

A Clarification Of Obviousness-Type Double Patenting

Law360, New York (November 05, 2012, 4:21 PM ET) -- In *Eli Lilly and Co. v. Teva Parenteral Medicines Inc.*, the Federal Circuit affirmed the U.S. District Court for the District of Delaware's decision that Eli Lilly's patent to pemetrexed is not invalid for obviousness-type double patenting. The Federal Circuit's decision provides important guidance on one of the most complex areas of U.S. patent jurisprudence and explains how information in the specification can be used in a double patenting analysis, discusses when obviousness-type double patenting may arise between product and method claims and notes that unexpected results may be relevant to obviousness-type double patenting.

The Patent at Issue

The patent at issue, U.S. Patent 5,344,932, relates to Eli Lilly's Alimta (pemetrexed) product, which is used in the treatment of advanced nonsquamous non-small cell lung cancer. Claims 1, 2 and 7 recite Markush groups that encompass a number of structurally related antifolate compounds, including pemetrexed. Claim 3 is directed specifically to pemetrexed.

Pemetrexed and the other structurally related antifolates claimed in the '932 patent exhibit anti-cancer activity by inhibiting folate-specific enzymes that selectively regulate DNA synthesis (TS inhibition), thereby inhibiting cancer cell growth and division. In contrast, prior art antifolates inhibit both DNA and RNA synthesis, which can be toxic for normal cells utilizing RNA synthesis.

The '932 patent is part of a family of patents that includes U.S. Patent 5,028,608 and U.S. Patent 5,248,775, both of which issued prior to the issuance of the '932 patent.

Claim 3 of the '608 patent recites an antifolate compound, which differs from pemetrexed only by having a five-member thiophene ring in the aryl region, as opposed to pemetrexed's six-member phenyl ring.

Claim 7 of the '775 patent recites an intermediate compound, which the '775 patent teaches can be used to produce pemetrexed.

The District Court Decision

Three generic drug manufacturers, Teva Parenteral Medicines Inc., Barr Laboratories Inc. and APP Pharmaceuticals, LLC (collectively Teva), filed abbreviated new drug applications (ANDAs) with paragraph IV certifications alleging that the '932 patent is invalid, unenforceable or not infringed by their proposed generic products. The invalidity issue before the Federal Circuit was whether the '932 patent is invalid for obviousness-type double patenting over claim 3 of the '608 patent or claim 7 of the '775 patent.

Teva presented the following arguments:

- The '608 Patent: Pemetrexed is obvious over the '608 Compound claimed in the '608 patent because prior art antifolate compounds had a phenyl group in the aryl position (the sole difference between pemetrexed and the '608 Compound), providing "conventional wisdom" to substitute a phenyl group for the thiophene ring of the '608 Compound.
- The '775 Patent: Pemetrexed is an obvious use for the '775 Intermediate, particularly when viewed in light of the '775 specification, which describes a process of synthesizing pemetrexed using the '775 Intermediate. Even without that disclosure, a skilled chemist presented with the '775 Intermediate "would have recognized pemetrexed as an obvious end product."

The district court disagreed with Teva's arguments.

Addressing the '608 patent, the district court stated that a skilled artisan would not have only focused on the aryl region, as Teva contends, but "would have pursued changes outside of the aryl region to improve TS inhibition and would have avoided introducing a phenyl group into the '608 Compound based on previous reports of toxicity with analogous antifolate structures."

For example, methotrexate, an antifolate compound with a phenyl group at the aryl position, was well known in the art and exhibits undesirable side effects related to toxicity.

Addressing the '775 patent, the district court noted that the '932 patent does not claim the '775 Intermediate, and so, "the teachings from the '775 patent's specification were inapplicable." The court also stated that pemetrexed would not have been obvious over the '775 Intermediate because of the "many possible choices" available to the skilled artisan for using the intermediate.

The Federal Circuit Decision

Teva presented similar arguments to the Federal Circuit:

The '608 Patent

- Citing the Federal Circuit's 2009 decision in *Amgen Inc. v. Hoffman-La Roche Ltd.*, Teva argued that the district court erred because "the correct analysis involves only the differences between the claims at issue, so that any features held in common between the claims — in this case, all but the aryl regions of the '608 Compound and pemetrexed- — would be excluded from consideration."
- Teva repeated its "conventional wisdom" argument based on prior art antifolates.
- Teva argued that the district court erred in finding "a phenyl group undesirable within the structural context of the '608 Compound."
- Teva argued that "principles of bioisosterism" would have led to the replacement of the thiophene group with a phenyl group.

The '775 patent

Citing the CCPA's 1931 decision in *In re Byck* and the Federal Circuit's 2010 decision in *Sun Pharmaceutical Industries Ltd., v. Eli Lilly and Co.*, Teva argued that the '775 patent's disclosure of using the '775 Intermediate to make pemetrexed renders obvious the '932 patent claim to pemetrexed.

The Federal Circuit rejected Teva's arguments.

The Federal Circuit noted that, as in any obviousness analysis, in an obviousness-type double patenting analysis, differences between the claims "cannot be considered in isolation — the claims must be considered as a whole." Thus, the Federal Circuit concluded that the district court "did not err by examining whether one of ordinary skill in the art would have been motivated to modify the '608 Compound to create pemetrexed, considering the compounds as a whole."

