IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TEIJIN LIMITED, TEIJIN PHARMA LIMITED, and TAKEDA PHARMACEUTICALS U.S.A., INC.,	)	
Plaintiffs,	)	
v.	)	C.A. No. _____
INDOCO REMEDIES LIMITED,	)	
Defendant.	)	

COMPLAINT

Plaintiffs Teijin Limited ("Teijin Ltd."), together with its subsidiary Teijin Pharma Limited ("Teijin Pharma Ltd.") (collectively, "Teijin"), and Takeda Pharmaceuticals U.S.A., Inc. ("Takeda") (collectively, "Plaintiffs"), for their Complaint against Defendant Indoco Remedies Limited ("Indoco"), hereby allege as follows:

PARTIES

1. Plaintiff Teijin Ltd. is a Japanese corporation, having a principal place of business at 6-7, Minami-Hommachi 1-chome, Chuo-ku, Osaka 541-8587, Japan.

2. Plaintiff Teijin Pharma Ltd. is a Japanese corporation, having its principal place of business at 2-1, Kasumigaseki 3-chome, Chiyoda-ku, Tokyo 100-8585, Japan.

3. Plaintiff Takeda is a Delaware corporation, having its principal place of business at 1 Takeda Parkway, Deerfield, Illinois 60015.

4. Upon information and belief, Defendant Indoco is a corporation organized and existing under the laws of India, having its principal place of business at Indoco House, 166 CST Road, Kalina, Santacruz (East), Mumbai 400098, India.

5. Upon information and belief, Indoco, either directly or through an agent acting at its direction, is in the business of, *inter alia*, developing, manufacturing, and packaging active pharmaceutical ingredients and pharmaceutical products for sale in the United States market, including in this judicial district.

NATURE OF THE ACTION

6. This is a civil action for infringement of United States Patent Nos. 7,361,676 ("the '676 patent"), 8,372,872 ("the '872 patent"), and 9,107,912 ("the '912 patent") (collectively, the "patents-in-suit"). This action arises under the Patent Laws of the United States, 35 U.S.C. § 100 *et seq*.

JURISDICTION AND VENUE

7. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

8. This Court has personal jurisdiction over Indoco because, *inter alia*, Indoco has committed or aided, abetted, contributed to, or participated in the commission of, the tortious act of patent infringement under 35 U.S.C. § 271(e)(2) and intends a future course of conduct that includes acts of patent infringement in Delaware. These acts have led and will lead to foreseeable harm and injury to Plaintiffs, including Takeda Pharmaceuticals U.S.A. Inc., a Delaware corporation. This Court has personal jurisdiction over Indoco for the additional reasons set forth below and for other reasons that will be presented to the Court if jurisdiction is challenged.

9. This Court has personal jurisdiction over Indoco because it has previously been sued in this district and has not challenged personal jurisdiction, and has affirmatively availed itself of the jurisdiction of this Court by filing counterclaims in this district. *See, e.g.*, *Bristol-Myers Squibb Co. et al. v. Indoco Remedies Ltd.*,17-cv-404.

10. Upon information and belief, Indoco and/or its affiliates have submitted, either directly or through an agent acting at its direction, over four Abbreviated New Drug Applications ("ANDAs") to the U.S. Food and Drug Administration ("FDA").

11. Upon information and belief, Indoco has received numerous approvals for pharmaceutical products and sells pharmaceutical products throughout the United States, including in this judicial district.

12. Upon information and belief, Indoco and/or its affiliates or agents will market and sell tablets containing 40 and 80 mg of the active ingredient febuxostat ("Indoco's Generic Product") in Delaware, and will derive substantial revenue from these activities, upon final approval of ANDA No. 210292 ("Indoco's ANDA") by the FDA.

13. Upon information and belief, Indoco and/or its affiliates or agents will market, offer for sale, and/or sell Indoco's Generic Product upon final approval of Indoco's ANDA by the FDA, with the reasonable expectation or knowledge and intent that such product will ultimately be purchased and used by consumers in this judicial district.

