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Supplementing your understanding of supplementary protection certificates

The Milan Court of First Instance recently addressed the validity of a supplementary protection certificate (SPC) held by Amgen based on a first marketing authorisation in Italy filed by Hoffmann La Roche (HLR), relating to the drug Kadcyla, which is used in the treatment of breast cancer. HLR argued that:

- Amgen had no right to base its SPC on HLR's first market authorisation, since no agreement or relationship existed between the parties which would permit this; and
- the active agent of Kadcyla did not fall within the scope of the relevant patent.

The court held that the SPC was invalid based on the second issue, thus leaving open the first issue.

Facts

Amgen is the holder of SPC UB2014CCP1383 (the ‘‘383 SPC’) designating as the basic patent EP 0 865 448 B2 (the ‘‘448 patent’). In the ‘383 SPC application Amgen relied on HLR’s first market authorisation for the drug Kadcyla, which contains the active agent trastuzumab emtansine.

The claims of the ‘448 patent were directed to anti-HER2 monoclonal antibodies, which are active against mammary tumours expressing HER2. The inventive concept of the ‘448 patent was that these antibodies are not only used as a carrier for a cytotoxic agent, but are also active themselves since they induce apoptosis (ie, programmed cell death) in the tumour cells. Importantly, the ‘448 patent did not disclose that the antibodies could be conjugated with a cytotoxic moiety. Amgen has no such product on the market and thus relied on HLR’s first market authorisation in the ‘383 SPC application.

Trastuzumab emtansine is a conjugate of the anti-HER2 monoclonal antibody trastuzumab, which is covalently coupled to the cytotoxic molecule DM1 (emtansine) by a stable thioether linker. Thus, it is a new substance with respect to the already known monoclonal antibody trastuzumab and it has a different structure and biological activity. Trastuzumab emtansine is the subject of European Patent 1 689 846 B1 and a separate SPC, UB2013CCP1342 in the name of ImmunoGen Inc, with HLR as the licensee.

Legal background

In 2015 HLR sued Amgen before the Milan Court of First Instance, arguing that Amgen's ‘383 SPC was invalid because:

- Amgen did not own the first market authorisation for Kadcyla (trastuzumab emtansine) and HLR had not authorised the use of its first market authorisation to Amgen;
- Amgen's '448 patent only claimed certain antibodies with apoptotic activity, not a conjugate of an antibody with a cytotoxic compound; and
- HLR was not infringing Amgen's patent.

In support of its first argument, HLR noted that Article 3(a) of EU Regulation 383/2009 allows an SPC to be granted only if:

- there is a valid basic patent covering the drug product; and
- the owner obtains first market authorisation for the drug product.

HLR also maintained that a first market authorisation can be relied on under Regulation 383/2009 only where a commercial relationship exists between two parties.

With respect to the second argument, HLR noted that the '448 patent covered only antibodies having apoptotic activity as such and did not disclose that the antibodies could be conjugated with a cytotoxic moiety.

In response, Amgen argued that Article 3(b) of Regulation 383/2009 does not require that the SPC applicant be the owner of the respective first market authorisation. Therefore, HLR's position was contrary to the general principle that the grounds for nullity of an industrial property right are statutory. Amgen also asserted that HLR's position was contrary to the European Court of Justice (ECJ) case law in Biogen (C-181-95) where the court did not object per se to an SPC being based on a third-party first market authorisation.

In addition, Amgen argued that HLR had erroneously interpreted the claims and the description of the '448 patent. According to Amgen, the ECJ allows an SPC to be granted even when it relates to active principles that are not explicitly mentioned in the claims of the basic patent, with the proviso that the active principle or product must nonetheless be identified in the claims, if not structurally, at least in a functional way (ie, that the claims would be interpreted as referring implicitly, but necessarily and in a specific manner to the active principle which is the subject of the SPC). Amgen argued that the claims of the '448 patent should be construed to refer in a functional way to trastuzumab emtansine.

Milan Court of First Instance decision

In Italian patent litigation proceedings, the judge, who typically does not have a technical background, usually appoints a technical expert selected from Italian and European patent attorneys who are registered in a list allowing them to act before the court. The judge is not bound by the expert's opinion, but he or she usually follows it unless there are obvious objections to the expert's opinion raised by the parties in the proceedings. In the present case, the judge followed the opinion of the court-appointed expert who concluded that the compound trastuzumab emtansine did not fall within the scope of the claims of the '448 patent, thus leaving unanswered the question of whether Amgen could rely on HLR's first market authorisation in the '383 SPC application.

The court first examined the claims of the '448 patent on the basis of the patent specification in order to reach a proper claim construction. The description of the '448 patent clearly states that the claimed antibodies are a selection of possible anti-HER2 antibodies, some of which were already known. The antibodies selected and claimed by the inventors are those that have apoptotic activity per se (ie, they can induce programmed cell death in the target cells). These antibodies are combined with a different active principle (ie, a cytotoxic or cytostatic compound). The antibodies allow the composition to induce apoptosis, making it possible to decrease the amount of cytotoxic drug with the advantage of decreasing its side effects, in particular its toxicity against non-tumour cells.

The court rejected Amgen's argument that the claims should be interpreted as providing a means to carry and target a second apoptotic drug to the tumour cells. This targeting function was already obtainable by known anti-HER2 antibodies which did not display apoptotic activity.

The court also rejected Amgen's argument that the term 'antibody' should mean both the antibody itself and a conjugated antibody. Referring to the patent description, the court noted that the claimed antibodies can recognise a specific region or epitope of HER2, which is different from the epitopes addressed by known anti-HER2 antibodies, and that they display apoptotic activity through binding. The '448 patent did not disclose or claim conjugated antibodies.

The court analysed whether HLR's Kadcyla (trastuzumab emtansine) fell within the scope of the claims of Amgen's '448 patent. In so doing, the court considered whether HLR's product had apoptotic activity and concluded that this activity was absent, based on both the assessment report of Kadcyla and the implicit admission of Amgen, which had not provided evidence of any apoptotic activity of trastuzumab emtansine. In addition, no evidence supported the claim that the conjugate trastuzumab emtansine might be equivalent to trastuzumab alone. Thus, HLR's product did not fall within the scope of Amgen's claims. Also for these reasons, previous EU case law (Medeva and Eli Lilly) was deemed inapplicable.

The court concluded that Amgen's '383 SPC should be revoked, since the conjugate trastuzumab emtansine did not fall within the scope of the '448 patent's claims.

In assessing the infringement issue the court held that the conventional criteria for infringement should be followed, which are less stringent than those set out by ECJ case law concerning SPCs. In view of the absence of an apoptotic effect of the antibody in the trastuzumab emtansine conjugate, the court concluded that infringement must be excluded.

Comment

The Milan Court of First Instance decided on the invalidity of Amgen's '383 SPC by applying a rule of reason based on non-compliance, from a technical point of view, of the product subject to the first market authorisation with the claims the '448 patent on which the SPC was based. Unfortunately, this finding of invalidity rendered moot the other, perhaps more interesting question of whether an SPC application can refer to a third party's first market authorisation in the absence of a specific contractual relationship between the SPC applicant and the first market authorisation owner. This decision is subject to appeal, thus the question remains open.

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