UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

ELI LILLY AND COMPANY,	)	
	)	
Plaintiff/Counter Defendant,	)	
	)	
v.	)	Case No. 1:17-cv-02865-TWP-MPB
	)	
APOTEX, INC.,	)	
	)	
Defendant/Counter Claimant.	)	

ENTRY ON CLAIM CONSTRUCTION

This patent infringement case is before the Court for construction of patent terms relevant to methods of administering the compound pemetrexed disodium, which is a pharmaceutical product manufactured and sold by Plaintiff Eli Lilly and Company ("Lilly") as ALIMTA®. Lilly brought this patent infringement action against Defendant Apotex, Inc. ("Apotex"). In lieu of conducting a *Markman* hearing, the parties submitted comprehensive briefs, exhibits, and proposed findings of fact and conclusions of law concerning the proper construction of disputed terms and phrases of the patent at issue, U.S. Patent No. 7,772,209 (the "'209 patent").

I. FACTUAL BACKGROUND

Lilly is a corporation organized and existing under the laws of the State of Indiana with its principal place of business in Indianapolis, Indiana. Lilly is a company involved in the formulation, manufacture, and selling of pharmaceuticals. Apotex is a corporation organized and existing under the laws of Canada, having a place of business in Toronto, Ontario, Canada. Apotex is in the business of manufacturing, marketing, and selling generic drug products.

The patent at issue in this infringement suit, the '209 patent, is titled "Antifolate Combination Therapies" and relates to Lilly's anti-cancer agent ALIMTA®. The '209 patent was

issued on August 10, 2010, and Lilly is the assignee of the '209 patent. ALIMTA® is used to treat patients with malignant pleural mesothelioma or for the initial treatment of locally advanced or metastatic nonsquamous non-small cell lung cancer. ALIMTA® is also indicated as a single-agent for the treatment of patients with locally advanced or metastatic nonsquamous non-small cell lung cancer after prior chemotherapy. Further, ALIMTA® is indicated for maintenance treatment of patients with locally advanced or metastatic nonsquamous non-small cell lung cancer whose disease has not progressed after four cycles of platinum-based first-line chemotherapy. Lilly sells ALIMTA® in the United States pursuant to a New Drug Application that has been approved by the Food and Drug Administration ("FDA").

Lilly contends that the New Drug Application filed by Apotex with the FDA for the manufacture and sale of its Pemetrexed for Injection (100 mg/vial and 500 mg/vial) products before the '209 patent expires infringes upon the '209 patent. Lilly further contends that Apotex's Pemetrexed for Injection products will be marketed as a competing product to ALIMTA®. As a result, Lilly filed this infringement action against Apotex on August 21, 2017.

ALIMTA® (pemetrexed disodium) is an antifolate drug that is known to disrupt the folic acid pathway which can contribute to the reduction of cancer cells. The '209 patent relates to a method of administering pemetrexed disodium along with folic acid and vitamin B12, a methylmalonic acid lowering agent, in order to reduce the toxicities associated with the administration of pemetrexed disodium. This discovery made by Lilly results in a reduction of certain toxic effects caused by the administration of antifolates through the presence of a methylmalonic acid lowering agent without adversely affecting the therapeutic efficacy of the antifolate (Filing No. 88-1 at 3–4).

The parties agreed on the construction of the claim terms or phrases "patient," "vitamin B12," "methylmalonic acid lowering agent," and the preamble of claim 1 (Filing No. 85 at 1). The parties initially disagreed about claim 12's "an improved method for administering pemetrexed disodium" and "improvement." *Id.* at 6. Lilly asserted that the phrase and term are part of a *Jepson* claim and thus do not require additional construction[1]. Apotex initially asserted that the phrase is a preamble, and the term "improvement" should be construed as "the improvement is the addition of the administration of vitamin B12 in a method that." *Id.* However, in its Responsive *Markman* Brief, Apotex acknowledged that "there may no longer be a relevant dispute" concerning "improvement." (Filing No. 113-1 at 41.) In its proposed findings of fact and conclusions of law, Apotex suggested the following language, which is consistent with Lilly's position that the phrase and term do not require the Court's construction:

> 418. The parties disputed the meaning of the term "improvement" as it is used in claim 12 of the '209 patent. ECF 85 at 6.
>
> 419. Based on the parties' subsequent briefing, however, the Court finds that the parties now agree that there is no need to construe this term. ECF 88 at 27 ("The Court should not separately construe this legal term of art."); ECF 113-1 at 35 ("Based on Lilly's opening brief, there may no longer be a relevant dispute.").
>
> 420. The Court, therefore, declines to construe the "improvement" term because there is no longer a material dispute.

