United States District Court,
S.D. Indiana, Indianapolis Division.

ELI LILLY AND COMPANY,
Plaintiff.

and

Massachusetts Institute of Technology and Interneuron Pharmaceuticals, Inc,
Involuntary Plaintiffs.
v.
TEVA PHARMACEUTICALS USA, INC,
Defendant.

No. IP 02-0512-C-B/S

July 21, 2003.

Dominick A Conde, Fitzpatrick Cella Harper & Scinto, New York, NY, Brian H Corcoran, Katten Muchin Zavis Rosenman, Washington, DC, Donald Knebel, Barnes & Thornburg, Jeffrey C McDermott, Krieg Devault Alexander Capehart, Indianapolis, IN, Timothy J Vezeau, Katten Muchin Zavis Rosenman, Chicago, IL, for plaintiffs.

Steven J Lee, Kenyon & Kenyon, New York, NY, David O Tittle, Bingham McHale, LLP, Indianapolis, IN, for defendants.

ENTRY ON CLAIM CONSTRUCTION

SARAH EVANS BARKER**, District Judge.**

This matter comes before the Court for the purposes of construing certain patent terms at the center of the underlying infringement action. Plaintiff Eli Lily & Company ("Lilly") and Defendant Teva Pharmaceuticals USA, Inc. ("Teva") have each presented the Court with proposed constructions for certain terms used in Claim 2 of U.S. Patent No. 4,971,998 ("the '998 patent"). Following a *Markman* hearing on April 8, 2003, and additional briefing on the matters addressed at that hearing, we make the following factual and legal findings related to the construction of the disputed patent language.

Factual Background

This patent infringement suit deals with the drug fluoxetine, an active ingredient in the anti-depressant Prozac marketed by Lilly. Fluoxetine belongs to a subclass of drugs called selective serotonin reuptake inhibitors, which are used to treat a variety of disorders that exhibit mood- and appetite-related symptoms. In 1987, Drs. Richard and Judith Wurtman filed a patent application with the U.S. Patent and Trademark

Office ("PTO") for the use of fluoxetine to treat Prementrual Syndrome ("PMS"). Also in 1987, the American Psychiatric Association ("APA") published its Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised ("DSM-III-R"). The DSM-III-R notes that "[m]any females report a variety of physical and emotional changes associated with specific phases of the menstrual cycle." App. for Decl. of Jean Endicott, Exh. 6. Immediately following this general statement, the DSM III R describes late luteal phase dysphoric disorder ("LLPDD") as "a pattern of clinically significant emotional and behavioral symptoms that occur during the last week of the luteal phase [of the menstrual cycle] and remit within a few days after the onset of the follicular phase." FN1 *Id*. The reference to "premenstrual syndrome" in the index of the DSM-III-R leads to the entry titled "late luteal phase dysphoric disorder." *Id*.

FN1. As explained by the parties, the luteal phase begins with ovulation and ends with menses, and the follicular phase begins with menses and ends with ovulation.

In 1990, the PTO issued U.S. Patent 4,971,998 (the '998 patent) to the Wurtmans. Lilly subsequently obtained the rights to this patent and conducted the necessary clinical trials to file a Supplementary New Drug Application with the U.S. Food and Drug Administration ("FDA") for fluoxetine to treat LLPDD, later referred to as premenstrual dysphoric disorder ("PMDD"). Lilly then undertook preparations to market fluoxetine under the brand name Sarafem. In March 2000, Lilly and the FDA negotiated the appropriate labeling for Sarafem, which process culminated in the FDA's decision to exclude the term "PMS" from the label.

In July 2000, just prior to the expiration of the last patent covering Prozac, Lilly gained FDA approval to market fluoxetine under the Sarafem trademark. Sarafem is approved for treatment of LLPDD/PMDD, and, as originally approved by the FDA, is designed to be dosed continuously throughout a woman's entire monthly cycle. However, in June 2002, the FDA approved a change in the dosing regimen for Sarafem that provided two alternative dosing schemes: either "continuously (every day of the menstrual cycle) or intermittently (defined as starting a daily dose 14 days prior to the anticipated onset of menstruation through the first full day of menses and repeating with each new cycle)." Decl. of Laura Miller para. 18.

On November 30, 2001, Teva filed an Abbreviated New Drug Application ("ANDA"), seeking permission to manufacture and market fluoxetine for the treatment of PMDD. The ANDA included the statutorily required certification that such activities would not infringe any valid and enforceable patents listed by Lilly in the FDA Orange Book. On February 19, 2002, as required by the applicable statute, Teva gave notice to Lilly of its ANDA and the factual and legal bases for the position that its activities with regard to fluoxetine would not infringe Lilly's listed patents.

