that the district court had imposed such a requirement. The panel seemed uninterested in exploring this point.

[4] Merck & Co. v. Teva Pharmaceuticals USA, Inc., 395 F.3d 1364 (Fed. Cir. 2005) (reversed district court in its analysis of commercial success because the earlier patent and FDA regulatory approval depressed incentives for others to invent the weekly-dosing scheme).

[5] Galderma Laboratories, L.P. v. Tolmar, Inc., 737 F.3d 731 (Fed. Cir. 2013) (reversed district court finding of commercial success due to earlier patents owned by Galderma that may have "blocked" competition to market the FDA-approved product by any entity other than Galderma).

[6] Acorda Therapeutics, Inc. v. Roxane Laboratories, Inc., case no. 2017-2078 and -2134, decided September 10, 2018, well after the district court opinion and after the parties briefed the Allergan appeal.

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