IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants:	Elliot Ehrich		
Application No.:	13/871,534	Group No.:	1627
Filed:	April 26, 2013	Examiner:	Carter, Kendra D.
Confirmation No.:	5842		
For:	NALTREXONE LONG ACTING FORMULATIONS AND METHODS OF USE		

APPEAL BRIEF

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P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Brief is being filed pursuant to 37 CFR §41.37. The required sections (i-v) under 37 CFR §41.37(c)(1) are set forth below under separate headings.

(i) The Real Party In Interest

The real party of interest in this appeal is the assignee, Alkermes Pharma Ireland Limited by virtue of the assignment recorded on October 16, 2015 at Reel 036809 and Frame 0447.

(ii) Related Appeals, Interferences, and Trials

There are no related appeals, interferences, or trials at this time known to the Appellant, the assignee or its representative which will directly affect or be directly affected by or have a bearing in the Board's decision in the pending appeal.

(iii) Summary of Claimed Subject Matter

Independent claim 1 recites a method for treating an individual in need of naltrexone comprising the step of administering by intramuscular injection a long acting formulation comprising naltrexone to the individual wherein the serum AUC of

naltrexone is at least about two times greater than that achieved by 50 mg/day oral administration, wherein the long acting formulation of naltrexone is administered only once during at least a two week period, and comprises between 160 and 240 mg of naltrexone or about 310 to about 480 mg of naltrexone. Support for claim 1 is found on page 3, lines 7-11 and 29-31; page 4, line 1; page 6, lines 3-6 and 24-31; and page 7, line 1.

Claim 6 depends directly from claim 1 and further recites that the long acting formulation releases naltrexone for a period of about four weeks. Support for claim 6 is found on page 6, lines 24-25.

Claim 7 depends directly from claim 1 and further recites that the long acting formulation is administered in a dose of about 380 mg of naltrexone. Support for claim 7 is found on page 4, lines 1-2.

Claim 11 depends directly from claim 1 and further recites that the long acting formulation is administered over a period of about 24 weeks or longer. Support for claim 11 is found on page 2, lines 19-22.

Claim 14 depends directly from claim 1 and further recites that the individual is an individual afflicted by alcohol dependency. Support for claim 14 can be found on page 7, lines 21-24.

Claims 16-17 depend directly from claim 1 and further recite that the long acting formulation comprises a polylactide polymer, a poly lactic acid polymer, or a polylactide-co-glycolide polymer. Support for claims 16 and 17 can be found on page 4, lines 10-12.

Claim 18 depends directly from claim 1 and further recites that the naltrexone is present in the long acting formulation at a concentration of about 35% by weight. Support for claim 18 can be found on page 5, lines 24-27.

Claim 22 depends directly from claim 11, which depends directly from claim 1, and further recites that the method of claim 11 further comprises a second administration of the long acting formulation comprising naltrexone at least about 28 days after the first administration. Support for claim 22 can be found on page 7, lines 5-8.

(iv) Argument

A. Claims 1, 6, 7, 11, 14, 16-18, and 22 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Heinala et al. (Journal of Clinical Psychopharmacology, 2001, vol. 21, pp. 287-292) as applied in claim 1 in view of Bartus et al. (Neuropsychopharmacology, 2003, vol. 28, pp. 1973-1982), Leavitt (Addiction Treatment Forum Ed., 2002, pp. 1-8), and Johnson (Therapeutics and Clinical Risk Management, 2007, vol. 3, no. 5, pp. 741-749).

Claim 1

The Examiner asserts that one of ordinary skill in the art at the time of the invention would have found it obvious and been motivated to modify the method of Heinala et al. and the claimed amounts of naltrexone administered according to the teachings of the secondary references. [Final Office Action dated March 17, 2015, page 7, first paragraph, through page 8; Upheld in Advisory Action dated August 4, 2015, page 2, first paragraph]

The Examiner continues on page 8 of the Final Action, asserting it is considered obvious that "once one administers the formulation and method of Heinala et al. in view of Bartus et al. and Leavitt, one would obviously obtain the pharmacokinetics claimed." Appellant respectfully disagrees.