Lilly filed this patent infringement lawsuit on April 5, 2002. Essentially, Lilly contends that the '998 patent, which explicitly covers the use of fluoxetine for PMS, also covers the use of the drug for PMDD because PMDD is one form of PMS. Lilly also contends that the '998 patent covers continuous dosing regimens for fluoxetine. Teva argues in response that the '998 patent covers only the use of the drug to treat PMS, but not PMDD, the distinct condition targeted by Teva's proposed generic form of Sarafem, and that the ' 998 patent covers only dosing of the drug during the "luteal" phase of the menstrual cycle, not continuous dosing throughout the month. The parties also dispute the meanings of the claim terms "disturbances of mood" and "disturbances of appetite." On April 8, 2003, the Court convened a *Markman* hearing, at which the parties presented videotaped deposition testimony and associated exhibits in support of their positions. With the post-hearing briefing now concluded, we shall resolve the issues presented by the parties.

Legal Issues

Claim construction is "the process of giving proper meaning to the claim language," the fundamental process that "defines the scope of the protected invention." Abtox, Inc. v. Exitron Corp., 122 F.3d 1019, 1023 (Fed.Cir.1997). Because the scope of a claim is necessarily determined by the language of the claim, claim construction analysis must start with these words. Teleflex, Inc. v. Ficosa North America Corp., 299 F.3d 1313, 1324 (Fed.Cir.2002); Markman v. Westview Instr., Inc., 52 F.3d 967, 976 (Fed.Cir.1995), *aff'd,* 517 U.S. 370 (1996). The words used in the claims are interpreted in light of the intrinsic record evidence, including written description, drawings, and the prosecution history, if in evidence. Teleflex, 299 F.3d at 1324. Absent an express intent to impart a novel meaning to claim terms, there exists a "heavy presumption" that a claim term carries its ordinary and customary meaning. Id. at 1325.

The ordinary meaning of a claim term may be divined by reviewing a variety of sources, including the claims themselves, other intrinsic evidence including the written description and the prosecution history, and extrinsic evidence such as dictionaries and treatises. *Id*. (citations omitted). Among all types of intrinsic evidence, courts have indicated that the specification is the "single best guide to the meaning of a disputed term." Vitronics, Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed .Cir.1996). While a claim must be read in light of its specification, particular formulations or examples appearing in the specification may not be read to limit the claim. Advanced Cardiovascular Sys., Inc. v. Scimed Life Sys., Inc., 261 F.3d 1329, 1338-39 (Fed.Cir.2001); Transmatic, Inc. v. Gulton Indus., Inc., 53 F.3d 1270, 1277 (Fed.Cir.1995). Conversely, the specification must not be read in any manner to expand the scope of the claim beyond the plain language of the claim. Novo Nordisk of N. Am. v. Genentech, 77 F.3d 1364, 1369 (Fed.Cir.1996); Transmatic, Inc., 53 F.3d at 1278. In all cases, however, the ordinary meaning must be determined from the standpoint of a person of ordinary skill in the relevant art. Teleflex, 299 F.3d at 1325.

"Extrinsic evidence consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." Markman, 52 F.3d at 980. In its discretion, a court may receive extrinsic evidence to aid in understanding the patent. *Id*. However, if the meaning of the claim terms is unambiguous, and the court can determine that meaning from the intrinsic evidence, it need not rely on extrinsic evidence in construing the claim. Vitronics, Corp., 90 F.3d at 1583. FN2

FN2. In the FDA Orange Book, more formally referred to as "Approved Drug Products with Therapeutic Equivalence Evaluations," Lilly listed three patents as covering Sarafem. Two of these patents-U.S. Patent Nos. 5,114,976 and 5,744,501-were licensed by Lilly from Dr. Michael Norden and claim the use of fluoxetine specifically to treat PMDD. Lilly does not address or attempt to distinguish these patents from the '998 patent in its claim construction briefing. We do not find these patents or their prosecution histories directly relevant to our claim construction analysis.

A. Intrinsic evidence FN3

FN3. Teva makes several arguments regarding the prosecution history of the '998 patent. Upon careful review, however, accepting these arguments would require us to make analytical leaps between language used by individuals in later proceedings regarding other patent claims and the plain language of the '998 patent. Given the strict standards we must apply to determine the scope of the claim terms at issue, we decline to make such leaps. Moreover, to the extent such arguments hinge on the meanings assigned to certain terms by the DSM-IV, which the parties agree was not the version of the treatise in circulation at the

time the patent was filed, we find them unpersuasive.

