Beyond patent enforcement: the Herceptin phoenix

While Western pharmaceutical companies struggle to enforce their IP rights in India, Roche has taken an unorthodox but surprisingly effective stance, as Debashish Banerjee and Shukadev Khuraijam explain.

Roche sprung a surprise of sorts at the expense of Indian biopharmaceutical company Biocon and US drugmaker Mylan when it succeeded in securing an interim injunction restraining them from relying upon, or otherwise referring to, Herceptin, Herclon or Biceltis or using any data relating to the drug trastuzumab marketed as Herceptin, Herclon or Biceltis including data relating to its manufacturing process, safety, efficacy and sales.

The injunction extended to any press releases, public announcements, promotional or other materials for their drugs Canmab and Hertraz and stopped them claiming any similarity with Herceptin, Herclon or Biceltis.

Trastuzumab is a $6 billion per year biological drug sold by Roche under the brand names Herceptin, Herclon or Biceltis and is a blockbuster drug for the treatment of human epidermal growth factor receptor 2-positive (HER2+) breast cancer. Roche obtained approval for import and marketing of trastuzumab in India in 2002 and patent protection for 'Herceptin' was also secured under Indian patent 205534, which had a term up to May 2019.

There is interesting history to this drug. The Indian Ministry of Health had mooted the idea of issuing a compulsory license under Section 92 of the Indian Patents Act, 1970, which pertains to compulsory licences in circumstances of national emergency or extreme urgency or public non-commercial use, mainly owing to prohibitive pricing in India. However, in July 2013, the Department of Industrial Policy and Promotion (DIPP) refused to grant a compulsory licence, following which the Ministry of Health recommended the government exercise its powers under Section 66 of the patents statute to revoke the Herceptin patent in the public interest. In a remarkable turn of events, Roche chose to let its Indian Herceptin patent lapse prematurely by not paying the renewal fee. Apparently, pursuant to the lapse of the Herceptin patent, Biocon and Mylan co-developed a purportedly biosimilar version of trastuzumab under the brand names Canmab and Hertraz respectively.

IP enforcement of a biological drug is unprecedented in the developing hotbed of Indian IP jurisprudence—big ticket pharma patent battles have so far stuck to the more traditional turf of chemical pharmaceuticals. Biosimilars differ from generic chemical drugs because their active ingredients are huge molecules with intricate structures which are almost impossible to replicate in minute detail. A biosimilar drug is similar to the innovator biopharmaceutical product only in view of the structural and manufacturing complexities involved in the production of biopharmaceuticals. Due to the unique starting material and complex manufacturing processes, it is not possible to precisely reproduce a biological in the same way a pharmaceutical chemical generic can be reproduced.

In the matter at hand, Roche's argument was two-pronged. Its first allegation was that Biocon and Mylan were allegedly misrepresenting their drugs as "trastuzumab", "biosimilar trastuzumab" and a "biosimilar version of Herceptin" without following the due process for their drugs being approved as biosimilars in accordance with the Guidelines on Similar Biologics issued in 2012. The second limb of its challenge accused Biocon and Mylan of passing off their goods as "Trastuzumab", "biosimilar Trastuzumab" and a "biosimilar version of Herceptin". The Drug Controller General of India (DGCI) was also made a party to the suit for giving permission to Mylan and Biocon to launch Canmab and Hertraz.

The guidelines prescribe specific standards for the development and evaluation of biosimilar biologics and seek to ensure the comparability of safety, efficacy and quality between the innovator biologic and the biosimilar molecule, prior to approving the latter as a biosimilar product. A "similar biologic" is defined thus: a "biological product/ drug produced by genetic engineering techniques and claimed to be 'similar' in terms of safety, efficacy and quality to a reference biologic, which has been granted a marketing authorization in India by the DCGI on the basis of a complete dossier, and with a history of safe use in India."

At the first hearing—heard *ex parte*—Roche contended that all applications for manufacturing and marketing authorisation of similar biologics in India are required to be evaluated under the guidelines and only approved products may be represented as biosimilar products. Roche argued that Biocon's and Mylan's approvals could not be said to have satisfied the requirements for a biosimilar drug under the guidelines, because the protocol and design study for Canmab was filed and approved by the DCGI prior to the guidelines becoming effective. Further, the approval had had been granted very quickly which made a weak case for compliance with the guidelines.

Roche also drew the court's attention to the fact that there was no publicly available record of registration of Phase I and Phase II clinical trials by Biocon and Mylan for the "purportedly biosimilar trastuzumab". This clearly contravened an official notification effective June 15, 2009, stipulating that registration of all phases of a clinical trial with the Clinical Trials Registry in India was mandatory prior to the initiation of any such clinical trials.

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Roche sought to restrain Biocon and Mylan from introducing their drugs to the Indian market as biosimilar products, until appropriate tests and studies prescribed under the guidelines were conducted and appropriate approvals obtained.

In addition, Roche also sought to restrain Biocon and Mylan from using its trademark Herceptin and the reputation and goodwill attached to it.

After hearing the arguments, Biocon was directed by the court to disclose the nature of approvals it had obtained for its biosimilar product at the time of the next hearing, which was fixed for February 28, 2014. Further, the court agreed with Roche that the misrepresentations made by Biocon and Mylan by referencing the brand name Herceptin amounted to passing off since the latter companies' impugned statements alleged their drugs were of the same safety, efficacy and quality as Herceptin. These misrepresentations were likely to deceive patients, the court found. It held that Biocon and Mylan were likely to derive unfair advantage from the reputation and goodwill enjoyed by Herceptin, and that Roche would suffer prejudice and irreparable injury if an interim order were not passed in the matter. It therefore granted the injunction, pending the February 28 hearing.

Biocon and Mylan responded swiftly and challenged the order by filing appeals before the Division Bench (two judge bench) of the Delhi High Court. After hearing the appeals, the bench directed they be treated as applications and listed before the same judge who had granted the injunction. When the applications were heard, Biocon and Mylan conveyed that they would forbear from using the trademarks Herceptin, Herclon or Biceltis in any press releases or public announcements for their drugs Canmab and Hertraz. However, Biocon and Mylan pressed for modification or vacation of the earlier order in view of the hardship it was causing them, given the drugs in question had already been launched.

The primary bone of contention at the hearing was whether Biocon and Mylan were entitled to use the package insert currently in circulation while marketing their drugs in the country. It was their contention that the package insert was duly approved by the Drug Authority, making it fit for use while marketing the drugs in question, unless the approval was first revoked by the Drug Controller.

Roche argued against the use of the package insert since no approval had been granted by the Drug Controller for the package insert *per se*. It asserted that Biocon's package insert slavishly reproduced its own package insert, albeit with various misrepresentations. While Biocon had submitted evidence to prove that the label, carton and package insert were submitted to the Drug Controller, no document established that the package insert in question had been specifically approved.

Weighing the circumstances, the court allowed Biocon to use the package insert in question until the February 28 hearing, with the caveat that it should have the necessary approval of the package insert in the first place. The court clarified that if the approval had not been obtained, the interim order passed earlier would continue without modification.

Biocon and Mylan would have not seen this action coming. The proceeding is significant in that it heralds something unparalleled in the area of biologic drugs enforcement. It remains to be seen whether Roche is triumphant with a confirmatory order or whether Biocon and Mylan manage a reprieve. ■

Debashish Banerjee is a managing associate at Remfry & Sagar. He can be contacted at: debashish.banerjee@remfry.com

Shukadev Khuraijam is a partner – designate at Remfry & Sagar. He can be contacted at: shukadev.khuraijam@remfry.com