14. Alternatively, should the Court find that the above facts do not establish personal jurisdiction over Indoco in this action, this Court may exercise jurisdiction over Indoco pursuant to Fed. R. Civil P. 4(k)(2) because (a) Plaintiffs' claims arise under federal law; (b) Indoco is a foreign defendant not subject to personal jurisdiction in the courts of any state; and (c) Indoco has sufficient contacts with the United States as a whole, including but not limited to submitting various ANDAs to the FDA, and manufacturing and selling active pharmaceutical ingredients that are used in pharmaceutical products distributed throughout the United States, such that this Court's exercise of jurisdiction over Indoco satisfies due process.

15. This Court also has personal jurisdiction over Indoco by virtue of, *inter alia*, the fact that it has availed themselves of the rights and benefits of Delaware law, and have engaged in substantial and continuing contacts with the State.

16. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391 and 1400(b).

THE PATENTS-IN-SUIT

17. On April 22, 2008, the ’676 patent, titled “Solid Preparation Containing Single Crystal Form,” was duly and legally issued. A copy of the ’676 patent is attached as Exhibit A.

18. Teijin Ltd. is the owner of the ’676 patent. Teijin Pharma Ltd. and Takeda hold exclusive licenses with respect to the ’676 patent.

19. On February 12, 2013, the ’872 patent, titled “Methods For Concomitant Treatment of Theophylline and Febuxostat,” was duly and legally issued. A copy of the ’872 patent is attached as Exhibit B.

20. Takeda is the owner of the ’872 patent.

21. On August 18, 2015, the ’912 patent, titled “Methods For Concomitant Treatment of Theophylline and Febuxostat,” was duly and legally issued. A copy of the ’912 patent is attached as Exhibit C.

22. Takeda is the owner of the ’912 patent.

ACTS GIVING RISE TO THIS ACTION

23. Takeda holds New Drug Application (“NDA”) No. 21-856 for oral tablets containing 40 or 80 mg of the active ingredient febuxostat. Takeda markets and sells these tablets in the United States under the brand name “Uloric®.”

24. Pursuant to 21 U.S.C. § 355(b)(1), the ’676, ’872, and ’912 patents are listed in the FDA’s publication titled, *Approved Drug Products with Therapeutic Equivalence Evaluations* (also known as the “Orange Book”), as covering Uloric® or its use.

25. Upon information and belief, Indoco submitted ANDA No. 210292 to the FDA under § 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355(j)). Upon information and belief, Indoco’s ANDA seeks FDA approval to engage in the commercial manufacture, use, sale, or offer for sale of tablets containing 40 and 80 mg of febuxostat prior to the expiration of the ’676, ’872, and ’912 patents.

26. Upon information and belief, pursuant to § 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act, Indoco certified in ANDA No. 210292 that the claims of the ’676, ’872, and ’912 patents are invalid, unenforceable, or would not be infringed by the commercial manufacture, use, sale, or offer for sale of Indoco’s Generic Product.

27. Plaintiffs received written notification of Indoco’s ANDA and its accompanying § 505(j)(2)(A)(vii)(IV) certification by a letter dated May 9, 2017 (“Notice Letter”).

28. Indoco’s Notice Letter contains limited information about the crystal form or forms of the febuxostat materials for which Indoco filed ANDA No. 210292.

29. The information relating to Indoco’s Generic Product produced by Indoco to date does not demonstrate that the product Indoco is asking the FDA to approve for sale will not fall within the scope of an issued claim of the ’676 patent, the ’872 patent, or the ’912 patent.

30. Indoco’s Notice Letter does not refer to a certification with respect to U.S. Patent Nos. 5,614,520 (“the ’520 patent”) and 6,225,474 (“the ’474 patent”), and does not provide any detailed statement with regard to the ’520 and ’474 patents. Accordingly, upon

information and belief, Indoco's ANDA contains "Paragraph III" certifications with respect to the '520 and '474 patents pursuant to 21 U.S.C. § 505(j)(2)(A)(vii)(III). The expiration date of the '520 patent is March 25, 2019 and the expiration date of the '474 patent is June 18, 2019.