Claim 2 states that the patent pertains to:

A method for treating disturbances of mood, disturbances of appetite, or both, associated with pre-menstrual syndrome, comprising administering to a woman prior to the onset of her menstrual period a composition consisting essentially of approximately 5 mg to 120 mg of fluoxetine.

The specification further guides our understanding of the claim language. Specifically, the specification mentions that the term "pre-menstrual syndrome" was commonly known as late luteal phase syndrome (citing, despite an obvious typographical error, the repeatedly mentioned DSM-III-R) and also contains descriptions of the mood and appetite disturbances commonly associated with the abovementioned condition. As to possible dosing regimens, the specification states:

The length of time during which a serotoninergic drug or drugs will be given varies on an individual basis, but will generally begin 1 to 14 days prior to menstruation and may continue for several days (e.g. 3 days) after the onset of menstruation.

Finally, the specification states that "[t]hose skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described specifically herein. Such equivalents are intended to be encompassed in the scope of the following claims." FN4

FN4. Although this language cannot be construed to broaden the claims beyond the scope of their actual terms, it does inform our understanding of the claim language.

B. Extrinsic evidence

Each side proffered an expert to support its respective interpretation of the disputed claim terms. Lilly offered the declaration of Dr. Jean Endicott, currently a professor of clinical psychology at College of Physicians and Surgeons, Columbia University, Department of Psychiatry. She has held this position since 1983, throughout which time she has also served as Director of the Premenstrual Evaluation Unit at Columbia Presbyterian Medical Center. Dr. Endicott has authored or co-authored more than 50 publications dealing with PMS and LLPDD/PMDD. She has also been involved with the design and execution of clinical trials relating to PMS/LLPDD/PMDD since 1982. Dr. Endicott also served as a member of the workgroup that proposed the definition of LLPDD appearing in the DSM III R, published by the APA in 1987.

Dr. Endicott testified, based on her experience and review of the relevant literature of the time, that "PMS has a wide spectrum of severity from mild PMS to the most severe form, which is diagnosed as LLPDD/PMDD." Decl. of Jean Endicott at 4. She identified numerous instances in the relevant literature that described or characterized LLPDD as a severe form of PMS, manifesting some unique symptoms and some common to the milder forms of PMS. Dr. Endicott also testified that "prior to the onset of her menstrual period" did not have a specialized meaning in 1987, and that those skilled in the art would understand it to mean anytime before the menstrual period begins and continuing daily for as long as needed.

Teva offers the testimony of Dr. Laura Miller, presently chief of the Women's Services Division, Department of Psychiatry at the University of Illinois at Chicago. Dr. Miller is a board certified psychiatrist and has experience in the area of women's reproductive-related mental illness. She graduated Harvard Medical School in 1982, and completed an internship at Michael Reese Hospital in Chicago in 1983. Thereafter, she completed a residency in psychiatry at the University of Chicago in 1986, and from that time until accepting her current position in 1998, she held various positions at the aforementioned schools, including assistant and associate professor of psychiatry, co-director of the women's clinic, and director of women's inpatient treatment. Over the years, she has authored numerous articles on psychiatric conditions in women, although, as she admitted on cross-examination, at the time of the patent filing she had authored no articles specifically addressing PMS or PMDD, and she has not participated in the design or execution of any clinical trials regarding PMS or PMDD.

Dr. Miller testified, based on her own experience and review of the relevant literature, that "pre-menstrual syndrome" or "PMS" is "a term used to describe the constellation of physical and psychological changes experienced by many women during the luteal phase of their menstrual cycles. There is no universally accepted definition of PMS or universally accepted set of diagnostic criteria ." Decl. of Laura Miller para. 6. She further clarified that although the term PMS has no generally accepted medical definition, it is a commonly used linguistic term to describe a variety of symptoms occurring in varying degrees.

Dr. Miller testified that, by constrast, LLPDD/PMDD is a separate and distinct clinical disorder, affecting only 3-8% of menstruating women. Dr. Miller asserts that the diagnostic criteria for LLPDD/PMDD were set forth in the DSM-III-R in 1987, and substantially differentiate the condition from PMS. Finally, Dr. Miller states that "prior to the onset of her menstrual period" would be understood by physicians in 1987 to mean a dosing regimen encompassing part or all of the luteal phase, but not continuous dosing throughout the month.

