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Astrazeneca vs. Teva

Court of Milan, 24 December 2020, docket number 8782/2020

Headnote

The last available decision on Fulvestrant in Italy was handed down by the Court of Milan on 24 December 2020, which held invalid/ineffective three patents of AstraZeneca. With a detailed and extensive reasoning, the Court declared EP'573 invalid for lack of inventive step, EP'138 invalid both for lack of inventive step and for lack of support, and IT'490 ineffective as it merely claimed part of the invention the subject matter of EP' 138.

Summary

On 24 December 2020 the Court of Milan issued its decision on the alleged infringement and validity of the patents EP 2266573 (EP'573), EP 1250138 (EP'138), and IT 1333490 (IT'490) of Astrazeneca by the generic of Fulvestrant marketed by Teva Italia S.r.l. ("Teva").

Astrazeneca AB and Astrazeneca UK LIMITED (jointly "AZ" or "Plaintiffs") sought a declaration of infringement of the Italian portion of EP'573 and EP'138 – and, of the corresponding Italian patent IT'490. All patents - belonging to the same family – claimed a specific pharmaceutical formulation prolonged-release that contains "Fulvestrant" as active ingredient for the treatment of breast cancer.

Teva, in return, submitted a counterclaim seeking a declaration of invalidity of the patents.

This judgment followed other non-final judgments, which have held invalid the same patents in proceedings between the patentee and Actavis.

The Court of Milan followed the same reasoning adopted by the previous national decisions[1]. The choice of the Court to follow the previous judgments – repeatedly mentioned in the grounds of the decision – allowed the Court to reach a decision quickly without staying the proceedings to wait for the previous decisions to become *res judicata*.

The Court of Milan declared EP'573 invalid for lack of inventive step, EP'138 invalid both for lack of inventive step and for lack of support, and IT'490 ineffective as it merely claimed part of EP'138 invention.

The subject matter of EP'573 was a particular formulation - for the treatment of breast cancer - made with a base of castor oil that allows for extended release and administrated by intramuscular

[1] Court of Milan 24 July 2019 (no. 7427/2019) declared EP'573 invalid. Court of Appeal of Turin 12 June 2020 (no. 624/2020) declared EP'138 invalid and IT'490 ineffective.

administration. In order to assess the validity of the patent, the Court applied the so-called *problem solution approach.* The person skilled in the art was identified in a team of experts, including at least one pharmacologist and one chemist specialised in pharmaceuticals with extensive knowledge of formulations based on steroids and, optionally, an oncologist specialized in the treatment of breast cancer. The closest prior art was identified in a publication of Howell ("H.") – published in the British Journal of Cancer in 1996.

The technical problem to be solved as the subject of the patented invention was defined as: make available a pharmaceutical formulation with a base of castor oil containing Fulvestrant in high concentration which allows for sufficient release of Fulvestrant over a prolonged period of time, so that it is therapeutically effective, safe and well tolerated by patients in the treatment of breast cancer.

The invention was considered obvious by combining H. with another publication (McLeskey) which disclosed the only feature of the invention missing in H. (i.e. the co-solvents - ethanol and benzyl alcohol - used in EP'573 to solubilize Fulvestrant in castor oil).

The Court rejected *inter alia* the argument of the plaintiffs that in H. there was a technical prejudice to use a high concentration of Fulvestrant.

As to the lack of inventive step of EP'138, a patent having as subject matter a second medical use of the same formulation of EP '573, the person skilled in the art was the same team of experts identified for EP'573 and the Court based its conclusions on the same publications which led to the invalidity of EP '573.

In particular, H.'s publication was considered as the closest prior art document. H. described a clinical study - performed on 19 patients - in which the pharmacological and anticancer effects of Fulvestrant were evaluated. H. in his article disclosed all the characteristics claimed by EP'138, except for the presence in the formulation of co-solvents.

The Court rejected AZ's argument that the therapeutically effective plasma level (claimed by the patent) could not be deduced from H.'s study because of the small and then unreliable number of patients involved in the study. The Court held that the study was reliable as it had been included in the dossier for the marketing authorization for Faslodex (the medicine based on Fulvestrant, marketed by AZ) sent to the regulatory authorities.

It is worth noting that the Court rejected the patentee's argument that H. could not be considered as part of the state of art because it did not describe in detail the Fulvestrant formulation thus not allowing to reproduce the teaching. According to the Court, differently from the assessment of novelty, the reproducibility requirement is not decisive to assess whether a document is part of the state of the art.

AZ alleged that the technical problem had to be identified in maintaining the characteristics of the Fulvestrant formulation. However, the Court observed that starting from H. the technical problem had to be identified as providing a formulation with high doses of Fulvestrant therapeutically effective, safe, and well tolerated by the patient.

According to the Court, the solution of the technical problem was obvious in the light of the publication of M. In particular, the Court held that i) M.'s study is a publication in the same field; ii)

it expressly cites H.'s publication; iii) it develops a pre-formulation with the desired concentration of Fulvestrant on a castor oil base; iv) the pre-formulation is suitable for intramuscular administration; v) the pre-formulation is capable of providing effective and long-lasting plasma levels; vi) the pre-formulation appears to be well tolerable vii) the formulation of H. does not seem to include alcohol, and thus the person skilled in the art would have sought to modify it without adding an excessive quantity of irritant alcohol.

EP'138 was held invalid also for lack of support because of the amendments to the claims which followed the opposition proceedings before EPO (concluded in 2015). Indeed, the original claims were product-related and were amended to second medical use claims. According to the Court, this led to an "inadequacy" of the patent description.

The Court observed that the patent met the requirement of sufficient disclosure only with respect to formulation, but in order to reproduce the invention in its entire claimed scope of protection - referred to second medical use - experimental research and trials would be necessary. Such activity would amount to an undue effort for the person skilled in the art who would be compelled to work by trial and error. Hence, according to the Court the evaluation of sufficient disclosure requires the verification of all the steps characterizing the invention and thus the steps related with the therapeutic treatment.

Finally, IT'490 was declared ineffective because its subject matter - a pharmaceutical formulation containing Fulvestrant for the treatment of breast cancer - falls within the scope of EP'138's claims covering any malignant and benign disease of breast and reproductive system. The Court applied article 59 of the Italian intellectual property Code according to which, if both an Italian patent and an European patent (validated in Italy with the same priority or filing date) have been granted to the same inventor for the same invention - the national patent ceases to produce its effects from the date on which the opposition procedure is concluded maintaining the European patent. The Court observed that such provision is implicitly applicable also to the case where the national patent protects only part of the same invention protected by the European patent.

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