31. This action was commenced within 45 days of the Notice Letter.

INFRINGEMENT BY INDOCO OF THE '676 PATENT

32. Plaintiffs re-allege paragraphs 1-31 as if fully set forth herein.

33. By seeking approval of ANDA No. 210292 to engage in the commercial manufacture, use, sale, or offer for sale within the United States, or importation into the United States of Indoco's Generic Product prior to the expiration of the '676 patent, including filing its § 505(j)(2)(A)(vii)(IV) certification, Indoco has infringed one or more claims of the '676 patent under 35 U.S.C. § 271(e)(2)(A).

34. If Indoco manufactures, uses, offers to sell, or sells within the United States, or imports into the United States Indoco's Generic Product prior to the expiration of the '676 patent, subject to any patent term extension or exclusivity for the '676 patent to which Plaintiffs are or become entitled, Indoco will infringe one or more claims of the '676 patent under 35 U.S.C. § 271.

35. Plaintiffs are entitled to relief provided by 35 U.S.C. § 271(e)(4), including an order from this Court that the effective date of the approval of Indoco's ANDA No. 210292 be a date that is not earlier than the expiration date of the '676 patent, subject to any patent term extension or exclusivity for the '676 patent to which Plaintiffs are or become entitled.

36. Plaintiffs are entitled to a declaration that if Indoco commercially manufactures, uses, offers for sale, or sells Indoco's Generic Product within the United States,

imports Indoco's Generic Product into the United States, or induces or contributes to such conduct, Indoco will infringe the '676 patent under 35 U.S.C. § 271.

37. Plaintiffs will be irreparably harmed by Indoco's infringing activities unless those activities are enjoined by this Court. Plaintiffs do not have an adequate remedy at law.

38. Upon information and belief, Indoco was aware of the existence of the '676 patent and was aware that the filing of its ANDA and certification with respect to the '676 patent constituted an act of infringement of that patent.

INFRINGEMENT BY INDOCO OF THE '872 AND '912 PATENTS

39. Takeda re-alleges paragraphs 1-38 as if fully set forth herein.

40. By seeking approval of ANDA No. 210292 to engage in the commercial manufacture, use, sale, or offer for sale within the United States, or importation into the United States of Indoco's Generic Product prior to the expiration of the '872 patent, including filing its § 505(j)(2)(A)(vii)(IV) certification, Indoco has infringed the sole claim of the '872 patent under 35 U.S.C. § 271(e)(2)(A).

41. Takeda is entitled to relief provided by 35 U.S.C. § 271(e)(4), including an order from this Court that the effective date of the approval of Indoco's ANDA No. 210292 be a date that is not earlier than the expiration date of the '872 patent, subject to any patent term extension or exclusivity for the '872 patent to which Takeda is or becomes entitled.

42. By seeking approval of ANDA No. 210292 to engage in the commercial manufacture, use, sale, or offer for sale within the United States, or importation into the United States of Indoco's Generic Product prior to the expiration of the '912 patent, including filing its

§ 505(j)(2)(A)(vii)(IV) certification, Indoco has infringed one or more claims of the '912 patent under 35 U.S.C. § 271(e)(2)(A).

43. Takeda is entitled to relief provided by 35 U.S.C. § 271(e)(4), including an order from this Court that the effective date of the approval of Indoco's ANDA No. 210292 be a date that is not earlier than the expiration date of the '912 patent, subject to any patent term extension or exclusivity for the '912 patent to which Takeda is or becomes entitled.

44. Uloric®, as of February 2009, was contraindicated for patients treated with theophylline. The prescribing information stated "CONTRAINDICATIONS. ULORIC is contraindicated in patients being treated with azathioprine, mercaptopurine, or theophylline," and "Do not take ULORIC if you: … take Theophylline (Theo-24®, Elixophyllin®, Theochron®, Theolair®, Uniphyl®)." Exhibit D.

