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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEPTUNE GENERICS, LLC,
Petitioner,

v.

ELI LILLY & COMPANY
Patent Owner.

Case IPR2016-00237
Patent 7,772,209 B2

Before MICHAEL P. TIERNEY, JACQUELINE WRIGHT BONILLA, and TINA E. HULSE, *Administrative Patent Judges*.

TIERNEY, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Neptune Generics, LLC ("Petitioner"), filed a Petition requesting an *inter partes* review of claims 1–22 of U.S. Patent 7,772,209 B2 (Ex. 1001, "the '209 patent"). Paper 1 ("Pet."). Patent Owner, Eli Lilly & Company, ("Patent Owner") timely filed a Preliminary Response (Paper 10, "Prelim. Resp.") to the Petition. We have jurisdiction under 35 U.S.C. § 314.

To institute an *inter partes* review, we must determine that the information presented in the Petition shows "a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). For the reasons set forth below, upon considering the Petition and the Preliminary Response, we conclude that the information presented in the Petition establishes a reasonable likelihood that Petitioner will prevail in challenging claims 1–22 of the '209 patent. We authorize an *inter partes* review to be instituted as to those claims.

Our factual findings and conclusions at this stage of the proceeding are based on the evidentiary record developed thus far. This decision to institute trial is not a final decision as to patentability of claims for which *inter partes* review is instituted. Our final decision will be based on the full record developed during trial.

A. Related Proceedings

The '209 patent is the subject of litigation in the Southern District of Indiana, including *Eli Lilly & Co. v. Teva Parenteral Medicines, Inc.*, et al., Case No. 1:10-cv-1376. Pet. 2, Prelim. Resp. 2.

Additionally, Petitioner notes that the '209 patent also was challenged in IPR2013-00356 by Accord Healthcare, Inc. Pet. 2.[1]

The '209 patent has also been challenged in IPR2016-00240 by Petitioner, and in IPR2016-00318 by Sandoz Inc.

B. The '209 Patent

The '209 patent claims priority benefit of a series of applications, the earliest of which was filed on June 30, 2000. Ex. 1001, 1:2–10.

"As cancer cells actively proliferate, they require large quantities of DNA and RNA." Declaration of W. Archie Bleyer, Ex. 1025 ¶ 67. Antifolates are a well-studied class of antineoplastic agents that inhibit one or several key folate-requiring enzymes of the thymidine and purine biosynthetic pathways. Ex. 1001, 1:36–41. As antifolates interfere with DNA and RNA synthesis, antifolates are used as chemotherapeutic drugs to treat certain types of cancer. Ex. 1025 ¶ 67.

A limitation on the use of antifolate drugs is "that the cytotoxic activity and subsequent effectiveness of the antifolates may be associated with substantial toxicity for some patients." Ex. 1001, 1:62–64. Homocysteine levels have been shown to be a predictor of cytotoxic events

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[1] The Board declined to institute in IPR2013-00356, holding that the petition was not filed within the time limit imposed by 35 U.S.C. § 315(b). *Accord Healthcare, Inc., USA v. Eli Lilly and Co.*, Case IPR2013-00356, slip op. 4 (PTAB Oct. 1, 2013) (Paper 13).

related to the use of certain antifolate enzyme inhibitors. *Id*. at 2:16–26. The '209 patent states that folic acid has been shown to lower homocysteine levels. *Id*. Additionally, the patent states that it was known in the art to treat and prevent cardiovascular disease with a combination of folic acid and vitamin B12. *Id*. at 2:50–54.

The '209 patent describes "[a] method of administering an antifolate to a mammal in need thereof." Ex. 1001, abstract. The method is said to improve the therapeutic utility of antifolate drugs by administering a methylmalonic acid ("MMA") lowering agent, such as vitamin B12, to the host undergoing treatment. *Id*. at 2: 37–46. The '209 patent also states that a combination of a MMA lowering agent, such as B12, and folic acid "synergistically reduces the toxic events associated with the administration of antifolate drugs." *Id*. at 2:47–50

The term antifolate is said to encompass chemical compounds that inhibit at least one key folate-requiring enzyme of the thymidine or purine biosynthetic pathways. *Id*. at 4:28–34. Pemetrexed disodium is the most preferred antifolate for the '209 patent. *Id*. at 4:28–43. Pemetrexed is also referred to in the art as the "multitargeted antifolate" ("MTA"). Ex. 1022, 129, Abstract 620P.

C. Illustrative Claims

The '209 patent contains twenty-two claims, all of which are challenged by Petitioner. Independent claim 1 is directed to a method for administering pemetrexed disodium to a patient in need thereof, where folic acid and a MMA lowering agent, such as B12, is administered, followed by administering an effective amount of the pemetrexed disodium. Independent claim 12 is written in a Jepson claim format, where the preamble defines the

admitted prior art as administering pemetrexed disodium to a patient in need of a chemotherapeutic treatment. Independent claim 12 further recites specific dosage amounts of folic acid and vitamin B12 that are administered to the patient prior to the first administration of the pemetrexed disodium. Dependent claim 2 requires the MMA lowering agent of claim 1 to be vitamin B12 and the remaining dependent claims recite various dosages of folic acid and B12, and times for administering folic acid. Certain claims also require the administration of cisplatin to the patient. Claims 1 and 12 are illustrative of the challenged claims and are reproduced below:

1. A method for administering pemetrexed disodium to a patient in need thereof comprising administering an effective amount of folic acid and an effective amount of a methylmalonic acid lowering agent followed by administering an effective amount of pemetrexed disodium, wherein

the methylmalonic acid lowering agent is selected from the group consisting of vitamin B12, hydroxycobalamin, cyano-10-chlorocobalamin, aquocobalamin perchlorate, aquo-10-cobalamin perchlorate, azidocobalamin, cobalamin, cyanocobalamin, or chlorocobalamin.

12. An improved method for administering pemetrexed disodium to a patient in need of chemotherapeutic treatment, wherein the improvement comprises:

a) administration of between about 350 μg and about 1000 μg of folic acid prior to the first administration of pemetrexed disodium;

b) administration of about 500 μg to about 1500 μg of vitamin B12, prior to the first administration of pemetrexed disodium; and

c) administration of pemetrexed disodium.

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