IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

TAKEDA PHARMACEUTICALS U.S.A., INC.,	)	
Plaintiff,	)	
v.	)	Civ. No. 14-1268-SLR
WEST-WARD PHARMACEUTICAL CORPORATION, HIKMA AMERICAS, INC. and HIKMA PHARMACEUTIALS PLC,	)	
Defendants.	)	

Mary W. Bourke, Esquire and Daniel M. Attaway, Esquire of Womble Carlyle Sandridge & Rice, LLP, Wilmington, Delaware. Counsel for Plaintiff. Of Counsel: Tryn T. Stimart, Esquire of Womble Carlyle Sandridge & Rice, LLP, Jeffrey I. Weinberger, Esquire, Ted G. Dane, Esquire, Elizabeth Laughton, Esquire, Eric K. Chiu, Esquire and Amy L. Greywitt, Esquire of Munger, Tolles & Olson LLP.

Dominick T. Gattuso, Esquire of Proctor Heyman Enerio LLP, Wilmington, Delaware. Counsel for Defendants. Of Counsel: John T. Bennett, Esquire, Elaine H. Blais, Esquire, William G. James, Esquire and Elizabeth J. Holland, Esquire of Goodwin Procter LLP, and Steffen N. Johnson, Esquire, Charles B. Klein, Esquire and Samuel S. Park, Esquire of Winston & Strawn LLP.

MEMORANDUM OPINION

Dated: May 18, 2016
Wilmington, Delaware

ROBINSON, District Judge

I. INTRODUCTION

On October 3, 2014, Takeda Pharmaceuticals U.S.A., Inc. ("Takeda") filed suit against West-Ward Pharmaceutical Corporation, Hikma Americas Inc., and Hikma Pharmaceuticals PLC (collectively, "Hikma"), asserting induced infringement of five patents under 35 U.S.C. § 271(b).[1] (D.I. 1) Takeda is the owner of the asserted patents, which contain one or more claims covering methods of use of Takeda's colchicine product, Colcrys®. (D.I. 109 at 8) Colcrys® is used primarily for preventing and treating gout flares. (*Id.* at 5)

Hikma has launched the accused product, Mitigare™, an oral single-ingredient colchicine product, "indicated for prophylaxis of gout flares in adults." (D.I. 1, ex. H at 1) Although Mitigare™ has the same active ingredient, route of administration, and strength as Colcrys®, Hikma did not file its application with the Food and Drug Administration (FDA) as an Abbreviated New Drug Application ("ANDA"). Instead, Hikma sought approval through the New Drug Application ("NDA") pathway under § 505(b)(2) of the Hatch-Waxman Act. Moreover, in its proposed label, Hikma has omitted specific mention of uses for which Takeda has patent protection.

On October 5, 2014, Takeda requested a temporary restraining order ("TRO") to preserve the status quo while the parties more fully briefed (and the court considered)

---

[1] The relevant patents owned by Takeda may be divided into three groups: the "drug-drug interaction patents" ("DDI Patents"), the "Acute Gout Treatment Patents" (the "Acute Flare Patents"), and the "COLCRYS® Patents." (D.I. 109 at ¶¶ 29-31). Takeda's amended complaint refers to these patents as the Acute Gout Treatment Patents, and Hikma refers to these patents as the Acute Flare Patents. The court refers to these patents as the Acute Flare Patents.

Takeda's motion for a preliminary injunction. (D.I. 5) On October 9, 2014, the court issued a memorandum order granting Takeda's motion for a TRO. (D.I. 21) The parties jointly stipulated to extend the period for which the TRO was in force through the end of November 4, 2014. (D.I. 54) The court reviewed Takeda's motion for a preliminary injunction and concluded that "[b]ecause Takeda has failed to demonstrate that it will likely prove induced infringement at trial or suffer irreparable harm, the extraordinary relief sought is not warranted." (D.I. 78 at 15) The court also concluded that, "given the significance of this dispute to both parties, [the court] will maintain the status quo pending appeal if: (1) Takeda takes an immediate appeal and requested expedited review of both the merits and this ruling by the Federal Circuit; and (2) the conditions included in [the court's] order of October 31, 2014 (D.I. 72) continue to govern the conduct of the parties, except that the bond shall increase $500,000 per day until further order of this court or the Federal Circuit." (*Id.*)