45. The prescribing information for Uloric® as revised in February 2009 further stressed the contraindication. In this regard, the prescribing information stated,

> "*Xanthine Oxidase Substrate Drugs-Azathioprine, Mercaptopurine, and Theophylline*: Febuxostat is an XO inhibitor. Drug interaction studies of ULORIC with drugs that are metabolized by XO (e.g., theophylline, mercaptopurine, azathioprine) have not been conducted. Inhibition of XO by ULORIC may cause increased plasma concentrations of these drugs leading to toxicity. ULORIC is contraindicated in patients being treated with azathioprine, mercaptopurine, and theophylline [*see Contraindications (4) and Drug Interactions (7)*].
> …
> Theophylline is a CYP1A2 and XO substrate. Although no ULORIC drug interaction study with theophylline has been conducted, concomitant administration of theophylline with allopurinol, a xanthine oxidase inhibitor at doses ≥600 mg per day, has been reported to increase theophylline plasma concentrations. Because ULORIC is a xanthine oxidase inhibitor and theophylline is a low therapeutic index drug, ULORIC could inhibit the XO-mediated metabolism of theophylline leading to increased plasma concentrations of theophylline that could induce severe theophylline toxicity." Exhibit D.

46. Research leading to the '872 patent and the '912 patent reveals that there is no need to contraindicate co-administration of febuxostat and theophylline. Co-administration

of febuxostat and theophylline can be carried out without adjusting the amount of theophylline administered for adverse drug interactions. The ’872 patent and the ’912 patent further disclose that dose adjustment of theophylline is required when it is co-administered with allopurinol.

47. As a result, Uloric®, is no longer contraindicated for patients treated with theophylline. The prescribing information states “CONTRAINDICATIONS. ULORIC is contraindicated in patients being treated with azathioprine or mercaptopurine.” The prescribing information documents as revised in January 2011, November 2012, and March 2013 are attached as Exhibits E, F, and G, respectively.

48. Upon information and belief, Indoco’s prescribing information provided with the Indoco Generic Product is expected to carry the same or substantially same contraindications as quoted in paragraph 47.

49. The absence of the above-referenced contraindication in the prescribing information for Uloric® on Indoco’s prescribing information, aided by the fact that the use in such population was previously contraindicated, induces the practice of the invention of the ’872 patent and/or the ’912 patent by a medical practitioner, a patient, or any other person to co-administer or cause the co-administration of febuxostat and theophylline without adjusting the amount of theophylline.

50. The recent and current revisions of Uloric® prescribing information contain express statements that no dose adjustment is necessary. The prescribing information states,

> “*Theophylline*: No dose adjustment is necessary for theophylline when co-administered with ULORIC. Administration of ULORIC (80 mg once daily) with theophylline resulted in an increase of 6% in C_{max} and 6.5% in AUC of theophylline. These changes were not considered statistically significant. However, the study also showed an approximately 400-fold increase in the amount of 1-methylxanthine (one of the major theophylline metabolites) excreted in urine as a result of XO inhibition by ULORIC. The safety of

> long-term exposure to 1-methylxanthine has not been evaluated. This should be taken into consideration when deciding to co-administer ULORIC and theophylline.
> …
> ULORIC is an XO inhibitor. Based on a drug interaction study in healthy subjects, febuxostat altered the metabolism of theophylline (a substrate of XO) in humans [*see Clinical Pharmacology (12.3)*]. Therefore, use with caution when coadministering ULORIC with theophylline.
> …
> *Xanthine Oxidase Substrate Drugs-Azathioprine, Mercaptopurine, and Theophylline*: Febuxostat is an XO inhibitor. A drug-drug interaction study evaluating the effect of ULORIC upon the pharmacokinetics of theophylline (an XO substrate) in healthy subjects showed that coadministration of febuxostat with theophylline resulted in an approximately 400-fold increase in the amount of 1-methylxanthine, one of the major metabolites of theophylline, excreted in the urine. Since the long-term safety of exposure to 1-methylxanthine in humans is unknown, use with caution when coadministering febuxostat with theophylline." Exhibits E, F, and G.

51. Upon information and belief, Indoco's prescribing information provided with the Indoco Generic Product is expected to carry the same or substantially same affirmative statements as quoted in paragraph 50.

52. As a result of the removal of theophylline from the contraindications and the addition of the language discussing the co-administration of Uloric® with theophylline, the prescribing information encourages the co-administration of febuxostat and theophylline without adjusting the amount of theophylline.

53. Furthermore, the affirmative statements set forth in paragraph 50 induce the practice of the invention of the '872 patent and/or the '912 patent by a medical practitioner, a patient, or any other person to co-administer or cause the co-administration of febuxostat and theophylline without adjusting the amount of theophylline.

