

Litigation Notes

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IMPACT OF KSR v. TELEFLEX ON PHARMACEUTICAL INDUSTRY

The U.S. Supreme Court issued a unanimous decision reversing the Federal Circuit Court of Appeals in *KSR v. Teleflex* and in the process it wiped out approximately ten years of Federal Circuit case law that, for practical purposes, had eliminated obviousness as a meaningful basis for invalidating drug industry patents. The Federal Circuit had established a rigid rule against obviousness challenges except in cases where the prior art itself provided a teaching, suggestion or motivation, or TSM, to combine two or more prior art references so as to produce the patented invention. Because of the extreme dependence of pharmaceutical companies on their patent portfolios in order to make profits, a decision with as broad a reach as this one seems likely to have a meaningful impact on the profits of many companies in the branded drug industry over the next few years.

In our analysis, the impact of the decision is not likely to be felt evenly across the industry, but instead, it will impact some companies much more severely than others. In this report, we have attempted to identify some of the drugs that will be affected by the Supreme Court's decision and also to classify the types of patents that will be more easily challenged as a result of the decision. In general, we think that follow-on patents will be vulnerable once the basic patent on a compound has expired, and in this category we include formulation patents, controlled release patents, enantiomer patents and salt patents. In addition, we think that composition of matter patents will be at risk where the composition covers the second, third or subsequent drug in a particular class, where the composition is merely a combination of two known drugs or is merely combined with a delivery vehicle or where the composition is a relatively uncreative modification of a preexisting compound, such as the substitution of a methyl group for an ethyl group in a heterocyclic ring.

We do not believe that too much guessing is needed to see what the new patent environment will be like, since we already have the benefit of Chief Judge Michel's March 23, 2007 decision in the *Norvasc* case, in which he identified the likely changes in the court's obviousness jurisprudence. Cf. *Litigation Notes*, March 31, 2007. As discussed, we think that Judge Michel was positioning the *Norvasc* case for a relatively speedy reargument en banc, thereby providing the judges with an efficient vehicle to reach a consensus in the wake of the Supreme Court's decision. A few of the principles reflected in Judge Michel's opinion are as follows:

- (1) routine testing to optimize a single parameter, rather than numerous parameters, is obvious;
- (2) an approach that is obvious to try is also obvious where normal trial and error procedures will lead to the result;
- (3) unexpected results cannot overcome an obviousness challenge unless the patentee proves what results would have been expected;

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- (4) a reasonable expectation of success does not have to be a predictable certainty but rather it can be an expectation that can be satisfied by routine experimentation; and
- (5) motivation can be found in common knowledge, the prior art as a whole or the nature of the problem itself.

We thought that Judge Michel's Norvasc decision was a pretty good effort at predicting what the U.S. Supreme Court was planning, although we are not so cynical as to believe that someone took him aside and told him what was coming. What did come was considerably more ambiguous and nonspecific than we had expected, leaving a lot of room for the Court of Appeals to fill in the gaps. One patent law commentator, who had hoped for something much more specific, declared that the Supreme Court had done nothing more than to substitute one amorphous, hard-to-define test for another amorphous, hard-to-define test. We are not persuaded by this view. Also, observers who had been anticipating a wholesale rejection of TSM were also surprised; TSM is still alive, but it may no longer be applied as a rigid rule.

What the Supreme Court did was in effect to inject a common sense requirement in place of what had been a rigid, mechanical rule that, in the end, could be satisfied comfortably only by concluding that obviousness had not been shown. The quotable quotes from the opinion were few in number, but were adequate to explain what the Supreme Court was trying to accomplish:

- (1) It said that "a person of ordinary skill is also a person of ordinary creativity, not an automaton."
- (2) It also said that it was wrong to believe that person attempting to solve a problem would look only to those elements of the prior art that are designed to solve the same problem.
- (3) It said that familiar items may have obvious uses beyond their primary purposes.
- (4) "Rigid, preventative rules that deny factfinders recourse to common sense," it said, "are neither necessary under our case law nor consistent with it."
- (5) Finally, it said that "where there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp."

As we mentioned above, there are certain types of patents in the pharmaceutical industry that will have to be looked at, or looked at again, in light of the Supreme Court's opinion. We happen to believe that enantiomer patents are especially vulnerable, at least in cases in which the technology to separate them was available in the public domain at the time the separation was made. However, we do not believe that the courts will permit a massive extermination of drug industry patents or that a meat-axe approach to them will be used. Rather, we think the Supreme Court's only demand is that common sense be injected into the determination of what a person of ordinary *creative* skill in the art would do.