On November 5, 2014, Takeda filed a notice of appeal to the United States Court of Appeals for the Federal Circuit, appealing the order denying its motion for preliminary injunction and seeking expedited review. (D.I. 80) Hikma then filed a notice of cross appeal to the Federal Circuit on November 10, 2014. (D.I. 82) On appeal, the Federal Circuit affirmed this court's order denying Takeda's motion for a preliminary injunction. *Takeda Pharmaceuticals U.S.A., Inc. v. West-Ward Pharmaceutical Corp.*, 785 F.3d 625, 627 (Fed. Cir. 2015). On September 10, 2015, Takeda filed its first amended complaint. (D.I. 109) Presently before the court is Hikma's motion to dismiss Takeda's first amended complaint pursuant to Federal Rule of Civil Procedure 12(b)(6). (D.I. 112) The court has jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

II. BACKGROUND

A. Takeda's Amended Complaint

In its amended complaint, Takeda alleges that Hikma's Mitigare™ products induce infringement of the Acute Flare Patents, and supports this claim with allegations related to the Mitigare™ and Mitigare™ AG product labels, Hikma's FDA correspondence, and Hikma's marketing and sales activities. The amended complaint also alleges induced infringement of the DDI Patents and supports this claim with allegations related to the Mitigare™ and Mitigare™ AG product labels and Hikma's FDA correspondence.

1. The Acute Flare Patents

In asserting that Hikma infringes its Acute Flare Patents, Takeda describes three aspects of Hikma's Mitigare™ product: the Mitigare™ and Mitigare™ AG product labels, Hikma's correspondence with the FDA, and Hikma's marketing and sales activities.

a. The MITIGARE™ and MITIGARE™ AG product labels

Takeda states that "Colcrys® is approved for both prophylaxis and treatment of acute gout flares, while Mitigare™ is approved only for prophylaxis. Nevertheless, the same 0.6 mg of colchicine can and is being used for either prophylaxis or treatment of acute gout flares." (D.I. 109 at ¶ 35) Takeda then describes the Mitigare™ product label which instructs patients: "If you have a gout flare while taking Mitigare™, tell your healthcare provider." (*Id.* at ¶ 36) Takeda asserts that this instruction means that "[w]ith respect to acute treatment, upon information and belief, [Hikma] know[s] and intend[s] that healthcare providers will prescribe the Mitigare™ Products for the treatment of acute gout flares according to the Colcrys® product label and the [American College of

Rheumatology] guidelines []." (*Id.*) Further, Takeda states that the only reference in the product labels to the treatment of acute gout flares is a statement that "the safety and effectiveness of Mitigare™ [or "colchicine capsules"] for acute treatment of gout flares during prophylaxis has not been studied." (*Id.* at ¶ 37) (alterations in original). Takeda bolsters this statement by alleging that while Hikma "may not have performed studies" to examine the effect of its capsule product in treating acute gout flares, Hikma is aware that Mutual, a pharmaceutical company and former affiliate of Takeda, "did study the safety and effectiveness of its pharmacologically-identical 0.6 mg colchicine tablet product in treating acute gout flares, as described in the Colcrys® product labeling." (*Id.*) Finally, Takeda states that the medication guides for Hikma's products "do not instruct patients to refrain from taking [Mitigare™] for treatment of acute gout flares[,] [n]or do they prescribe the proper dosage of [Mitigare™]." (*Id.* at ¶ 38)

b. FDA correspondence

Takeda states that the FDA "recognized the high likelihood that a drug suitable both for the treatment and the prophylaxis of acute gout flares likely would be prescribed for both," and that the FDA consequently informed Hikma that "if Mitigare is being used for prophylaxis, it may be natural for the provider to use it for acute treatment as well." (*Id.* at ¶ 41) According to Takeda, Hikma's product label stating "If you have a gout flare while taking Mitigare™, tell your healthcare provider" indicates that Hikma "intended to encourage and facilitate the use of [Mitigare] to treat acute gout flares in accordance with Takeda's patented methods." (*Id.* at ¶ 42).

c. Marketing and sales activities

Takeda alleges that Hikma's October 3, 2014 domestic launch of Mitigare™ and its January 9, 2015 domestic launch of Mitigare™ AG are indicative of efforts by Hikma to "manufacture, advertise, promote, market, offer to sell, and sell the Mitigare™ Products to compete directly with Colcrys®[]." (*Id.* at ¶¶ 43-45) In support of this assertion, Takeda proffers that Hikma's representatives informed prescribers that "thirty capsules of Mitigare™...could last a patient up to one year." (*Id.* at ¶ 48) Takeda states that Hikma's "sales representatives have also explicitly informed prescribers that [Mitigare] can be used to treat acute gout flares." (*Id.*) Further, Takeda states that Hikma has entered into at least two "sole-source contracts" with specific insurance providers that "effectively guarantee that, for all patients covered by these insurance providers, the only single oral colchicine option available to them for the treatment of acute gout flares will be [Mitigare™] or [Mitigare™] AG product."[2] (*Id.* at ¶ 52) According to Takeda, "by intending, or being willfully blind to, the use of Takeda's patent-protected low-dose regimen, Hikma [] actively induce[d] infringement of one or more claims of the [Acute Flare Patents]." (*Id.* at ¶ 54).

