

## Patent For Cholesterol Drug Livalo Is Valid, Judge Rules

By **Cara Salvatore**

Law360, New York (September 20, 2017, 10:54 PM EDT) -- Japanese drugmaker Kowa Co. Ltd. won a patent infringement trial against Amneal and Apotex on Wednesday when a New York federal judge delivered the verdict that Kowa's patent for the statin Livalo was valid and that the defendants were not able to show it was anticipated or obvious.

U.S. District Judge Paul Crotty also found that Toronto-based Apotex Inc. infringed the patent. New Jersey-based Amneal Pharmaceuticals LLC has already admitted to infringement.

New Jersey-based Amneal and Toronto-based Apotex were two of the eight defendants originally sued by Kowa over two patents for Livalo; the other six have settled. U.S. District Judge Paul Crotty ruled on the first patent in April, and today's 98-page ruling concerned the second patent, called the '993 patent, for "Crystalline Forms of Pitavastatin Calcium." The bench trial took place early this year.

The judge said that a 1992 European patent issued to Nissan Chemical Industries Ltd., which has assigned patent rights to Kowa and was also a party in the suit, did not inherently anticipate the '993 patent. The European patent is called '406, and its "Example 3" chemical recipe was the subject of contention here, as the parties argued about which crystalline polymorphic forms could be gotten out of that recipe, and whether it would always produce the "Form A" polymorph, as it had been known to do at least twice.

The recipe didn't include some key parameters, like the time, temperature and air pressure under which drying would occur, which can affect the water content — one of the key things in determining crystalline form. For that vagueness and other reasons, Judge Crotty said that the '406 patent can plausibly lead to polymorphs other than Form A.

"There is insufficient evidence to clearly and convincingly find that following the parameters of EP '406 Example 3 would necessarily produce Form A of the '993 patent," the judge said.

The judge did call it a "close question" — but the burden of proof is a high one, "clear and convincing," and the defendants didn't meet it, he said.

Livalo hit the U.S. market in 2010 and began to compete with the six other statins then on the market. The '993 patent was issued in 2013 with a priority date of February 2003.

Furthermore, the patent examiner had considered the '406 history in issuing the patent, and found it was different, because it didn't include crystalline or amorphous forms. He said this analysis and her sign-off on each document in the file history, suggesting she decided that '406 didn't anticipate '993, deserved an ample degree of deference.

Next the judge turned to obviousness, where he also found a lack of clear and convincing proof. That statins produce polymorphic forms was known in the industry by February 2003, and researchers were actively trying to suss out such forms. So the defendants' expert had testified that researchers would have known by early 2003 to do the "polymorph screen" that would help discover the forms of crystalline pitavastatin calcium.

Nonetheless, “defendants’ obviousness argument is driven by impermissible hindsight,” the judge said. “Crystallization and polymorphism are unpredictable ... the unpredictable possible results a [person of ordinary skill in the art] could obtain from performing a polymorph screen of pitavastatin calcium are a far cry from evidence of a ‘finite number of identified, predictable solutions’ that the Federal Circuit has declared ‘might support an inference of obviousness,’” citing a 2008 decision called Eisai Co.

And prior art didn’t flag pitavastatin calcium as a compound that could be polymorphic, the judge said, so that knowledge may not have been there in any case.

Commercial success is also a factor that suggests the invention was not obvious, and the judge found that Livalo was commercially successful. Its gross U.S. sales were \$235 million in 2015, and even more in Japan in 2016. “The absolute dollars and produced volumes are really quite substantial.”

Results surprising to those familiar with the art can also indicate nonobviousness. Some surprising results of Livalo were its higher tolerance by patients and a relatively low rate of interactions with other drugs, the judge said.

As a final note, the judge also remarked on the fact that six of the eight original defendants in the case have settled, a suggestion that those defendants thought the patent was valid, the judge said.

Then he had to look at Apotex’s infringement — only Apotex’s, because Amneal had admitted infringement. The judge credited Kowa’s expert’s testimony that Apotex’s product was, in fact, structurally a Form A. It shared the same general characteristic peaks in a diffractogram as Form A. Kowa’s experts convinced the judge that some variation in peak intensity is expected.

Representatives for the parties were not immediately available for comment.

Kowa is represented by Kathleen Carr and David Conlin of Mintz Levin.

Amneal is represented by Steven Maddox of Maddox Edwards PLLC. Counsel information for Apotex was not immediately available.

The case is Kowa Co. Ltd. et al. v. Amneal Pharmaceuticals LLC, case number 1:14-cv-02758, in the U.S. District Court for the Southern District of New York.

--Editing by Alanna Weissman.