The primary examples of enantiomer patents that we regard as vulnerable include **Forest Labs'** Lexapro, **Bristol-Myers'** Plavix, **AstraZeneca's** Nexium and **Johnson & Johnson's** Levaquin. We think that all four of these drugs are especially vulnerable now, in light of the new, broader scope of obviousness. In the case of Levaquin, Mylan Labs lost at the district court level in a case that it should have won, even under the law as it existed at the time, and then it was affirmed by Judge Pauline Newman, a pro-industry Federal Circuit judge, in a non-precedential decision without opinion. In a new case, if obviousness is in the mix and if Judge Newman is avoided on appeal, then Levaquin will be a generic drug.

In most cases, it is probably impossible to determine with clarity that a drug patent that was valid under the old rules is no good now, but we do think it is meaningful to consider some of the more likely drugs that may be affected by the decision. Below, we discuss the impact of the decision on many of the drugs that are on our radar screen. The list of drugs discussed below is not an exhaustive list of such drugs, since many others also are currently the subject of patent litigation.

Forest Labs' Lexapro: Forest won this case before Judge Joseph Farnan, a strongly pro-patentee judge in the U.S. District Court in Delaware, and is scheduled to defend the decision in the Federal Circuit on May 9, 2007. Since the lower court gave no meaningful analysis of the obviousness issues, we think that a reversal in light of KSR would be reasonable to expect so as to give the lower court a chance to consider these issues again. We plan a report on the case later this month.

Bristol-Myers' Plavix: The district court trial is over, post-trial briefs have been submitted and the case is under submission to the district court judge, who will probably be influenced by the Norvasc decision, in which obviousness invalidated the patent where there were a relatively small number of options to try.

AstraZeneca's Nexium: This slow-moving case in New Jersey is in the pre-trial phase, but is subject to the fundamental problem that separation of the enantiomers of omeprazole is likely to be considered obvious.

Procter & Gamble's Actonel: Trial of this case was completed before Judge Farnan in Delaware last November, and the post-trial briefs were submitted in January of this year. Teva's fundamental argument is premised on obviousness, and therefore it would have had little chance of winning prior to the KSR and Norvasc decisions. That said, we think that Judge Farnan is unlikely to change his pro-patentee bias, but a Teva win could come out of the Court of Appeals.

Sanofi Aventis' Allegra and Allegra D: These slow-moving cases, pending in New Jersey, entail obviousness challenges made by Novartis' Sandoz, Barr, Ranbaxy, Teva, Impax and Mylan to an extensive list of method patents.

Shire's Adderall XR: Shire settled with Barr and Impax last year but is still litigating against Teva, and Andrx, as of last October, was also seeking to enter the market for this drug. Impax had made a strong obviousness argument against the Adderall XR patent in light of the Dexadrine Spansule, and it also had a good noninfringement argument based on the definition of "delayed release."

Johnson & Johnson's Topamax: Judge Chesler in New Jersey granted Johnson & Johnson a preliminary injunction last November, but in his opinion he emphasized TSM as the basis for discarding obviousness. He possibly could be persuaded to lift the injunction in light of the KSR decision, which will certainly change his view of the law when the case goes to trial.

Eisai's Aciphex: Trial in early March in New York indicates that the generics will probably lose on their claim that the Aciphex patent is invalid for inequitable conduct, but an obviousness charge was previously dismissed because of inadequate TSM, and this ruling will probably have to be revisited before the case goes to the Court of Appeals.

Eisai's Aricept ODT: Eisai's other major drug is subject to a patent challenge filed last summer by Mutual Pharmaceutical, which is likely to benefit by the new interpretation of obviousness in challenging this oral delivery formulation.

AstraZeneca's Seroquel: AstraZeneca's case against Teva, pending in New Jersey since 2005, is subject to a potent obviousness argument articulated by Teva in its amended answer filed in January of this year. AstraZeneca had overcome an obviousness rejection based on two prior patents by asserting unexpected results about the lower probability of inducing undesirable dyskinesias, but it neglected to compare the product to the closest prior art, which a person of ordinary skill would have predicted to have antipsychotic activity and lower side effects. AstraZeneca sued Sandoz, the generic drug subsidiary of Novartis, in another Seroquel case filed three weeks ago, also in New Jersey.

Adams Respiratory's Mucinex: Adams settled with the only challenger to date, and it was clear to us that otherwise the challenger, a private company, would have won. Anyone who is serious about getting back into the guaifeneson marketplace will not find Adams' patent position to be a meaningful obstacle.