2. The DDI Patents

---

[2] To support its allegation that Hikma's representatives intended to infringe Takeda's patented gout care patents, Takeda points to Hikma's agreement with Kaiser Permanente, whose medication guide "currently contains dosing instructions for acute treatment that describe Takeda's patented method...[but] does not contain any instructions for prophylactic use, which is the only FDA-approved use for MITIGARE™." (*Id.* at ¶ 52) Takeda claims that Hikma was aware of the contents of the medication guide, and that the medication guide demonstrates that Hikma "know[s] and intend[s], or [is] at a minimum [] willfully blind to the fact that, healthcare organizations, physicians, and pharmacists will use MITIGARE™ to treat patients for acute gout flares in accordance with the claimed methods in the Acute [Flare] Patents." (*Id.* at ¶ 53).

In describing Hikma's alleged infringement of the DDI Patents, Takeda focuses on the Mitigare product labels and Hikma's FDA correspondence.

a. The Mitigare™ and Mitigare™ AG product labels

Takeda alleges that the Mitigare product labels instruct doctors and patients that, "when coadministering [Mitigare™] with CYP3A4 or P-gp inhibitors, the dose of [Mitigare™] should be adjusted by either reducing the daily dose or reducing the dose frequency, and the patient should be monitored for colchicine toxicity."[3] (*Id.* at ¶ 55) Further, Takeda asserts that Hikma knows that Mutual "studied dose adjustments of colchicine in the presence of CYP3A4 and P-gp inhibitors and that dose reduction instructions are contained in the [Colcrys®] product label;" therefore, Hikma knows or intends, or is willfully blind to the fact, that the Mitigare product labels "fail to specify how to reduce the dose or dose frequency when the Mitigare products are concomitantly administered with [inhibitors], [and that] at least some doctors and patients will consult the dose regimens set forth in the [Colcrys®] product labeling, and adjust the colchicine dosing according to the instructions in the FDA-approved [Colcrys®] label." (*Id.* at ¶ 57).

b. FDA correspondence

Takeda states that the FDA denied more than one of Hikma's proposed product labels and that, when Hikma conducted its own drug-drug interaction study, the FDA found the study's results non-conclusive. Takeda further states that "[t]he only specific instructions for how to reduce colchicine dosages when the drug is coadministered with

[3] Takeda's amended complaint also states that "[t]hese labels expressly name clarithromycin, ketoconazole, and verapamil as CYP3A4 inhibitors ["the CYP3A4 inhibitors"] for which a dose is necessary, but do not specify the amount by which the daily dose of colchicine should be reduced." (*Id.* at ¶ 55).

the CYP3A4 or P-gp inhibitors are the patented dosing reductions contained in the COLCRYS® label, which the [American College of Rheumatology] has adopted as the standard of care for colchicine treatment." (*Id.* at ¶ 62) According to Takeda, this demonstrates that Hikma "knew and intended, or [was] willfully blind to the fact that at least some physicians, pharmacists, or healthcare organizations, would consult the FDA-approved COLCRYS® label and/or the [American College of Rheumatology] guidelines to determine the specific amount of dose reductions required for concomitant administration with CYP3A4 and/or P-gp inhibitors." (*Id.*)

III. STANDARDS OF REVIEW

A. Motions to Dismiss

A motion filed under Federal Rule of Civil Procedure 12(b)(6) tests the sufficiency of a complaint's factual allegations. *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555 (2007); *Kost v. Kozakiewicz*, 1 F.3d 176, 183 (3d Cir. 1993). A complaint must contain "a short and plain statement of the claim showing that the pleader is entitled to relief, in order to give the defendant fair notice of what the . . . claim is and the grounds upon which it rests." *Twombly*, 550 U.S. at 545 (internal quotation marks omitted) (interpreting Fed. R. Civ. P. 8(a)). Consistent with the Supreme Court's rulings in *Twombly* and *Ashcroft v. Iqbal*, 556 U.S. 662 (2009), the Third Circuit requires a two-part analysis when reviewing a Rule 12(b)(6) motion. *Edwards v. A.H. Cornell & Son, Inc.*, 610 F.3d 217, 219 (3d Cir. 2010); *Fowler v. UPMC Shadyside*, 578 F.3d 203, 210 (3d Cir. 2009). First, a court should separate the factual and legal elements of a claim, accepting the facts and disregarding the legal conclusions. *Fowler*, 578 F.3d. at 210-11. Second, a court should determine whether the remaining well-pled facts sufficiently

