(2015) 11 DEL CK 0270

In the Delhi High Court

Case No : CS (OS) No. 3284/2015

Genentech Inc. and Others — APPELLANT

Vs

Drugs Controller General of India and Others — RESPONDENT

Date of Decision : 02-11-2015

Acts Referred:
Civil Procedure Code, 1908 (CPC) — Order 39 Rule 1, Order 39 Rule 2, 149, 80(2)

Citation : (2016) 65 PTC 107

Hon'ble Judges : Manmohan Singh, J.

Bench : Single Bench

Advocate : Rajiv Nayar, Sandeep Sethi, Sr. Advs., Niti Dixit, Darpan Wadhwa, N. Mahavir, Samiksha Godiyal and Roshni, Advocates, for the Appellant; Amit Mahajan, and Rishi Kant Singh, Advocates, for the Respondent

Judgement

Manmohan Singh, J.

Caveat No. 1151/2015

Since the counsel for the caveator has appeared, the caveat is discharged.

I.A. No. 23044/2015 (under Section 149 CPC)

Counsel for the plaintiffs states that the court fee shall be furnished within three days. In view of the statement made by the learned counsel for the plaintiffs, the application is disposed of.

I.A. No. 23042/2015 (under Section 80(2) CPC)

Issue notice. Let reply be filed by the next date.

At this stage without going into the merit of the case, the plaintiffs are granted permission to file the suit against the defendants No. 1 and 2 also.

I.A. No. 23043/2015 (exemption)

Exemption allowed, subject to just exceptions.

The application is disposed of.

CS(OS) No. 3284/2015 and I.A. No. 23041/2015 (u/o XXXIX R.1 & 2 CPC)

1. Let the plaint be registered as a suit.

2. Issue summons in the main suit and notice in the application. Counsel appearing on behalf of the defendants No. 1 and 3 accept same. Written statement be filed by the defendants No. 1 and 3 within four weeks. Summons and notice be issued to the defendant No. 2, on filing of process fee and Regd. A.D. Covers, returnable on 17th November, 2015.

3. Learned counsel for the plaintiffs is pressing for ad-interim order. The same is opposed by the learned counsel appearing on behalf of the defendant No. 3. Both the parties have made their submissions for some time. Counsel for the defendant No. 3 admitted that the approval of the drug was granted on 2nd June, 2015. The drug in question has not been launched in the market. However, she states that approval of label and carton is granted recently.

4. The present suit has been filed by the Plaintiffs to seek injunctions against the Defendants on account of the imminent threat and credible apprehension of the approval and launch of a purported biosimilar version of the Plaintiffs'' biological drug Trastuzumab (the "Plaintiffs'' Trastuzumab") for the treatment of HER2+ metastatic breast cancer, HER2+ early breast cancer and HER2+ metastatic gastric cancer (collectively, the "Indications"), by Defendant No. 3 (the "Defendant''s Drug"), without the Defendant''s Drug having been adequately tested for any of the Indications in accordance with the Drugs and Cosmetics Act, 1940, as amended (the "Drugs Act"), the Drugs and Cosmetics Rules, 1945, as amended (the "Drugs Rules"), the Guidelines on Similar Biologies, 2012 (the "Biosimilar Guidelines").

5. Mr. Rajiv Nayar, learned senior counsel for the plaintiffs, states that the approvals of the defendant No. 3''s drug granted by the defendant No. 1 are contrary to the rules and various provisions of The Drugs and Cosmetics Act, 1940. The averments are made in para 25 to 34 of the plaint. He submits that neither clinical tests of Phase I and Phase II have been conducted by the defendant No. 3 nor the same are registered with the defendant No. 1. The said fact has not been denied by the learned counsel for the defendant No. 1 and defendant No. 3. He states that the said approvals have been granted on the basis of clinical test of Phase III which itself is contrary to the Rule 122 of the Drugs Act and the Biosimilar Guidelines. The second submission of the learned counsel for the plaintiffs is that the original application was filed by the defendant No. 3 only for one indication i.e. Metastatic HER2-Overexpressing Breast Cancer. However, approvals have been granted for two other indications without conducting any clinical trials.

6. As far as Biosimilar Guidelines are concerned, counsel has referred para 5 and 6 of Guidelines on Similar Biologics: Regulatory Requirements for Marketing

Authorization in India.

7. Mrs. Prathiba M. Singh, learned senior counsel appearing on behalf of the defendant No. 3, has denied all the arguments of the plaintiffs'' counsel who stated that the plaintiffs are misleading the Court as the approvals have been granted as per Rules as well as Biosimilar Guidelines, 2012. Counsel states that the clinical trials of Phase I and Phase II have been abbreviated under sub rule (1) (iv) (b) and sub-rule (3) of Rule 1 of Schedule Y and Rule 122A and 122B of the Drugs Act. On query, learned senior counsel appearing on behalf of the defendant No. 3, submits that conducting of clinical trials of Phase I and Phase II takes number of years. She also submits that the Drug Authority may or may not exempt/abbreviate the Phase I and Phase II by exercising its discretion. In the present case, the discretion is exercised in favour of the defendant No. 3 to exempt Phase I and Phase II as per Rules. Therefore, the Civil Court should not interfere with the same.

8. In reply, Mr. Sandeep Sethi, learned Senior counsel appearing on behalf of the plaintiffs, has referred Schedule Y and submits that the defendant No. 3 was supposed to conduct the clinical trials of all phases. In the present case, the approval is granted without the clinical trials of Phase I and Phase II. The act of the defendant No. 1 is contrary to the provision of sub-rule (1) (iv) (a) of Rule 1 of Schedule Y read with Rule 122, Form No. 44 and Appendix 1. He referred the requirement of the clinical trial of Phase I and Phase II in support of his submissions. The same reads as under:

"(6) Human Pharmacology (Phase I) -

(i) The objective of studies in this Phase is the estimation of safety and tolerability with the initial administration of an investigational new drug into human(s). Studies in this Phase of development usually have non-therapeutic objectives and may be conducted in healthy volunteers subjects or certain types of patients. Drugs with significant potential toxicity e.g. cytotoxic drugs are usually studied in patients. Phase I trials should preferably be carried out by investigators trained in clinical pharmacology with access to the necessary facilities to closely observe and monitor the Subjects.