C. Claim construction

1. Premenstrual syndrome

In light of the claim language, the patent specification, and the expert testimony on the meaning of this term, we find that the intrinsic and extrinsic evidence supports Lilly's position: that at the time of the patent filing, "PMS" was most likely understood by those skilled in the art as an umbrella term covering a variety of premenstrual conditions, including those severe forms described as LLPDD, or, later PMDD. The claim language contains no helpful description of the two conditions to guide our analysis. However, we find support for this interpretation in both the claim specification and the literature from the relevant time frame. At the time of the patent filing, the relationship between the conditions was acknowledged by the DSM III R, which contrasted the two conditions only in terms of their essential features and the severity of their symptoms. It did not go so far as to distinguish them on the basis of their etiologies or the available universe of treatment. Although we credit Dr. Miller's testimony that medical practitioners at the time of the patent filing probably used the term PMS in imprecise ways to describe varying constellations of symptoms in varying degrees, we find more credible Dr. Endicott's testimony that the term generically described a class of symptoms, of which LLPDD/PMDD was a severe subcategory. Adopting a construction of PMS that includes LLPDD/PMDD in no way broadens the claim term, but merely recognizes the relationship of the two terms as understood as of the filing date of the patent by those skilled in the art. Therefore, we find that the claim term "pre-menstrual syndrome" as it appears in the language of Claim 2 of the '998 patent includes the more serious form of the disorder then known as LLPDD, now referred to as PMDD.

2. Disturbance of mood***/disturbance of appetite***

Lilly contends that the patent claim term "disturbances of mood ... associated with premenstrual syndrome" should be interpreted to mean "an interruption of a person's normal mood associated with premenstrual syndrome." Teva, by contrast, argues that the claim term should be interpreted to mean simply "depressed mood." Our analysis necessarily begins with the claim language itself. Nowhere in the plain language of the claim can we divine any term that would limit "disturbances of mood" to "depressed mood." Such a narrow interpretation is also refuted by the accompanying specification. Immediately following its mention of "disturbances of mood," the patent specification contains the qualifying language "(e.g., depression, anxiety)." This explanatory phrase, and specifically the use of the term "anxiety," demonstrates that the "disturbances of mood" encompasses more variations than simply depressed mood.

In addition, the expert testimony on this point counsels in favor of construing these terms consistent with their plain, ordinary meaning. Dr. Miller's declaration states, with regard to the symptoms commonly associated with PMS, that "[t]here have been reports in the literature of over 150 possible premenstrual symptoms, including anxiety, anger, [and] irritability." Decl. of Laura Miller para. 6. Thus, the claim language, the specification, and even Teva's proffered expert testimony on this point weigh against limiting "disturbances of mood" to "depressed mood."

The same analysis applies to the term "disturbances of appetite," which Teva contends should include simply carbohydrate cravings. The claim language contains no such limitation. The specification provides examples of appetite disturbances, specifically carbohydrate cravings and weight gain, but does not in any way suggest that these two conditions represent the universe of possible appetite changes. Adopting the narrow meaning Teva advocates would require us to impose a limitation absent from the claim language and inconsistent with the specification. Accordingly, based on the intrinsic and extrinsic evidence as to the meanings of these claim terms, we construe "disturbances of mood" to mean negative changes in a person's normal mood associated with PMS. In addition, we construe the term "disturbances of appetite" to mean negative changes to a person's normal appetite associated with PMS.

3. Prior to onset of menstrual period

Claim 2 of the '998 patent explicitly covers administration of fluoxetine for treatment of PMS "prior to the onset of [a woman's] menstrual period." The claim itself does not mention any specific dosing regimen. However, the specification mentions possible dosing regimens for fluoxetine and other serotoninergic drugs. Lilly contends that Claim 2 should be given its plain, ordinary meaning, covering any dosing scheme of any duration that begins at any point before menstruation during any month. Teva argues that one skilled in the art would understand "prior to the onset of her menstrual period" to mean the time period from 14 days before menstruation to up to three days after. The claim language does not contain such an explicit time frame. The specification mentions such a time frame as one possible dosing regimen, but recognizes that regimens may vary among individuals. Without contradicting the ordinary meaning of the claim language, the specification leaves open the possibility of varying dosing schemes. Therefore, we find that the plain language of Claim 2 embraces a wide array of dosing schemes, including continuous dosing.

Conclusion

For the reasons set out in detail above, we adopt the following constructions for the disputed terms from the '998 patent: 1) the term "pre-menstrual syndrome" as used in Claim 2 of the '998 patent includes

LLPDD/PMDD; 2) the term "disturbances of mood" we construe to mean negative changes in a person's normal mood associated with PMS; 3) the term "disturbances of appetite" we construe to mean negative changes to a person's normal appetite associated with PMS; and 4) "prior to the onset of her menstrual period" we construe to include not only late-luteal phase dosing regimens, but all dosing regimens that begin prior to the onset of a woman's menstrual period, including those that go on continuously thereafter.

S.D.Ind.,2003.
Eli Lilly and Co. v. Teva Pharmaceuticals USA, Inc.