

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEPTUNE GENERICS, LLC,
APOTEX INC., APOTEX CORP.,
TEVA PHARMACEUTICALS USA, INC.,
and FRESENIUS KABI USA, LLC,

PETITIONERS,

V.

ELI LILLY & COMPANY,
PATENT OWNER.

Case IPR2016-00240^{1,2}
Patent 7,772,209

PETITIONER'S REPLY TO PATENT OWNER'S RESPONSE

¹ Cases IPR2016-01191 and IPR2016-01343 have been joined with the instant proceeding.

² An identical Reply has been filed in IPR2016-00237 under that IPR caption. All paper and exhibit numbers herein refer to IPR2016-00237's papers and exhibits unless otherwise noted.

TABLE OF CONTENTS

I.	INTRODUCTION	1
II.	DR. CHABNER APPLIES THE WRONG OBVIOUSNESS STANDARDS TO REACH HIS OPINIONS.	2
III.	DR. CHABNER’S OPINIONS ARE INCONSISTENT WITH CONTEMPORANEOUS EVIDENCE OF HOW A POSA WOULD INTERPRET THE PRIOR ART.	6
IV.	A POSA WOULD HAVE BEEN MOTIVATED TO ADDRESS PEMETREXED’S KNOWN TOXICITIES.....	11
V.	FOLIC ACID IS NOT PEMETREXED’S ANTIDOTE.	12
1.	A POSA Would Have Understood that Folic Acid is Not Pemetrexed’s Antidote.....	12
2.	A POSA Would Have Reasonably Expected Folic Acid Pretreatment to Improve Pemetrexed’s Therapeutic Index.....	14
3.	A POSA Would Not Have Compared Hammond and Rinaldi for the Efficacy of Folic Acid Supplementation.....	16
4.	A POSA Would Have Understood that Folic Acid Supplementation Does Not Cause Tumor Growth.	17
VI.	A POSA WOULD HAVE BEEN MOTIVATED TO SUPPLEMENT PEMETREXED WITH FOLIC ACID AND B ₁₂ WITH A REASONABLE EXPECTATION OF SUCCESS.....	18
A.	The Prior Art Taught that <i>Pretreatment</i> Elevated Homocysteine Predicts Pemetrexed Toxicity.....	18
B.	A POSA Would Have Had a Reasonable Expectation that B ₁₂ Supplementation with FA Would Successfully Reduce Pemetrexed Toxicity.	23
C.	A POSA Would Not Have Been Concerned about a B ₁₂ Methyl Trap .	27
D.	A POSA Would Have Understood that B ₁₂ Supplementation Would Not Cause Tumor Growth.....	28

VII. THE '209 PATENT'S CLAIMED DOSE AND SCHEDULE ARE NOT CRITICAL AND WERE STANDARD IN THE ART.....30

VIII. LILLY'S ALLEGED SECONDARY CONSIDERATIONS ARE INSUFFICIENT TO DEFEAT OBVIOUSNESS.31

TABLE OF AUTHORITIES

Cases

<i>Amazon.com, Inc. v. Barnesandnoble.com</i> , 239 F.3d 1343 (Fed. Cir. 2001).....	3
<i>Bayer Healthcare Pharms., Inc. v. Watson Pharms., Inc.</i> , 713 F.3d 1369 (Fed. Cir. 2013).....	33
<i>Custom Accessories, Inc. v. Jeffrey-Allan Indus.</i> , 807 F.2d 955 (Fed. Cir. 1986).....	3
<i>Ex Parte Erlich</i> , 1992 Pat. App. Lexis 2, (Bd. Pat. App. & Interferences Jan. 16 1992).....	7
<i>Ex Parte McGaughey</i> , 1988 Pat. App. LEXIS 2, (Bd. Pat. App. & Interferences Mar. 4, 1988).....	7
<i>Ex Parte Raychem</i> , 1992 Pat. App. LEXIS 21, (Bd. Pat. App. & Interferences June 30, 1992).....	7
<i>Hoffman-LaRoche Inc. v. Apotex, Inc.</i> , 748 F.3d 1326 (Fed. Cir. 2014).....	3
<i>In re Fulton</i> , 391 F.3d 1195 (Fed. Cir. 2004).....	25
<i>In re Hogan</i> , 559 F.2d 595 (C.C.P.A. 1977)	7
<i>In re Wilson</i> , 311 F.2d 266 (C.C.P.A. 1962)	6
<i>KSR Int’l Co. v. Teleflex Inc.</i> , 550 U.S. 398 (2007).....	4
<i>Medichem S.A. v. Rolabo S.I.</i> , 437 F.3d 1157 (Fed. Cir. 2006).....	15
<i>Organik Kimya AS v. Rohm & Haas Co.</i> , IPR2014-00185, Paper 42-2 (P.T.A.B. Dec. 18, 2014).....	32
<i>Ortho-McNeil Pharm., Inc. v. Teva Pharms. Indus., Ltd.</i> , 344 F. App’x 595 (Fed. Cir. 2009)	11

<i>Pharmastem Therapeutics, Inc. v. Viacell, Inc.</i> , 491 F.3d 1342 (Fed. Cir. 2007).....	11, 32, 33
<i>Randall Mfg. v. Rea</i> , 733 F.3d 1355 (Fed. Cir. 2013).....	19
<i>Std. Oil Co. v. Am. Cyanamid Co.</i> , 774 F.2d 448 (Fed. Cir. 1985).....	3
<i>Thomas & Betts Corp. v. Litton Sys., Inc.</i> , 720 F.2d 1572 (Fed. Cir. 1983).....	6
<i>ViiV Healthcare UK Ltd. v. Lupin Ltd.</i> , 6 F. Supp. 3d 461 (D. Del. 2013).....	32
Rules	
Fed. R. Evid. 801(d)(2)	7

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.