UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC., TEVA PHARMACEUTICALS USA, INC. and AKORN INC.,[1]
Petitioners,

v.

ALLERGAN, INC.
Patent Owner.

Case IPR2016-01127 (US 8,685,930 B2)
Case IPR2016-01128 (US 8,629,111 B2)
Case IPR2016-01129 (US 8,642,556 B2)
Case IPR2016-01130 (US 8,633,162 B2)
Case IPR2016-01131 (US 8,648,048 B2)
Case IPR2016-01132 (US 9,248,191 B2)

PETITIONERS' REPLY
37 C.F.R. §42.24(c)

---

[1] Cases IPR2017-00576 and IPR2017-00594, IPR2017-00578 and IPR2017-00596, IPR2017-00579 and IPR2017-00598, IPR2017-00583 and IPR2017-00599, IPR2017-00585 and IPR2017-00600, and IPR2017-00586 and IPR2017-00601, have respectively been joined with the captioned proceedings. The word-for-word identical paper is filed in each proceeding identified in the caption pursuant to the Board's Scheduling Order (Paper 10).

TABLE OF CONTENTS

I. INTRODUCTION

It is undisputed that the claimed formulation falls squarely within the ranges disclosed in the prior art Ding '979 patent. Allergan attempts to weave a tale of unexpected results and criticality of the claimed formulation based on an alleged superiority, but none has been demonstrated. The prior art Sall reference demonstrates therapeutic equivalence between the 0.05% and 0.10% CsA formulations. Allergan conjures a theory that the ratio of CsA-to-castor oil is critical to therapeutic efficacy. But the very ratio used in the claimed formulation is already disclosed in Ding '979, and nothing in the record indicates that using this ratio for a 0.05% CsA formulation changes its therapeutic efficacy. Allergan's arguments are not only unsubstantiated entirely, they are repeatedly and soundly contradicted by the evidence of record.[2]

Allergan's criticality arguments hinge on an alleged improvement in categorized Schirmer Tear Test ("STT") scores in Sall Figure 2 for the 0.05% CsA formulation over the 0.10% CsA formulation. Allergan's arguments contradict the

---

[2] Because of the near-identity of issues in each of the IPRs addressing the related '930, '111, '556, '162, '048, and '191 patents ("patents-at-issue"), Petitioners' Reply is identical in each IPR and provides citations to the page numbers in IPR2016-01127 as exemplary citations for all six proceedings.

teachings of Sall, Stevenson (EX1015 reporting Phase 2 results), and the shared specification of the patents-at-issue. Sall, in fact, demonstrates substantially equivalent therapeutic efficacy between the two formulations. EX1007, 634-36. Any alleged difference between the two formulations is neither significant nor material. Unexpected equivalent efficacy (or even potentially marginally increased efficacy) between the two formulations does not demonstrate a difference in kind.

Allergan's thermodynamic theory is so theoretical its experts never even bothered to attempt to quantify it. Allergan's suggestion that a thermodynamic effect would be large enough to render the claimed formulation inoperative is directly contradicted by Ding '979's teachings that its emulsions had "reasonably high thermodynamic activity," and that "the therapeutic level of cyclosporin was found in the tissues of interest after dosage." EX1006, 3:25-28, 5:15-24.

Allergan's two PK studies confirm that any theoretical thermodynamic effect was not large enough to matter, demonstrating each formulation delivered well-above-therapeutic levels of CsA to the tissues. Further, Allergan's employee, Dr. Attar, compared these two, completely different types of studies (steady-state, measuring tissue concentrations after 9.5 days of twice-daily 50 µL doses, versus single-dose, measuring tissue concentrations after just one 28.5 µL dose), and still failed to demonstrate a statistically significant difference in CsA delivery to the lacrimal glands, the "most important" target tissue.

Allergan's remaining alleged objective indicia of non-obviousness fail for lack of nexus. Allergan's Orange Book listing of both U.S. Patent No. 4,839,342 (EX2002) and Ding '979 render it impossible to attribute commercial sales to any allegedly novel features of the claims. EX1032, ADA36. Allergan forcefully drove sales through heavy direct-to-consumer marketing and other strategic initiatives. Thus, Allergan's sales numbers provide no information about any alleged relative benefit from or criticality of the claimed formulation as compared to the prior art alternatives. Moreover, the alleged objective indicia are not relevant to the formulation claims because those are also anticipated.

II. LEGAL STANDARDS

Allergan must show that a POSA would have expected the claimed formulation to lack therapeutic efficacy or operate differently for treating dry eye/KCS. Paper 8, 17-19. Allergan must also produce evidence of objective indicia of nonobviousness to rebut Petitioners' evidence of obviousness. *Prometheus Labs., Inc. v. Roxane Labs., Inc.*, 805 F.3d 1092, 1101-02 (Fed. Cir. 2015). Objective indicia require "a nexus to establish that the evidence relied upon traces its basis to a novel element in the claim and not to something in the prior art." *Biomarin Pharmaceutical Inc. v. Genzyme Therapeutic Products L.P.*, IPR2013-00537, Paper 79, 22; *Institute Pasteur & Universite Pierre et Marie Curie v.*

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.