show that the plaintiff "has a 'plausible claim for relief.'" *Id.* at 211 (quoting *Iqbal*, 556 U.S. at 679). As part of the analysis, a court must accept all well-pleaded factual allegations in the complaint as true, and view them in the light most favorable to the plaintiff. *See Erickson v. Pardus*, 551 U.S. 89, 94 (2007); *Christopher v. Harbury*, 536 U.S. 403, 406 (2002); *Phillips v. Cnty. of Allegheny*, 515 F.3d 224, 231 (3d Cir. 2008). In this regard, a court may consider the pleadings, public record, orders, exhibits attached to the complaint, and documents incorporated into the complaint by reference. *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 322 (2007); *Oshiver v. Levin, Fishbein, Sedran & Berman*, 38 F.3d 1380, 1384-85 n.2 (3d Cir. 1994).

The court's determination is not whether the non-moving party "will ultimately prevail," but whether that party is "entitled to offer evidence to support the claims." *United States ex rel. Wilkins v. United Health Grp., Inc.*, 659 F.3d 295, 302 (3d Cir. 2011). This "does not impose a probability requirement at the pleading stage," but instead "simply calls for enough facts to raise a reasonable expectation that discovery will reveal evidence of [the necessary element]." *Phillips*, 515 F.3d at 234 (quoting *Twombly*, 550 U.S. at 556). The court's analysis is a context-specific task requiring the court "to draw on its judicial experience and common sense." *Iqbal*, 556 U.S. at 663-64.

B. Indirect Infringement

To establish indirect infringement, a patent owner has available two theories: active inducement of infringement and contributory infringement. *See* 35 U.S.C. § 271(b) & (c). Liability for indirect infringement may arise "if, but only if, [there is] ... direct infringement." *Limelight Networks, Inc. v. Akamai Technologies, Inc.*, 134 S. Ct. 2111,

2117 (2014) (citing *Aro Mfg. Co. v. Convertible Top Replacement Co.*, 365 U.S. 336, 341 (1961) (emphasis omitted)).

Under 35 U.S.C. § 271(b), "whoever actively induces infringement of a patent shall be liable as an infringer." "To prove induced infringement, the patentee must show direct infringement, and that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement." *Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1363 (Fed. Cir. 2012) (internal quotations omitted). "[I]nduced infringement under § 271(b) requires knowledge that the induced acts constitute patent infringement." *Global-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754, 766 (2011). The knowledge requirement can be met by a showing of either actual knowledge or willful blindness. *See id.* "[A] willfully blind defendant is one who takes deliberate actions to avoid confirming a high probability of wrongdoing and who can almost be said to have actually known the critical facts." *Id.* at 769 (citation omitted). "[I]nducement requires evidence of culpable conduct, directed to encouraging another's infringement, not merely that the inducer had knowledge of the direct infringer's activities." *DSU Medical Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006) (en banc in relevant part) (citations omitted).

To establish contributory infringement, the patent owner must demonstrate the following: (1) an offer to sell, sale, or import; (2) a component or material for use in a patented process constituting a material part of the invention; (3) knowledge by the defendant that the component is especially made or especially adapted for use in an infringement of such patents; and (4) the component is not a staple or article suitable for substantial non-infringing use. *See Fujitsu Ltd. v. Netgear Inc.*, 620 F.3d 1321, 1326

(Fed. Cir. 2010) (citing 35 U.S.C. § 271(c)). Defendant "must know 'that the combination for which his component was especially designed was both patented and infringing.'" *Global–Tech*, 563 U.S. at 763 (citing *Aro Mfg. Co. v. Convertible Top Replacement Co.*, 377 U.S. 476, 488 (1964)).

In *Takeda*, the Federal Circuit stated that "[i]nducement can be found where there is evidence of active steps taken to encourage direct infringement, which can in turn be found in advertising and infringing use or instructing how to engage in an infringing use." *Takeda*, 785 F.3d at 630-31 (citations and internal quotation marks omitted). Further, the court held that "mere knowledge of possible infringement by others does not amount to inducement; specific intent and action to induce infringement must be proven." *Id.* at 631 (citations omitted).