(ii) Studies conducted in Phase I, usually intended to involve one or a combination of the following objectives:-

(a) Maximum Tolerated Dose: To determine the tolerability of the dose range expected to be needed for later clinical studies and to determine the nature of adverse reactions that can be expected. These studies include both single and multiple dose administration.

(b) Pharmacokinetics, i.e., characterization of a drug''s absorption, distribution, metabolism and excretion. Although these studies continue throughout the development plan, they should be performed to support formulation development and determine pharmacokinetic parameters in different age groups to support

dosing recommendations.

(c) Pharmacodynamics: Depending on the drug and the endpoints studied, pharmacodynamic studies and studies relating to drug blood levels (pharmacokinetic/ pharmacodynamic studies) may be conducted in healthy volunteer Subjects or in patients with the target disease. If there are appropriate validated indicators of activity and potential efficacy, pharmacodynamic data obtained from patients may guide the dosage and dose regimen to be applied in later studies.

(d) Early Measurement of Drug Activity: Preliminary studies of activity or potential therapeutic benefit may be conducted in Phase I as a secondary objective. Such studies are generally performed in later phases but may be appropriate when drug activity is readily measurable with a short duration of drug exposure in patients at this early stage.

(7) Therapeutic Exploratory Trials (Phase II) -

(i) The primary objective of Phase II trials is to evaluate the effectiveness of a drug for a particular indication or indications in patients with the condition under study and to determine the common short-term side-effects and risks associated with the drug. Studies in Phase II should be conducted in a group of patients who are selected by relatively narrow criteria leading to a relatively homogeneous population. These studies should be closely monitored. An important goal for this Phase is to determine the dose(s) and regimen for Phase III trials. Doses used in Phase II are usually (but not always) less than the highest doses used in Phase I.

(ii) Additional objectives of Phase II studies can include evaluation of potential study endpoints, therapeutic regimens (including concomitant medications) and target populations (e.g. mild versus severe disease) for further studies in Phase II or Phase III. These objectives may be served by exploratory analyses, examining subsets of data and by including multiple endpoints in trials.

(iii) If the application is for conduct of clinical trials as a part of multi-national clinical development of the drug, the number of sites and the patients as well as the justification for undertaking such trials in India shall be provided to the Licensing Authority.

(8) Therapeutic Confirmatory Trials (Phase III) -

(i) Phase III studies have primary objective of demonstration or confirmation of therapeutic benefit(s). Studies in Phase III are designed to confirm the preliminary evidence accumulated in Phase II that a drug is safe and effective for use in the intended indication and recipient population. These studies should be intended to provide an adequate basis for marketing approval. Studies in Phase III may also further explore the dose- response relationships (relationships among dose, drug concentration in blood and clinical response), use of the drug in wider populations, in different stages of disease, or the safety and efficacy of

the drug in combination with other drug(s).

(ii) For drugs intended to be administered for long periods, trials involving extended exposure to the drug are ordinarily conducted in Phase III, although they may be initiated in Phase II. These studies carried out in Phase III complete the information needed to support adequate instructions for use of the drug (prescribing information).

(iii) For new drugs approved outside India, Phase III studies need to be carried out primarily to generate evidence of efficacy and safety of the drug in Indian patients when used as recommended in the prescribing information. Prior to conduct of Phase III studies in Indian subjects, Licensing Authority may require pharmacokinetic studies to be undertaken to verify that the data generated in Indian population is in conformity with the data already generated abroad.

(iv) If the application is for the conduct of clinical trials as a part of multi-national clinical development of the drug, the number of sites and patients as well as the justification for undertaking such trials in India should be provided to the Licensing Authority along with the application."

9. Mr. Sethi, learned senior counsel appearing on behalf of the plaintiffs, submits that the result of clinical trial of Phase III is dependent upon the results of trials of Phase I and Phase II. Thus, on the basis of clinical trial of Phase III even if valid cannot be treated as biosimilar product. Mr. Sethi also referred the newspaper reporting dated 1st November, 2015 of The Economic Times in which it is reported that Indian Pharmaceutical and Biotechnology firm Intas Biopharmaceuticals has curtailed the distribution of Razumab, a biosimilar of Genentech''s Lucentis, an injectable drug used for treating macular degeneration, barely two months after its launch following stray incidents of adverse reactions like inflammation in eyes. He says that since it is a biosimilar product and reference drug used in the process is of the plaintiffs'' drug, therefore in case the defendant No. 3 wishes to manufacture and market the drug in question, it has to comply all the requisite requirements.

10. After small hearing, it appears to the Court that the serious issues are raised in the matter. The Authority has granted the approval to the defendant No. 3 on 2nd June, 2015. The product has not been launched. The explanation given by the defendant No. 3 would have to be considered after filing of the reply. Let the reply be filed within ten days. Rejoinder thereto be filed by the next date. List the application for hearing on 17th November, 2015.

11. It is clarified that no adjournment shall be granted and the matter would be taken up on day-to-day basis. As soon as the hearing is concluded, the order would be passed. Both the parties are granted time to file the written submissions by 16th November, 2015.

12. Till the next date of hearing, the defendant No. 3 is directed not to launch the drug in question in the market.

13. Copy of the order be given Dasti to both the parties under the signatures of the Court Master.