Many of the facts related to this appeal are not in dispute.

1. Heinala does not teach long acting naltrexone formulations, intramuscular administration, or the pharmacokinetic profile

Heinala is relied upon to show that oral naltrexone (50 mg/day) can be used to treat alcohol dependence in non-abstinent alcoholics.

It is admitted that Heinala does not teach (1) administration of a long acting form of naltrexone (2) to achieve a pharmacokinetic profile of at least 2 times the oral dosage (as measured by the serum AUC) (3) by injection (4) on at least a biweekly or monthly schedule (5) over a period of 24 weeks or more of (6) formulations that comprise a

polylactide or PLGA. Thus, it appears to be admitted that Heinala does not teach any material limitation of the claim (the formulation, mode of administration, dosing regimen, dose or pharmacokinetic profile).

The Examiner does not dispute that Heinala also teaches oral administration of naltrexone on an as needed basis when the craving for alcohol is high (see the last 4 lines of the article) and that Heinala warns against the possibility that long term naltrexone use may produce supersensitivity of the opioid receptors and other side effects. Thus, the fact that Heinala also has teachings away from the claimed invention also does not appear to be in dispute.

The Examiner then relies upon three secondary references to teach these missing limitations in an effort to arrive at the claimed invention.

2. Leavitt does not teach long acting injections

Leavitt is relied upon to teach that naltrexone can be orally administered at doses ranging from 12.5 mg/day to 150 mg/day. Leavitt is a review article of several clinical trials of orally administered naltrexone. The Abstract suggests flexible dosing and, like Heinala, on an "as needed basis."

Leavitt does not teach that intramuscular injection of a 380 mg long acting formulation can achieve a serum AUC of twice 50 mg/day oral dosing. Nor does Leavitt teach that such a dose by injection (either 380 mg, for example, or twice the AUC of oral naltrexone) is desirable. In fact, since a long acting formulation would not be "flexible dosing" on an "as needed basis," it does not appear to be disputed that Leavitt, like Heinala, provide teachings away from the claimed invention.

3. Bartus does not teach the desired dosing or a method of manufacture

Bartus is relied upon to show a long acting formulation comprising PLGA and about 35% naltrexone, called Vivitrex® microspheres. Bartus administered 50 mg/kg of the microspheres to Sprague Dawley rats and repeated the dose after 34 days to a group of these rats.

It is not disputed that Bartus does not teach (1) that it is desirable to administer naltrexone to achieve an AUC that is at least twice that of the 50 mg/day oral dose in humans, (2) the human dose in mg of naltrexone, (3) how one would select a human dose from the rat dose, or (3) a method for manufacturing Vivitrex® microspheres.

Therefore, it is not disputed that Bartus does not teach the missing limitations of the claims relating to the human dose and pharmacokinetic profile or a method of manufacturing the product.

4. Johnson is not prior art and does not teach how to make the product

Johnson was published in 2007. The effective filing date for the present claims is 2004. It is not in dispute that Johnson is not available as prior art.

In spite of this fact, the Examiner states that Johnson is "an evidentiary art to prove what is in VIVITREX." [Advisory Action, Page 5] and that Vivitrex® is naltrexone formulated into poly-(lactide-co-glycolide) microspheres. [Final Action, page 11, first paragraph]. It appears that the Examiner admits that Bartus does not teach what is in Vivitrex® microspheres and that one must resort to literature that is not prior art.

Johnson is not relied upon, and cannot be relied upon, to provide a teaching of the state of the art at the time of the invention. Additionally, while Johnson does state that Vivitrex® microspheres contain PLGA and naltrexone, like Bartus, Johnson also does not provide a teaching of how to make Vivitrex® microspheres.

5. 2003 Alkermes Press Release is improperly cited, is not prior art and does not teach how to make the product

In the Advisory Action dated August 4, 2015, the Examiner asserts that the Alkermes Press Release of December 8, 2003 teaches a 380 mg naltrexone injectable suspension with the poly-lactide co-glycolide polymer can be administered once a month to humans. [Advisory Action, page 2, third paragraph; page 5, lines 1-4; page 8, last seven lines].

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