IV. DISCUSSION

A. Analytical Framework

The Federal Circuit's decision in *Warner-Lambert Co. v. Apotex Corp.,* 316 F.3d 1348 (Fed. Cir. 2003), sets the framework for analyzing the issue at bar.[4] In *Warner-Lambert*, the patentee received approval from the FDA to market gabapentin,[5] a drug used for treating epilepsy. Warner-Lambert's patent for use of gabapentin in treating

---

[4] The court acknowledges that Hikma sought approval for Mitigare™ through the NDA pathway under § 505(b)(2) of the Hatch-Waxman Act, rather than through an ANDA. Therefore, Takeda has asserted its induced infringement claims under § 271(b) and not § 271(e)(2), as applicable in *Warner-Lambert* and its progeny. However, the court finds the *Warner-Lambert* construct instructive; notably, the Federal Circuit relied on *Warner-Lambert* in affirming the court's denial of a preliminary injunction at bar on the issue of whether Takeda's induced infringement claim was likely to succeed on the merits. *Takeda*, 785 F.3d at 630-633.

[5] Gabapentin was marketed under the trade name Neurontin®.

epilepsy had expired, but Warner-Lambert had an unexpired patent claiming the use of gabapentin for treating neurodegenerative disease.[6] The latter use of the drug, however, had not been approved by the FDA. Apotex, a generic manufacturer, filed an ANDA seeking approval to market a generic form of gabapentin for the approved use of treating epilepsy upon the expiration of Warner-Lambert's epilepsy method patent. After Apotex notified Warner-Lambert that it had filed the ANDA and a Paragraph IV certification, Warner-Lambert instituted suit within 45 days in the United States District Court for the Northern District of Illinois, alleging that Apotex's submission of an ANDA for gabapentin was an act of infringement of its neurodegenerative method patent under 35 U.S.C. § 271(e)(2). Following discovery, the district court granted Apotex's motion for summary judgment of non-infringement, concluding that there was no evidence that Apotex actively induced physicians to prescribe its product for neurodegenerative diseases or that Apotex knew its product would be prescribed for neurodegenerative diseases. *Warner-Lambert Co. v. Apotex Corp.*, 2001 WL 1104618, at *3 (N.D. Ill. Sept. 14, 2001).

On appeal, the Federal Circuit expressed concern that permitting a cause of action under § 271(e)(2) for off-label method of use patents would "confer substantial additional rights on pioneer drug patent owners that Congress quite clearly did not intend to confer." *Warner-Lambert,* 316 F.3d at 1359. Moreover, the panel determined that "Warner-Lambert would have needed to demonstrate the existence of a genuine issue of material fact to support a traditional infringement claim, i.e., that Apotex

---

[6] Neurodegenerative diseases include stroke, Alzheimer's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, and Parkinson's disease.

induced or will induce infringement of the neurodegenerative method patent." *Id.* at 1356. Upon considering Warner-Lambert's cause of action under § 271(b), the Court concluded that, "[i]n the absence of any evidence that Apotex has or will promote or encourage doctors to infringe the neurodegenerative method patent, there has been raised no genuine issue of material fact." *Id.* at 1364. The Federal Circuit, therefore, affirmed the district court's grant of summary judgment, holding that a method of use patent holder may not bring an action under § 271(e)(2) for infringement of a method of use patent that does not claim a FDA-approved use. S*ee also Allergan, Inc. v. Alcon Laboratories, Inc.*, 324 F.3d 1322 (Fed. Cir. 2003) (holding the generic drug applicant could not be liable for infringement under § 271(e)(2)(A), even though brimonidine had other uses not approved by the FDA for which the drug was effective in patients who took the drug for the approved purpose of reducing intraocular pressure).

More recently, the Federal Circuit addressed the *Warner-Lambert* construct at the pleading stage in *AstraZeneca Pharmaceuticals LP v. Apotex Corp.*, 669 F.3d 1370 (Fed. Cir. 2012). AstraZeneca markets a cholesterol-lowering drug, rosuvastatin calcium under the brand name CRESTOR®, and holds rights to the two method patents at issue in that appeal. Collectively, the two patents claim methods of using rosuvastatin compounds to treat heterozygous familial hypercholesterolemia ("HeFH") and to lower the cardiovascular disease risk for individuals with elevated circulating C-reactive protein ("CRP"). Each patent is listed in the FDA's Orange Book and covers an approved indication for use of CRESTOR®.