Sanofi Aventis' Ambien CR: Sanofi's suit against Barr, filed in New Jersey in March, seeks to defend its patent position for a controlled release version of an existing drug used as a sleep aid. Patents on controlled release versions of existing drugs used for known functions are often considered obvious.

Sepracor's Brovana: Dey sued Sepracor in March on its patent covering bronchodilator compositions, but Sepracor will now be able to argue that formoterol was in the prior art and that finding an adequately stable aqueous solution for use in a nebulizer was obvious to a skilled drug developer.

Pfizer's Caduet: This drug is nothing more than a combination of Lipitor and Norvasc. Pfizer sued Ranbaxy, the first-filer, in Delaware in March. We expect that a primary argument against the patent will be that it was obvious to combine the two drugs to achieve lower blood pressure.

Altana's and Wyeth's Protonix: This litigation has had a contorted procedural history since it was filed in New Jersey in 2004, but the primary grounds for invalidity asserted by Teva, Schwarz/KUDCO and Sun are obviousness and obviousness-type double patenting.

Abbott's Biaxin XL: Abbott managed to prevail before Chicago Judge David Coar on its preliminary injunction motion against Teva, which had asserted a powerful obviousness argument that the extended release version of clarithromycin was obvious in light of the immediate release version, the patent on which had expired. In light of the KSR ruling, Abbott's position has been substantially weakened.

PDL Biopharma's humanized antibody patents: PDL sued Alexion in Delaware in March for infringement of its patents, the European versions of which recently survived a European Patent Office challenge on the issue of "inventive step," which is the European version of nonobvious. Alexion's product, Soliris, treats paroxysmal nocturnal hemoglobinuria.

Tyco Healthcare's Restoril: This suit against Pharmaceutical Holdings, filed in New Jersey in March, seeks enforcement of three patents covering the use of a low-dose version of an existing drug for use as a sleep aid.

Barr's Seasonale: The patent on Seasonale was reissued by the PTO, which we regarded as a bit of a miracle since the obviousness rejection made by the examiner was quite powerful. With the benefit of the new interpretation of obviousness in light of KSR, we think Watson Pharmaceuticals, the challenger, should have a fairly strong position.

Wyeth's Effexor XR: Johnson & Johnson sued Wyeth last year for infringement of a controlled release patent that covers Wyeth's biggest selling product, Effexor XR, which is responsible for \$3.5 billion in sales. In a pending reexamination proceeding, the primary issue is obviousness in light of two prior art patents that teach delivery of highly soluble agents. The KSR decision makes it easier to explain why a person of ordinary skill would have been motivated to combine the teaching of the two patents. Wyeth has its own patents, asserted against Lupin Pharmaceuticals in a case filed last month in Baltimore, but the obviousness arguments it makes against Johnson & Johnson may haunt it in the Lupin case.

Pfizer's Celebrex: Pfizer prevailed against Teva after trial in New Jersey in a ruling issued a month ago in which Pfizer's COX-2 inhibitor was held to be unobvious. Judge Lifland stated in footnote 3 that he

recognized that TSM might be rejected by the Supreme Court in the KSR case but that he believed his findings on obviousness would stand up even if TSM were rejected by the Supreme Court. Nevertheless, Teva will be able to make a pointed argument for reversal in the Federal Circuit, to which it has appealed.

Eli Lilly's Zyprexa: Lilly prevailed both at trial and on appeal against Dr. Reddy's and Teva in a challenge to Lilly's Zyprexa patent, a \$4.4 billion drug, but because of the narrow interpretation of obviousness in effect at that time, the case was decided on the basis of anticipation. A broader view of obviousness could jeopardize Lilly's current patent in light of the now expired genus patent, subsequent prior art articles by the inventor and a certain German publication that actually disclosed the Zyprexa compound, albeit with two rather conspicuous mistakes that a person of ordinary skill should have been able to correct. However, a new challenger would not have the incentive of a 180-day exclusivity if it were to prevail.

Eli Lilly's Gemzar: Lilly's second biggest drug, an injectable chemotherapy that generated \$1.4 billion last year, is subject to challenge on obviousness grounds by Sicor Pharmaceuticals, Teva and Mayne Pharma. The case was filed against Sicor and Teva in February, 2006 and was assigned to Lilly-friendly Judge Sarah Evans Barker in Lilly-friendly territory, the U.S. District Court in Indianapolis. The case against Mayne is a little more recent. The Federal Circuit undoubtedly recalls Judge Barker from the Prozac case, in which she did not even bother to discuss double patenting, which turned out to be the Federal Circuit's basis for invalidating Lilly's Prozac patent.