(Filing No. 163-1 at 128.) In light of this development, the Court declines to construe claim 12's phrase and term "an improved method for administering pemetrexed disodium" and "improvement."

[1] Drafting a claim in *Jepson* format (*i.e.*, the format described in 37 C.F.R. 1.75(e); see MPEP § 608.01(m)) is taken as an implied admission that the subject matter of the preamble is the prior art work of another. *In re Fout*, 675 F.2d 297, 301 (CCPA 1982) (holding preamble of *Jepson*-type claim to be admitted prior art where applicant's specification credited another as the inventor of the subject matter of the preamble).

II. LEGAL STANDARD

"Victory in an infringement suit requires a finding that the patent claim covers the alleged infringer's product or process, which in turn necessitates a determination of what the words in the claim mean." *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 374 (1996) (citation and quotation marks omitted). The construction of patent claims, which requires determining the meaning and scope of the claims, is a matter of law for the court. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 988 (Fed. Cir. 1995), *aff'd* 517 U.S. 370. The Federal Circuit has explained, "[i]t is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (citations and quotation marks omitted); *see also Vitronics Corp. v. Conceptronic*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) ("First, we look to the words of the claims themselves . . . to define the scope of the patented invention.").

The words in patent claims are "given their ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips*, 415 F.3d at 1312–13 (citations omitted); *see also Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004) ("customary meaning" refers to the "customary meaning in [the] art field"). "In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." *Phillips*, 415 F.3d at 1314.

There are two exceptions to the general rule of applying the ordinary meaning to claim terms: "1) when a patentee sets out a definition and acts as his own lexicographer, or 2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution."

Thorner v. Sony Comput. Entm't Am. LLC, 669 F.3d 1362, 1365 (Fed. Cir. 2012). To become one's own lexicographer, "a patentee must clearly set forth a definition of the disputed claim term other than its plain and ordinary meaning." *Id.* (citation and quotation marks omitted). "It is not enough for a patentee to simply disclose a single embodiment or use a word in the same manner in all embodiments[;] the patentee must 'clearly express an intent' to redefine the term." *Id.* (citation omitted). Additionally, "[t]he patentee may demonstrate an intent to deviate from the ordinary and accustomed meaning of a claim term by including in the specification expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1325 (Fed. Cir. 2002).

When interpreting claim terms, the court first looks to the intrinsic evidence, which includes the claims themselves, the specification, and the prosecution history. *See Interactive Gift Express, Inc. v. CompuServe Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001) ("[I]n interpreting an asserted claim, the court should look first to the intrinsic evidence of record, *i.e.*, the patent itself, including the claims, the specification and, if in evidence, the prosecution history. Such intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language."). And within that intrinsic evidence, courts first "look to the claim language." *Id.* When reviewing the claims, the specification, or the prosecution history, if these intrinsic sources define a claim term, that definition shall apply even if it differs from the term's ordinary meaning. *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366–67 (Fed. Cir. 2002). Although claims must be read in light of the specification, the court should not limit a claim by restricting its scope based on a preferred embodiment within the specification. *Phillips*, 415 F.3d at 1323. "Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in

the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Id.* at 1313.

In addition to relying on intrinsic evidence in ascertaining the scope of an invention's claim, the court also may look to extrinsic evidence, which includes evidence outside of the patent and prosecution history such as expert testimony, dictionaries, and learned treatises. *Id.* at 1317; *see also Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999). Courts may "rely on dictionary definitions when construing claim terms, so long as the dictionary definition does not contradict any definition found in or ascertained by a reading of the patent documents." *Phillips*, 415 F.3d at 1322–23 (internal citation omitted).

III. DISCUSSION

Similar to the Court's previous approach in the *Eli Lilly v. Teva Parenteral Medicines* case (No. 1:10-cv-1376-TWP-DKL), the Court will briefly discuss the background of the '209 patent, resolve the dispute concerning a person of ordinary skill in the art, and then construe the disputed claim terms and phrases at issue in this action.

A. The '209 Patent

The '209 patent, titled "Antifolate Combination Therapies," concerns the administration of pemetrexed disodium in combination with folic acid and a methylmalonic acid lowering agent to reduce the toxicity levels associated with the administration of pemetrexed disodium. Specifically, the antifolate, pemetrexed disodium, prevents other compounds, known as reduced folates, from binding to particular enzymes that are essential in the growth of potentially cancerous tumors. However, certain toxicities are associated with the administration of pemetrexed disodium. The '209 patent discloses a method of administering pemetrexed disodium in conjunction with certain

amounts of folic acid and a methylmalonic acid lowering agent, such as vitamin B12, to reduce toxicity levels without affecting the efficacy of the antifolate.