In addition to the two treatment indications claimed in the aforementioned patents, rosuvastatin calcium is also approved for uses not claimed by either of these

patents, including the treatment of patients with homozygous familial hypercholesterolemia ("HoFH") or hypertriglyceridemia. The defendant generic pharmaceutical companies filed ANDAs seeking to market generic rosuvastatin calcium for treating HoFH and hypertriglyceridemia while carving out the patented indications directed toward HeFH and elevated CRP. To do so, the generic manufacturers filed statements[7] averring that their ANDAs excluded all uses claimed in the asserted patents.

AstraZeneca brought suit for infringement of its method of use patents, asserting that the ANDA filings infringed and would cause infringement of the method of use patents under § 271(e)(2). AstraZeneca alleged that: (1) the ANDAs violated § 271(e)(2) as applications for a drug, the use of which is claimed in the patents; (2) if approved by the FDA, the generic manufacturers' proposed activities will induce infringement of the patents; and (3) the FDA will require labeling amendments explicitly incorporating the indications covered by the patents. The district court dismissed AstraZeneca's infringement claims for lack of subject matter jurisdiction, finding that

---

[7] The Hatch-Waxman Act requires each ANDA applicant to certify that (1) the Orange Book contains no patent information relevant to their ANDA ("Paragraph I certification"), (2) the listed patents have expired ("Paragraph II certification"), (3) the applicant will not enter the market until the listed patents expire ("Paragraph III certification"), or (4) the applicant believes that the listed patents are invalid or will not be infringed by the applicant's generic compositions ("Paragraph IV certification"). 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV) (2006). The Act specifies that filing an ANDA containing a Paragraph IV certification constitutes an act of infringement. 35 U.S.C. § 271(e)(2) (2006); *AstraZeneca,* 669 F.3d at 1374 (citation omitted). Where the Orange Book lists a method of use patent that "does not claim a use for which the applicant is seeking approval," an applicant may instead submit a statement under 21 U.S.C. § 355(j)(2)(A)(viii) averring that the ANDA excludes all uses claimed in the patent ("Section viii statement"). *Id.* (citing *Warner-Lambert*, 316 F.3d at 1360-61).

AstraZeneca had not presented a valid § 271(e)(2) claim based on the ANDA filings. *AstraZeneca Pharmaceuticals LP v. Apotex Corp.*, 2010 WL 5376310 (D. Del. Dec. 22, 2010), *aff'd*, 669 F.3d 1370 (Fed. Cir. 2012). The district court also held that AstraZeneca's claims were not ripe to the extent they relied on presumptive future labeling amendments. *Id.*

On appeal, the Federal Circuit disagreed with AstraZeneca's attempt to distinguish *Warner-Lambert* as involving a patent that claimed an unapproved or "off-label" use for which no generic could be approved through the ANDA process.[8] The Federal Circuit found the distinction between patents claiming unapproved and approved uses irrelevant for purposes of § 271(e)(2), explaining that when considering allegations that an ANDA filing infringes a patented method, § 271(e)(2) directs the analysis to the scope of approval sought in the ANDA. The panel noted that the Hatch-Waxman Act allows generic manufacturers to limit the scope of regulatory approval they seek, and thereby forego Paragraph IV certification and a § 271(e)(2) infringement suit by excluding patented indications from their ANDAs with a Section viii statement. *Id.* at 1379-80.

The Federal Circuit was also not persuaded by AstraZeneca's argument that pharmacists and doctors could substitute the generic product for all indications once the product became available, stating that finding infringement based on such speculative

---

[8] The Federal Circuit additionally addressed subject matter jurisdiction, finding that alleging infringement by the filing of an ANDA was sufficient to establish subject matter jurisdiction. The Federal Circuit also affirmed the district court's finding that AstraZeneca's allegation that the FDA would require future labeling amendments to include all FDA-approved indications for rosuvastatin calcium was insufficiently ripe for adjudication.

prescribing practices would enable infringement claims despite a Section viii statement and corresponding proposed labeling that explicitly and undisputedly carved out all patented indications for a particular product. *Id.* at 1380. Moreover, the Court expressed concern that a pioneer drug manufacturer could maintain de facto indefinite exclusivity over a pharmaceutical compound by obtaining serial patents for approved methods of using the compound and then wielding § 271(e)(2) as a sword against any competitor's ANDA seeking approval to market an off-patent drug for an approved use. *Id.* Accordingly, the Federal Circuit affirmed the district court's dismissal of AstraZeneca's complaint.

