

# Pfizer wards off Lipitor patent challenge from leading generics firm

Pharmaceutical giant Pfizer was celebrating its triumph recently as the UK's High Court upheld the exclusivity of the main patent covering atorvastatin, the active ingredient in Lipitor, until November 2011. Hiroshi Sheraton, an associate in the law firm of McDermott Will & Emery UK LLP, based in its London office, examines the issues at stake and scrutinises the ramifications of the judgement for other ongoing cases.

On 12 October 2005, Mr Justice Pumfrey handed down his judgment in the English High Court in relation to two patents owned by Warner-Lambert (now part of the Pfizer group) covering the blockbuster cholesterol-lowering drug atorvastatin – sold under the brand Lipitor. Lipitor is the world's best selling drug, the market being estimated at around \$12bn (€10bn) per year, of which half comes from the US and around 7% from the UK.

There are separate disputes in at least the US, Norway and Austria although most attention is focussed on the outcome of the US case, which is expected in the next few months. This article looks in more detail at the reasoning of the English judge and the impact that the decision might have beyond the shores of the UK.

## ... the UK case

Two patents were in issue: EP 0 247 633 ('633) and EP 0 409 281 ('281). '633 covers the API atorvastatin itself, whereas the '281 covers the Calcium salt of atorvastatin. The earlier of the two, the '633 patent actually expires later (in November 2011) than the '281 patent (which expires in July 2010) due to the additional protection of a supplementary protection certificate (SPC).

Three separate legal proceedings were heard together. The first case was brought by Ranbaxy who sought a declaration of non-infringement of '633 by the sale of their product. The second case was also brought by Ranbaxy for the revocation of '281. Arrow Generics also brought a case for revocation of '281.

In order to launch a generic product in the near future, the generics companies would have to succeed on both non-infringement and invalidity. If successful on non-infringement of '633 – but not on invalidity of '281 – the generics could launch in the UK in 2010.

## ... infringement of '633

The issue of infringement turned on the particular chemical structure claimed by the '633 patent. The patent set out a chemical formula which showed the atorvastatin molecule with specific stereochemistry whereas the patent itself only described how to make a racemic mixture of the two possible enantiomers. Ranbaxy argued that the claim covered only the racemate and not the individual enantiomer if sold on its own relying on the fact that a stereospecific chemical structure was commonly used to also refer to the racemate. Since Ranbaxy intended to sell only a single enantiomer, they said that they did not infringe the patent when properly interpreted.

The judge held that, at the time of the patent (1986), stereochemical issues would be well known to the skilled person reading the patent. Such a skilled person would know, for example, that a racemate is a



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mixture of two chemically identical structures, but which may well show very different biological activity.

The skilled person would also know that it was preferable to separate the enantiomers in order to have the purest product possible, consisting only of the biologically active isomer. He would also be able to follow straightforward resolving techniques to separate the two isomers from the racemate.

A patent should be interpreted with the knowledge of the skilled person. The judge placed particular emphasis on the commercial effect of the patent if it were to be interpreted as covering only the racemate

but excluding the pure biologically active enantiomer. This, he said, would be both surprising and, in the eye of the reader, immediately deprive the patent of any commercial effect.

Although the formula in the claim refers to the racemate (adopting the convention relied on by Ranbaxy), the claim was held to cover both the racemate *and* the individual isomers. The declaration of non-infringement sought was therefore refused.

## ... validity of '281

The '281 patent claims the preferred isomer of atorvastatin as the calcium salt. Ranbaxy and Arrow sought to revoke the patent on the basis that it lacked novelty over an earlier publication (WO 89/07598) and was obvious in the light of the published application for the '633 patent. In order to be held valid, a patent must be both new (i.e. novel) and inventive (i.e. not obvious) when compared with earlier publications in the field.

## ... lack of novelty

'598 describe ways of making racemic atorvastatin. Although it mentioned the process of separating out the preferred enantiomer, it did not give details of how to perform this step. The judge placed emphasis on the state of knowledge and desirability of separating the enantiomers using well known techniques. In a strongly worded conclusion, the judge held that there was a clear case for invalidity of '281 based on a lack of novelty over '598.

## ... lack of inventive step

The judge went on to consider whether the '281 patent represented an inventive step over the earlier '633 patent. The earlier publication described how to make the racemate and listed a number of possible pharmaceutically acceptable salts of the drug. On the other hand, the '281 patent specifically claimed the calcium salt of the biologically active enantiomer. Referring once again to the state of knowledge of in relation to racemates, the judge held that the differences were obvious.

He also held that the advantages of better handling characteristics said to arise from the choice of the particular Calcium salt over the sodium salt were not described in the '281 patent. For that reason, those advantages could not be used as a basis for providing a distinguishing inventive step over the earlier publication. This meant that arguments for validity relied on in the European Patent Office by Warner Lambert could not provide an answer. The '281 patent was therefore also held to be invalid for obviousness over the earlier '633 patent.

...continued

### ... the result

Although technically a positive result for both sides (attracting claims of success by each party), the result maintained Lipitor's monopoly position in the UK until November 2011. Similarly, both sides intend to appeal the decision, meaning that a degree of uncertainty will continue for a further 12-18 months.

### ... implications

Will this case impact on the decision in the US case? The strict answer is that it will not. Patent laws and the way patents are interpreted can be very different between the USA and UK and the specific wording of patent claims (which form the basis for any legal dispute) can vary widely.

On the other hand, judgments from the specialist UK patents judges are often considered to be a rigorous and in-depth analysis of the technical merits of the case. In this particular case, Mr Justice Pumfrey made findings relating to the "state of the art" in 1986 and, in particular, the inventiveness of obtaining a pure enantiomer from a racemic mixture and of using different salts as pharmaceutically acceptable products. Such findings may well translate directly into the technical background considered in other jurisdictions, although the legal effect of them may vary depending on how the law is applied. Rather than give an indication of the outcome of the case, these findings may therefore be seen as a first independent evaluation of the evidence.

What then, of other European markets? Unfortunately, the position is only slightly clearer. Each of the '633 and '281 patents in issue is a "European Patent", and therefore one might expect the decision to apply to the whole of the European area. Theoretically at least,

identical patents (with identical wording) exist in each European jurisdiction. Similarly, (at least in theory) the same law of interpretation applies in each state covered by the European Patent Convention. These factors go some way to suggest that other European jurisdictions would follow the UK result. It is certainly the case that judges of different European Courts (and particularly the UK) are making efforts to ensure that inconsistent results are not achieved. Conversely, slightly different applications of the same law and the same facts can lead to very different (or even opposite) results. For technically complex patent cases with so much at stake, nothing can be guaranteed without going to the expense of litigating in each country.

### ... conclusion

Nothing has been said so far of other patents that protect Lipitor's market. The Norwegian case involves entirely different patents covering production methods and intermediate compounds used in manufacture. There are also likely to be other patents or pending applications covering different forms, formulations or uses of the drug which the generic companies may need to deal with before launching competing products. Such supplemental patents are commonly used to extend the practical life of a blockbuster drug monopoly, although they are usually considered weaker than the main patent.

This case was indeed a bold attack by Ranbaxy on the scope of Pfizer's core Lipitor patent which was defended successfully. However, the invalidity of the '281 patent may suggest a weakness in Pfizer's patent armoury that could be exploited by the generic companies in years to come. Whatever the outcome on appeal or in the US, rest assured the battle will continue.\*

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