54. For "Dosage and Administration," the prescribing information for Uloric® states, *inter alia*, that

> "ULORIC is recommended at 40 mg or 80 mg once daily. The recommended starting dose of ULORIC is 40 mg once daily. For patients who do not achieve a serum uric acid

(sUA) less than 6 mg/dL after 2 weeks with 40 mg, ULORIC 80 mg is recommended." Exhibits D, E, F and G.

55. Upon information and belief, Indoco's prescribing information provided with the Indoco Generic Product is expected to carry the same or substantially same dosage and administration statements as quoted in paragraph 54.

56. Claim 1, the sole claim in the '872 patent, states, *inter alia*, that "administering to the hyperuricemic patient suffering from gout a therapeutically effective amount of febuxostat in a dose of 80 mg."

57. The affirmative statements set forth in paragraph 54 induce the practice of the invention of the '872 patent by a medical practitioner, a patient, or any other person to increase the dosage of febuxostat to 80 mg, such as by administering one 80 mg pill, or two 40 mg pills at the same time.

58. Therefore, for the reasons alleged in paragraphs 44-57 and other reasons that may be subsequently developed, the commercial manufacture, use, offer to sell, sale, or import of Indoco's Generic Product, if approved by the FDA, prior to the expiration of the '872 patent, subject to any patent term extension or exclusivity for the '872 patent to which Takeda or becomes entitled, would induce the infringement of the '872 patent under 35 U.S.C. § 271(b).

59. Takeda is entitled to a declaration that, if Indoco commercially manufactures, uses, offers for sale, or sells Indoco's Generic Product within the United States, imports Indoco's Generic Product into the United States, or induces or contributes to such conduct, Indoco will infringe the '872 patent under 35 U.S.C. § 271(b).

60. Claim 1, the sole independent claim in the '912 patent, states, *inter alia*, that "administering to a patient suffering from hyperuricemia and at least one second disease state, a therapeutically effective amount of [febuxostat] or a pharmaceutically acceptable salt

thereof, wherein the subject is also receiving concomitant administration of theophylline to treat the at least one second disease state…."

61. Therefore, for the reasons alleged in paragraphs 44-57 and other reasons that may be subsequently developed, the commercial manufacture, use, offer to sell, sale, or import of Indoco's Generic Product, if approved by the FDA, prior to the expiration of the '912 patent, subject to any patent term extension or exclusivity for the '912 patent to which Takeda is or becomes entitled, would induce the infringement of the '912 patent under 35 U.S.C. § 271(b).

62. Takeda is entitled to a declaration that, if Indoco commercially manufactures, uses, offers for sale, or sells Indoco's Generic Product within the United States, imports Indoco's Generic Product into the United States, or induces or contributes to such conduct, Indoco will infringe the '912 patent under 35 U.S.C. § 271(b).

63. Plaintiffs will be irreparably harmed by Indoco's infringing activities unless those activities are enjoined by this Court. Plaintiffs do not have an adequate remedy at law.

64. Upon information and belief, Indoco was aware of the existence of the '872 and '912 patents and was aware that the filing of its ANDA and certifications with respect to the '872 and '912 patents constituted an act of infringement of those patents.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs pray for judgment as follows:

A. That Defendant Indoco has infringed the '676, '872, and '912 patents;

B. That pursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of any approval of ANDA No. 210292 under § 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355(j)) shall not be earlier than the expiration of the '676, '872, and '912 patents,

subject to any patent term extension or exclusivity to which Takeda and/or Teijin are or become entitled;

C. That Defendant Indoco, its officers, agents, servants, and employees, and those persons in active concert or participation with any of them, be preliminarily and permanently enjoined from commercially manufacturing, using, offering to sell, selling, or importing into the United States Indoco's Generic Product and any other product that infringes or induces or contributes to the infringement of one or more claims of the '676, '872, and '912 patents prior to its expiration, subject to any patent term extension or exclusivity to which Takeda and/or Teijin are or become entitled;

D. That Plaintiffs be awarded the attorney fees, costs, and expenses that they incur prosecuting this action; and

E. That Plaintiffs be awarded such other and further relief as this Court deems just and proper.

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