United States Court of Appeals for the Federal Circuit

TEVA PHARMACEUTICALS USA, INC.,
Appellant

v.

CORCEPT THERAPEUTICS, INC.,
Appellee

2021-1360

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. PGR2019-00048.

Decided: December 7, 2021

JOHN CHRISTOPHER ROZENDAAL, Sterne Kessler Goldstein & Fox, PLLC, Washington, DC, argued for appellant. Also represented by UMA EVERETT, WILLIAM MILLIKEN, OLGA A. PARTINGTON, DEBORAH STERLING.

ERIC C. STOPS, Quinn Emanuel Urquhart & Sullivan, LLP, New York, NY, argued for appellee. Also represented by WILLIAM ADAMS, FRANK CHARLES CALVOSA, FRANCIS DOMINIC CERRITO, DANIEL C. WIESNER.

Before MOORE, *Chief Judge*, NEWMAN and REYNA, *Circuit Judges*.

MOORE, *Chief Judge*.

In a final-written decision, the Patent Trial and Appeal Board held that Teva Pharmaceuticals USA had failed to show claims 1–13 of U.S. Patent No. 10,195,214 would have been obvious. *Teva Pharms. USA, Inc. v. Corcept Therapeutics, Inc.*, PGR2019-00048, 2020 WL 6809812 (P.T.A.B. Nov. 18, 2020) (*Final Decision*). Teva appeals, arguing the Board misapplied our obviousness law.[1] For the following reasons, we affirm.

I

A

In the 1980s, mifepristone was developed as an antiprogestin. *See* J.A. 1009. But researchers soon realized mifepristone functions as a glucocorticoid reception antagonist, meaning it likely inhibits the effect of cortisol on tissues by competing with cortisol for receptor binding sites. *See* J.A. 870, 1037. As a result, they suggested using mifepristone to treat Cushing's syndrome, a disease caused by excessive levels of cortisol. J.A. 1034–38.

More than 20 years later, Corcept Therapeutics, Inc., initiated the first major clinical trial of mifepristone in patients with Cushing's syndrome. J.A. 1252. Over a 24-week period, 50 participants were given one daily dose of mifepristone, starting at a dosage of 300 mg per day and possibly increasing to a maximum dosage of 1200 mg per day. J.A. 1259. That administration "produced significant clinical and metabolic improvement in patients with [Cushing's syndrome] with an acceptable risk-benefit

---

[1] Teva also argues that, under the correct standards, the challenged claims would have been obvious. Because we discern no legal error, we need not reach that argument.

profile during 6 months of treatment." J.A. 1259; *accord* J.A. 1259–61.

Based on its successful study, Corcept filed a New Drug Application (NDA) for Korlym, a 300 mg mifepristone tablet. It sought approval for the administration of Korlym to control "hyperglycemia secondary to hypercortisolism" in certain patients with Cushing's syndrome. J.A. 982. The U.S. Food and Drug Administration approved Corcept's application, but imposed a few postmarketing requirements under 21 U.S.C. § 355(o)(3). One requirement was to conduct "[a] drug-drug interaction clinical trial to determine a quantitative estimate of the change in exposure of mifepristone following co-administration of ketoconazole (a strong CYP3A4 inhibitor)." J.A. 984.

To summarize the drug-drug interaction study requirement, the FDA provided Corcept with an Office of Clinical Pharmacology memorandum. *See* J.A. 865–900 (hereinafter, Lee). That memorandum explained that "[t]he degree of change in exposure of mifepristone when co-administered with strong CYP3A inhibitors is unknown . . . ." J.A. 865. Thus, Lee noted that co-administration "may present a safety risk" and that, without a drug-drug interaction study, a "lack of accurate knowledge" may "deprive the patients on strong inhibitors [of] the use of [m]ifepristone." *Id.* Lee also noted that, "[b]ased on the results of this study, the effect of moderate CYP3A inhibitors on mifepristone pharmacokinetics may need to be addressed." J.A. 866.

In approving Corcept's NDA, the FDA also approved the prescribing information for Korlym contained in its label. J.A. 839–49. The FDA-approved Korlym label "recommended [a] starting dose [of] 300 mg once daily" and allowed for increasing the dosage "in 300 mg increments to a maximum of 1200 mg once daily" based on clinical assessments. J.A. 839. In addition to those conditions, the Korlym label warned against using mifepristone "with strong

CYP3A inhibitors" and limited the "mifepristone dose to 300 mg per day when used with strong CYP3A inhibitors." J.A. 839.

B

Corcept conducted the drug-drug interaction study described in Lee, collecting data on co-administration of mifepristone with a strong CYP3A inhibitor. Based on that data, Corcept sought and received the '214 patent. The '214 patent relates to methods of treating Cushing's syndrome by co-administering mifepristone and a strong CYP3A inhibitor. Claim 1 is representative for purposes of this appeal:

> A method of treating Cushing's syndrome in a patient who is taking an original once-daily dose of 1200 mg or 900 mg per day of mifepristone, comprising the steps of:
>
> > reducing the original once-daily dose to an adjusted once-daily dose of 600 mg mifepristone,
> >
> > administering the adjusted once-daily dose of 600 mg mifepristone and a strong CYP3A inhibitor to the patient,
> >
> > wherein said strong CYP3A inhibitor is selected from the group consisting of ketoconazole, itraconazole, nefazodone, ritonavir, nelfmavir, indinavir, boceprevir, clarithromycin, conivaptan, lopinavir, posaconazole, saquinavir, telaprevir, cobicistat, troleandomycin, tipranivir, paritaprevir, and voriconazole.

After Corcept asserted the '214 patent against Teva in district court, Teva sought post-grant review of claims 1–13. Teva argued those claims would have been obvious in light of Korlym's label and Lee, optionally in combination

with FDA guidance on drug-drug interaction studies. In support of its petition, Teva provided a declaration from Dr. David J. Greenblatt. Most relevant here, Dr. Greenblatt opined that, based on the Korlym label and Lee, "it was reasonably likely that 600 mg [per day of mifepristone] would be well tolerated and therapeutically effective when co-administered with a strong CYP3A inhibitor." J.A. 681. The Board instituted review on all asserted grounds.

In its final-written decision, the Board held Teva had failed to prove claims 1–13 would have been obvious to a skilled artisan. It first construed the claims to require safe administration of mifepristone. *Final Decision* at *7–9. Then, the Board found Teva failed to show that a skilled artisan would have had a reasonable expectation of success for safe co-administration of more than 300 mg of mifepristone with a strong CYP3A inhibitor. *Id.* at *10–22. In doing so, it discredited the above-quoted statement from Dr. Greenblatt, finding it inconsistent with his later testimony and other evidence in the record. Teva appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(4).

II

Teva faults the Board for, in its view, committing two legal errors. First, it claims the Board required precise predictability, rather than a reasonable expectation of success, in achieving the claimed invention. That is, Teva argues the Board improperly required it "to show an expectation that the *specific* dose recited in the claims would have been safe." Appellant's Br. at 41. Second, Teva claims the Board ought to have applied our prior-art-range precedents. In Teva's view, the Board committed legal error when it found Teva had failed to prove the general working conditions disclosed in the prior art encompassed the claimed invention. We do not agree.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.