B. Analysis

The above reasoning applies to the case at bar. Takeda's Colcrys® drug is approved and used to treat and prevent acute gout flares, while Hikma's Mitigare™ is approved solely to prevent gout flares. To this point, the Mitigare™ label warns that "[t]he safety and effectiveness of MITIGARE™ for acute treatment of gout flares during prophylaxis has not been studied." (D.I. 109, ex. K at 1) Like the generic in *AstraZeneca*, Hikma has specified that Mitigare™ is for the prevention of gout flares and warned that its drug is not indicated for the treatment of acute gout flares. Allowing Takeda to proceed with its claims would be akin to allowing Takeda to expand the scope of its exclusivity over the treatment of gout with colchicine.

Specifically with respect to induced infringement, the Federal Circuit has stated that "[t]he pertinent question is whether the proposed label instructs the users to perform the patented method. If so, the proposed label may provide evidence of [the generic's] affirmative intent to induce infringement." *AstraZeneca LP v. Apotex, Inc.*,

633 F.3d 1042, 1060 (Fed. Cir. 2010). "The question is not ... whether a user following the instructions may end up using the device in an infringing way. Rather, it is whether [the] instructions teach an infringing use of the device such that we are willing to infer from those instructions an affirmative intent to infringe the patent." *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1329 n.2 (Fed. Cir. 2009); *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1322 (Fed. Cir. 2012) ("The question to be answered, then, is whether the FDA has approved the use of Yasmin to achieve the combination of the three effects claimed in the '652 patent."). In sum, the Federal Circuit has not found infringement when the product label does not address the patented methods.[9]

On its face, the Mitigare™ label does not infringe. Rather, the Mitigare™ label instructs patients to consult with a healthcare provider who may (or may not) consult Colcrys® prescribing information, and who may (or may not) follow the patented method of use for treatment of the acute gout flare. This is an insufficient basis upon which to establish induced infringement. "The label must encourage, recommend, or promote infringement. The mere existence of direct infringement by physicians, while necessary to find liability for induced infringement, is not sufficient for inducement." *Takeda*, 785 F.3d at 631 (citations omitted). Accepting the factual allegations viewed in the light most favorable to Takeda and under the more lenient standard at the pleading stage, Takeda has failed to meet its burden. The Mitigare™ label is not a sufficient catalyst to

[9] The court acknowledges that the Federal Circuit has found infringement when instructions in the label would cause at least some users to infringe. *AstraZeneca*, 633 F.3d at 1060. The circumstances here, however, are distinguishable, as the instructions on the Mitigare™ label require consultation with a physician rather than specific instructions, as did the label in *AstraZeneca* in compliance with FDA requirements.

constitute "active steps taken to encourage direct infringement" as it requires consultation with a physician. *Id.* at 630.

Takeda's arguments regarding Hikma's marketing and sales activities similarly fail. To survive a motion to dismiss, Takeda is charged with providing adequate factual allegations that set forth a plausible claim for relief such that there is a reasonable expectation that discovery will uncover relevant evidence. Despite the marketing of Mitigare™ for at least ten months, Takeda offers no such allegations. In this regard, Takeda added two allegations to its amended complaint based "upon information and belief," one concerning Mitigare™ sales representatives (D.I. 109 at ¶¶ 48-49)[10] and one concerning Hikma's entering contracts with health insurance providers. (D.I. 109 at ¶¶ 50-53).[11] Viewing these allegations in a light favorable to Takeda, (and despite having had at least ten months to observe the market's reaction to Mitigare™), the allegations are too conclusory to pass muster. With respect to the sales representatives, telling a patient that thirty capsules may last a year in no way

---

[10] According to Takeda, "MITIGARE™ sales representatives have informed prescribers that thirty capsules of MITIGARE™ or the MITIGARE™ AG product could last a patient up to one year, demonstrating Hikma's and West-Ward's intent to sell the MITIGARE™ Products for the treatment of acute gout flares" and that "MITIGARE™ sales representatives have also explicitly informed prescribers that MITIGARE™ or the MITIGARE™ AG product can be used to treat acute gout flares." (D.I. 109 at ¶¶ 48-49)

