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Paper 7
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ANTARES PHARMA, INC., LEO PHARMA A/S AND
LEO PHARMA INC.,
Petitioner,

v.

MEDAC GESELLSCHAFT FÜER KLINISCHE
SPEZIALPRÄPARATE MBH.,
Patent Owner.

Case IPR2014-01091
Patent 8,664,231 B2

Before TONI R. SCHEINER, ERICA A. FRANKLIN, and
JACQUELINE WRIGHT BONILLA, *Administrative Patent Judges.*

FRANKLIN, *Administrative Patent Judge.*

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

I. INTRODUCTION

Antares Pharma, Inc., Leo Pharma A/S and Leo Pharma Inc. (collectively, "Petitioner") filed a Petition requesting an *inter partes* review of claims 1–22 of U.S. Patent No. 8,664,231 B2 (Ex. 1001, "the '231 patent"). Paper 1 ("Pet."). Medac Gesellschaft für klinische Spezialpräparate mbH ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp.").

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is 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). Upon considering the Petition and Preliminary Response, we determine that Petitioner has shown a reasonable likelihood that it would prevail in showing the unpatentability of claims 1–22. Accordingly, we institute an *inter partes* review of those claims.

A. Related Proceedings

Petitioner and Patent Owner identify one district court action involving the '231 patent, titled *medac Pharma, Inc. v. Antares Pharma, Inc*, No. 1:14-cv-01498-JBS-KMW (D.N.J.). Pet. 1; Paper 5, 2.

B. The '231 Patent (Ex. 1001)

The '231 patent relates to a method for treating inflammatory autoimmune diseases, such as rheumatoid arthritis, juvenile rheumatoid arthritis, or psoriasis, comprising administering subcutaneously a concentrated methotrexate solution comprising more than 30 mg/ml of methotrexate. Ex. 1001, Abstract. Methotrexate is an effective cytostatic agent that is well known for treating breast cancer, leukemia in children, and

psoriasis. *Id*. at 1:24–30. "Over the years, methotrexate has become the gold standard in the treatment of rheumatoid arthritis." *Id*. at 2:34–36. As a basic therapeutic for rheumatoid arthritis, methotrexate is administered once a week, orally or parenterally. *Id*. at 64–67.

The invention is also directed to a ready-made syringe and carpule containing the methotrexate solution, as well as a pen-injector comprising the ready-made syringe and/or carpule. *Id*. at 1:10–13. Preparing methotrexate, including drawing it up in a syringe from a bottle, is subject to strict restrictions, such as requiring the preparation to occur within a suitable venting system. *Id*. at 2:7–17.

Previously, ready-made syringes were developed to avoid the step of preparing a methotrexate solution for injection. *Id*. at 2:18–19.) The '231 patent states, "[f]or the first time, the applicant in the present invention was able to have such ready-made syringes for subcutaneous application approved throughout Europe." *Id*. at 2:19–22. These ready-made syringes may be administered by the physician, medical staff, or by the patient as a self-application, without requiring any preparation of the injection. *Id*. at 22–25.

According to the Specification, the claimed invention provides a concentrated methotrexate solution for subcutaneous administration that allows a smaller volume of the solution to be injected, thereby overcoming the pain associated with subcutaneously injecting larger amounts of solution, e.g., up to 3 ml. *Id*. at 2:44–60.

C. Illustrative Claim

Claim 1 of the '231 patent, the only independent claim, is illustrative and is reproduced below:

> 1. A method for the treatment of inflammatory autoimmune diseases in a patient in need thereof, comprising subcutaneously administering to said patient a medicament comprising methotrexate in a pharmaceutically acceptable solvent at a concentration of more than 30 mg/ml.

D. The Prior Art

Petitioner relies upon the following prior art references:

Grint	US 6,544,504 B1, issued Apr. 8, 2003	Ex. 1003
Insulin Admin.	American Diabetes Assn., *Insulin Admin.*, 26 DIABETES CARE Supp. 1, S121–S124 (2003).	Ex. 1015
Alsufyani	Alsufyani et al., *The Role of Subcutaneous Adm. of Methotrexate in Children with Juvenile Idiopathic Arthritis Who Have Failed Oral Methotrexate*, 31:1 J. RHEUMATOLOGY 179–82 (2003).	Ex. 1006
The PDR	Edward R. Barnhart, Physicians' Desk Reference (39th ed. 1985).	Ex. 1007
Hospira	Hospira UK Ltd, *Product Summary for Methotrexate 100mg/ml Injection* (Rev. 2005)	Ex. 1009
Brooks	Brooks et al., *Pharmacokinetics of Methotrexate Adm. by Intramuscular and Subcutaneous Injections in patients with Rheumatoid Arthritis*, 33 ARTHRITIS AND RHEUMATOLOGY 91–94 (1990).	Ex. 1008

Hoekstra	Hoekstra et al., *Bioavailability of Higher Dose Methotrexate Comparing Oral and Subcutaneous Admin. in Patients with Rheumatoid Arthritis*, 31:4 J. RHEUMATOLOGY 645–648 (2004).	Ex. 1004
Jorgensen	Jorgensen et al., *Pain Assessment of Subcutaneous Injections*, 30 ANN. PHARMACOTHERAPY 729–32 (1996).	Ex. 1005

Petitioner also relies upon the declarations of Dr. Michael E. Weinblatt (Ex. 1012) and Dr. David C. Gammon (Ex. 1013).

E. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–22 of the '231 patent on the following grounds:

References	**Basis**	**Claims Challenged**
Grint	§ 102(b)	1, 2, 4–6, 11–13, 17, and 22
Grint and Insulin Admin.	§ 103(a)	7–10, 14–16, and 19–21
Grint and Alsufyani	§ 103(a)	18
The PDR or Hospira and Brooks	§ 103(a)	1–5, 11–13, 17, and 22
The PDR or Hospira, Brooks, and Insulin Admin.	§ 103(a)	7–10, 14–16, and 19–21
Hoekstra and Jorgensen	§ 103(a)	1–6, 11–13, 17, and 22
Hoekstra, Jorgensen, and Insulin Admin.	§ 103(a)	7–10, 14–16, and 19–21
Hoekstra, Jorgensen, and Alsufyani	§ 103(a)	18

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