B. Person of Ordinary Skill in the Art

Claim terms and phrases are construed from the perspective of a person of ordinary skill in the art ("POSA") to whom the patent is addressed. "The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation." *Phillips*, 415 F.3d at 1313. "The descriptions in patents are not addressed to the public generally, to lawyers or to judges, but, as section 112 [of Title 35] says, to those skilled in the art to which the invention pertains or with which it is most nearly connected." *Id.* (citation omitted).

Lilly asserts that, "[i]n this case, the art of the '209 patent deals with the medical problem of toxicity associated with chemotherapeutic treatment, and the POSA is therefore a medical oncologist." (Filing No. 88 at 13.) Lilly points out, "[a]ll of the experts in this case agree that the POSA for the '209 patent at least includes a medical oncologist, and this definition of the POSA is consistent with the definition previously adopted by the Court for the '209 patent." *Id.*

Apotex acknowledges the Court's previous determination of the person of ordinary skill in the art for the '209 patent as a medical oncologist, and then Apotex suggests that, "[i]n this *Lilly v. Apotex* case, however, Lilly's current theory of literal infringement implicates questions of pharmaceutical chemistry, dosage forms and formulations." (Filing No. 86 at 26.)

> Therefore, based on (1) the Court's description of the POSA in the Teva Case, and (2) Lilly's current literal infringement theory and description of the POSA, Apotex proposes that, for purposes of the claim construction disputes in this Apotex Case, the POSA would include a medical oncologist, as described by the Court above, as well as an individual with experience in drug formulation sufficient to address the pharmaceutical chemistry, dosage form, and formulation aspects of the '209 Patent.

Id.

After the parties submitted their claim construction briefs, the United States Court of Appeals for the Federal Circuit issued its decision in *Eli Lilly & Co. v. Hospira, Inc.*, 933 F.3d 1320 (Fed. Cir. 2019). Following that decision, "Lilly withdr[ew] its assertion of literal infringement against Apotex in this case." (Filing No. 248 at 1.) Because Apotex's proposal to include a person experienced in drug formulation is based upon Lilly's literal infringement theory, which is now withdrawn, the Court declines to include a drug formulator in the description of the person of ordinary skill in the art in this case. The parties agree that the person of ordinary skill in the art is a medical oncologist, and the Court sees no reason to depart from its previous determination that the person of ordinary skill in the art for the '209 patent is a medical oncologist. Therefore, the Court concludes that a medical oncologist is the person of ordinary skill in the art for the '209 patent in this matter.

C. The Disputed Terms and Phrases

The parties dispute various terms and phrases in the '209 patent for the purposes of claim construction. Each disputed term or phrase will be addressed in turn.

Claim 1 in the '209 patent is:

> A method of 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.

(Filing No. 88-1 at 7.)

Claim 12 in the '209 patent is:

> 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.

Id. at 8.

1. <u>"administration of pemetrexed disodium," "administering pemetrexed disodium," "administering an effective amount of pemetrexed disodium"</u>

Claim Term/Phrase	Lilly's Proposed Construction	Apotex's Proposed Construction
"administration of pemetrexed disodium" "administering pemetrexed disodium" "administering an effective amount of pemetrexed disodium"	"a liquid administration of an effective amount of pemetrexed disodium"	"administering/administration of an effective amount of pemetrexed disodium"

The parties dispute the meaning of the phrases "administration of pemetrexed disodium," "administering pemetrexed disodium," and "administering an effective amount of pemetrexed disodium" as they are referred to in the claims of the '209 patent.

Apotex acknowledges that the Court previously construed claim 12's "administration of pemetrexed disodium" phrase to mean "a liquid administration of pemetrexed disodium" in the Dr. Reddy case; however, Apotex argues that for purposes of the dispute in this case, the word "liquid" does not resolve the construction issues here. Apotex explains that the '209 patent describes general and specific routes of administration such as intravenous administration and oral administration, but claim 1 does not specify the route of administration, dosage form, or dose, and "liquid" is not a route of administration. Additionally, "liquid" can refer to many types of liquid dosage forms such as a "solution" and a "suspension." In a "suspension," the active ingredient remains in a solid form for administration. Thus, Apotex contends that simply construing

"administration of pemetrexed disodium" as "a liquid administration of pemetrexed disodium" is not appropriate.