[11] As to health insurance providers, Takeda alleges Hikma has entered into at least two "sole-source contracts" with specific insurance providers that "effectively guarantee that, for all patients covered by these insurance providers, the only single oral colchicine option available to them for the treatment of acute gout flares will be [Mitigare™] or [Mitigare™] AG product." (D.I. 109 at ¶ 52) In support, Takeda points to Hikma's agreement with Kaiser Permanente, whose medication guide "currently contains dosing instructions for acute treatment that describe Takeda's patented method . . . [but] does not contain any instructions for prophylactic use, which is the only FDA-approved use for MITIGARE™." (*Id.*)

constitutes "[e]vidence of active steps taken to encourage direct infringement." *Takeda*, 785 F.3d 630 (alteration in original). Moreover, a threadbare allegation stating that Mitigare™ **can** be used for acute gout flares is not the same as stating Mitigare™ **should** be used, explaining how to do so in an infringing manner, and establishing that patients have followed those instructions. The allegations directed at third-party insurance providers fare no better, as Hikma's allegation in this regard merely acknowledges potential infringement by others, not that Hikma has taken "active steps" itself "to encourage direct infringement." *Takeda*, 785 F.3d at 630. "[I]t is well-established that 'mere knowledge of possible infringement by others does not amount to inducement; specific intent and action to induce infringement must be proven.'" *Id.* at 631 (quoting *Warner-Lambert*, 316 F.3d at 1364).

Turning to the DDI Patents and based on the record currently before it, the court maintains its finding that Takeda has not adequately alleged direct (and consequently, induced) infringement. Direct infringement of the DDI Patents requires a 0.3 mg dose of colchicine per day; Mitigare™ is a 0.6 mg capsule that cannot be split.[12] Further, Takeda's amended complaint offers no factual allegations that infringement, either direct or indirect, has actually occurred, despite the marketing of Mitigare™ for at least ten months. Rather, Takeda speculates that "at least some doctors and patients **will** consult the dose regimens set forth in the Colcrys® product labeling, and adjust the colchicine dosing according to the instructions in the FDA-approved Colcrys® label." (D.I. 109 at ¶ 57) (emphasis added) Takeda then discusses Hikma's correspondence

[12] The court and Federal Circuit have already dispensed with Takeda's argument that the 0.3 mg doses may be accomplished by reducing the frequency of a 0.6 mg dose. *Takeda*, 785 F.3d at 635.

with the FDA during the approval process, devoid of any non-conclusory allegations of infringement. (D.I. 109 at ¶¶ 58-63) Viewed in the light most favorable to Takeda, these allegations are insufficient to raise a reasonable inference of infringement because (like the Acute Flare Patents discussed above), the doctors and patients may (or may not) consult Colcrys®' product labeling, and may (or may not) adjust the colchicine dosing according to the instructions in the FDA-approved Colcrys® label. On this record, Takeda has only pled speculative future infringement. "The mere knowledge of possible infringement will not suffice" (*Vita-Mix*, 581 F.3d at 1328); "[h]ypothetical instances of direct infringement are insufficient to establish [] indirect infringement." *ACCO Brands, Inc. v. ABA Locks Mfrs. Co.*, 501 F.3d 1307, 1313 (Fed. Cir. 2007) (citing *Dynacore Holdings Corp. v. U.S. Philips Corp.*, 363 F.3d 1263, 1274 (Fed. Cir. 2004)). Indeed, "inducement gives rise to liability only if the inducement leads to actual infringement ... [t]here is no such thing as attempted patent infringement." *Akamai Technologies, Inc. v. Limelight Networks, Inc.*, 692 F.3d 1301, 1308 (Fed. Cir. 2012), *rev'd on other grounds*, 134 S. Ct. 2111 (2014). It is undisputedly possible that the use of Mitigare™ will not ever practice the claimed method. *Vita-Mix*, 581 F.3d at 1329. Given the lack of factual allegations of infringement, the court is unable to find that Takeda has a "plausible claim for relief" at this time. *Iqbal*, 556 U.S. at 679.

V. CONCLUSION

For the foregoing reasons, the court grants Hikma's motion to dismiss. An appropriate order shall issue.

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

TAKEDA PHARMACEUTICALS U.S.A., INC.,	)	
Plaintiff,	)	
v.	)	Civ. No. 14-1268-SLR
WEST-WARD PHARMACEUTICAL CORPORATION, HIKMA AMERICAS, INC. and HIKMA PHARMACEUTIALS PLC,	)	
Defendants.	)	

ORDER

At Wilmington this 18th day of May, 2016, consistent with the memorandum opinion issued this same date;

IT IS ORDERED that defendants' motion to dismiss plaintiff's first amended complaint (D.I. 112) is granted.

United States District Judge