On the merits, the Federal Circuit emphasized that an obviousness-type double patenting analysis in a chemical context requires "some reason" for modifying a chemical structure, coupled with "a reasonable expectation of success" in doing so.

The Federal Circuit noted that Lilly had presented evidence of "contemporary experience and understanding in the TS field" that substituting a phenyl group into the '608 Compound would have been undesirable, given "earlier reports of associated inefficacy and toxicity." The court found no error in the way the district court weighed the evidence and decided the issue in Lilly's favor.

Addressing the '775 patent, the Federal Circuit emphasized that an obviousness-type double patenting analysis should rest on a comparison between the claims at issue "with the earlier patent's written description considered only to the extent necessary to construe its claims." This is because:

The focus of the obviousness-type double patenting doctrine ... rests on preventing a patentee from claiming an obvious variant of what it has previously claimed, not what it has previously disclosed.

The Federal Circuit addressed *Byck*, *Sun* and two other cases where the specification of the earlier patent was relied upon to invalidate the claims of the later patent under the doctrine of obviousness-type double patenting: *Geneva Pharmaceuticals Inc. v. GlaxoSmithKline PLC* (Fed. Cir. 2003) and *Pfizer Inc. v. Teva Pharmaceuticals USA Inc.* (Fed. Cir. 2008).

In *Byck*, the patent at issue claimed an insulated coil coated with a phenol-oil composition, but the patentee had already patented the same phenol-oil composition in a patent that disclosed its use for coating coils. In *Sun*, the patent at issue claimed methods of using gemcitabine for treating cancer, but the earlier patent claimed gemcitabine and taught that it was useful to treat cancer.

In *Geneva*, the patentee claimed methods of using clavulanic acid for treating antibiotic-resistant bacteria but owned an earlier patent that claimed clavulanic acid and disclosed its use against the same bacteria. In *Pfizer*, the patent at issue claimed methods of administering an anti-inflammatory drug, but the patentee had previously patented the same drug in a patent that disclosed its use in the same methods.

The Federal Circuit characterized these cases as representing “a limited exception:”

Byck, *Geneva*, *Pfizer* and *Sun* thus “address the situation in which an earlier patent claims a compound, disclosing the utility of that compound in the specification, and a later patent claims a method of using that compound for a particular use described in the specification of the earlier patent.”

Furthermore, in each of those cases, the claims held to be patentably indistinct had in common the same compound or composition — that is, each subsequently patented “use” constituted a, or the, disclosed use for the previously claimed substance.

The Federal Circuit distinguished the claims at issue:

- Pemetrexed and the '775 Intermediate are two distinct compounds
- Pemetrexed can be made by many different processes that do not require the '775 Intermediate
- The '775 patent “offered no protection for pemetrexed” and the '932 patent does “not incorporate or require use of the '775 Intermediate”

Accordingly, the Federal Circuit affirmed the district court’s decision finding that the '932 patent claims are not invalid for obviousness-type double patenting.

Unexpected Results

In a portion of the decision that might be dicta itself, the Federal Circuit noted that the district court’s refusal to consider Lilly’s evidence of unexpected results appears to have been based on misunderstood dicta in *Geneva*. In an effort to clarify this aspect of obviousness-type double patenting jurisprudence, the Federal Circuit stated:

[T]he district court relied on a footnote in *Geneva*, in which we remarked only that inquiry into secondary considerations is not required in every obviousness-type double patenting analysis, not that such evidence is off-limits or irrelevant. The district court’s categorical repudiation of Lilly’s evidence was therefore erroneous. When offered, such evidence should be considered; a fact-finder “must withhold judgment on an obviousness challenge until it has considered all relevant evidence, including that relating to the objective considerations.”

Obviousness-Type Double Patenting at the USPTO

Obviousness-type double patenting is one of the items on a U.S. Patent and Trademark Office examiner's checklist of issues to consider when examining a patent application. Manual of Patent Examining Procedure (MPEP) § 804 provides guidance on this issue and states, "[w]hen considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art."

However, the MPEP states further, "[t]his does not mean that one is precluded from all use of the patent disclosure." For example, according to the MPEP, permitted uses of the specification include "as a dictionary to learn the meaning of a term in the patent claim" and referring to "those portions of the specification which provide support for the patent claims."

Product Claims Vs. Method Claims

While patent holders may welcome the discussion in this decision on the rationale behind *Byck*, *Geneva*, *Pfizer* and *Sun*, those cases still leave applicants in a difficult position. A patent to a new product must disclose a practical use for that product in order to satisfy 35 USC §§ 101 and 112.

If the patentee also wants to claim methods of using that product, it may be precluded from doing so by the doctrine of obviousness-type double patenting. One way to avoid this issue is to present both product and method claims in the original patent application.

If the examiner issues a restriction requirement and requires the claims to be pursued in separate applications, 35 USC § 121 will shield the claims from obviousness-type double patenting, as long as the granted claims are consonant with the claims that were subject to the restriction requirement. Although this strategy does not work for every situation, it is one that applicants should keep in mind if they are interested in obtaining both product and method claims.

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