Apotex additionally argues that the '209 patent examiner understood that the claims would allow the administration of pemetrexed disodium both parenterally and orally. The patent application included oral administration via tablets, and the patent examiner understood the claim's scope would include such a solid compound. Lilly did not disclaim or disavow oral administration of pemetrexed disodium tablets, so, Apotex asserts, the claim should not be construed to mean only liquid administration of pemetrexed disodium.

Lilly first argues that Apotex's request to construe each of the constituent parts of these phrases is not helpful and not legally proper because claim terms must be interpreted in the context of the claim and in the context of the entire patent, including the specification.

Lilly asserts that Apotex's focus on a solid salt form of pemetrexed disodium is unfounded, and the only method for actually administering pemetrexed disodium is in the liquid form. Lilly asserts the Court already has addressed this issue in the Dr. Reddy and Hospira cases, and the Court determined that the phrase means a "liquid administration of pemetrexed disodium." Lilly acknowledges that pemetrexed disodium exists in a solid form, but when it is administered, it is done in a liquid form only. Pemetrexed disodium is administered as a solution, and there is no evidence that it has been administered to a patient in any other way. Lilly further asserts that administration of a solid form of pemetrexed disodium would exclude the preferred embodiment of the invention (*i.e.*, parenteral administration, specifically, intravenous injection), and construing a claim in a way that excludes the preferred embodiment is rarely, if ever, correct.

Lilly additionally argues that "administering pemetrexed disodium" entails administering a solution of an appropriate ratio of pemetrexed and sodium ions (1:2) regardless of how the

solution is made. The claim language does not concern how pemetrexed disodium is created before it is administered; the claim language simply recites administering pemetrexed disodium. The claim language also does not contain any source limitations for the pemetrexed and sodium ions. Lastly, Lilly asserts that the Court should not decide whether administering a hypothetical solid form of pemetrexed disodium falls within the claims because doing so would risk rendering an advisory opinion as to claim construction issues unrelated to the infringement controversy. Lilly's product is administered in a solution (liquid form). Apotex's product is to be administered in a solution (liquid form). Thus, deciding whether a solid pemetrexed disodium tablet is within the scope of the patent claims would be to decide an issue unnecessary for resolution of the infringement claim.

The Court is not persuaded by Lilly's position that construing constituent parts of the disputed phrases will necessarily take the terms and phrases out of context of the claims and the entire patent. While the Court recognizes that it previously has construed claim 12's "administration of pemetrexed disodium" phrase to mean "a liquid administration of pemetrexed disodium," the Court determines that limiting the phrase by the inclusion of the term "liquid" is not appropriate based upon the intrinsic evidence. The Court concludes that the phrases "administration of pemetrexed disodium" and "administering pemetrexed disodium" mean "administration of pemetrexed disodium" and "administering pemetrexed disodium" as the constituent terms are described below regardless of the "solid" or "liquid" state of the pemetrexed disodium.

The parties' experts note that pemetrexed disodium has been administered as a liquid solution. However, claim 1 of the '209 patent does not specify a "solid" or "liquid" state of pemetrexed disodium. Additionally, claim 1 does not specify the route of administration, dosage

form, or dose of pemetrexed disodium, folic acid, or a methylmalonic acid lowering agent. Claim 12 also does not specify the route of administration, dosage form, or dose of pemetrexed disodium, nor does it specify a "solid" or "liquid" state of pemetrexed disodium. Claims 2–11 and 13–22 similarly do not limit pemetrexed disodium to a "solid" or "liquid" state or provide the route of administration, dosage form, or dose of pemetrexed disodium.

The '209 patent specification explains the preferred embodiment of the invention as including the parenteral administration of the antifolate (*i.e.*, pemetrexed disodium), and later notes administration via intravenous injection. Yet, the specification does not rule out "solid" pemetrexed disodium. By declining to narrowly construe the phrase "administration of pemetrexed disodium" to mean "a liquid administration of pemetrexed disodium," the Court does not exclude the preferred embodiment of the invention (parenteral administration of the antifolate) as Lilly has argued. The preferred embodiment is still included in the claims.

The Court notes that the patent examiner recognized both parenteral and oral administration, referencing the Taylor '932 patent, which explained, "[t]he compounds can be administered orally but preferably are administered parenterally . . . . Parenteral routes of administration include intramuscular, intrathecal, intravenous and intra-arterial. . . . Oral dosage forms include tablets and capsules . . . ." (Filing No. 91-14 at 7–8; Filing No. 90-6 at 7; Filing No. 91-13 at 5.) There is no evidence that Lilly disclaimed or disavowed oral administration of tablets or other "solids."

Lilly acknowledged in its Responsive *Markman* Brief that "Lilly's prescribing information would make clear to the POSA that the sodium is bonded to pemetrexed when in solid form and dissociated into separate ions when in solution, and that 'pemetrexed disodium' ***can refer to either form***." (Filing No. 112 at 14 (emphasis added).)

The evidence leads to the Court's conclusion that the phrases "administration of pemetrexed disodium" and "administering pemetrexed disodium" mean "administration of pemetrexed disodium" and "administering pemetrexed disodium" as the constituent terms are described below regardless of the "solid" or "liquid" state of the pemetrexed disodium.

2. <u>"administering," "administration"</u>

Claim Term/Phrase	Lilly's Proposed Construction	Apotex's Proposed Construction
"administering" "administration"	This term will necessarily be construed as part of the term "administering pemetrexed disodium," or "administering an effective amount of pemetrexed disodium." [***<u>or</u>*** "administration of pemetrexed disodium."] The construction of this term separate and apart from those phrases is neither efficient nor proper here. To the extent a construction is required, however, it is: "prescribing that results in a patient receiving, directing that results in a patient receiving, or writing orders that results in a patient receiving, or putting on or in a patient's body"	"depending on the route of administration and dosage form: (1) prescription of, (2) direction of preparation/use of, (3) instruction to take, and/or (4) putting on or in"

As noted above, Lilly argues that the terms "administering" and "administration" should not be construed in isolation and should be construed only in connection with the longer phrase that includes the term "pemetrexed disodium." Lilly asserts that if the Court construes "administering" and "administration" separately, then the terms should be construed as "prescribing that results in a patient receiving, directing that results in a patient receiving, or writing orders that results in a patient receiving, or putting on or in a patient's body." Apotex

argues that "administering" and "administration" should be construed as "depending on the route of administration and dosage form: (1) prescription of, (2) direction of preparation/use of, (3) instruction to take, and/or (4) putting on or in."

Lilly argues that the Court should not adopt Apotex's construction because it is vague. Apotex's construction uses "and/or" and further uses the conditional phrase "depending on the route of administration and dosage form," which leaves uncertainty regarding what "administration" is and whether it has occurred. Lilly further argues that Apotex's construction is vague about whether a patient actually has to receive the pemetrexed disodium in order for the pemetrexed disodium to be "administered". Lilly asserts that its construction focuses on what the patient actually receives upon a doctor's orders rather than on the doctor's orders themselves.

Lilly explains that the specification uses "administration" and "treatment" interchangeably, and while a physician might not actually physically inject pemetrexed disodium into a patient, the medical oncologist would "administer" or "treat" the patient by writing the order that causes the patient to receive the pemetrexed disodium. Lilly points out that Apotex's expert conceded that pemetrexed disodium "hasn't been administered unless the patient actually receives it." (Filing No. 88-5 at 59.) Looking at the language of claims 5 and 21, Lilly asserts that vitamin B12 is "administered" for a period of time "until administration of pemetrexed disodium is discontinued." (Filing No. 88-1 at 8.) Discontinuing the administration of pemetrexed disodium necessarily means that the patient was actually receiving it. Lilly argues that the Court should not adopt Apotex's construction because it is vague and incomplete.

Apotex argues that the Court should adopt its construction because the claims and specification describe various routes of administration, dosage forms, and doses, which must be

chosen by a medical professional. Thus, Apotex asserts, its construction makes clear that administration depends upon those choices.

Lilly's argument and position are well taken. The Court agrees that the claims and specification of the '209 patent contemplate a patient actually receiving pemetrexed disodium, folic acid, and a methylmalonic acid lowering agent, and a person of ordinary skill in the art would understand such. Apotex's proposed construction does not adequately describe "administration" or "administering" to encompass the patient's receipt of pemetrexed disodium, folic acid, and a methylmalonic acid lowering agent. The Court also concludes that the use of "and/or" and the conditional phrase "depending on the route of administration and dosage form" creates uncertainties regarding what "administration" is and whether it has occurred. Lilly's proposed construction adequately addresses Apotex's concern about the various routes of administration, dosage forms, and doses that will be chosen by a medical professional. Therefore, the Court construes the terms "administering" and "administration" to mean "prescribing that results in a patient receiving, directing that results in a patient receiving, or writing orders that results in a patient receiving, or putting on or in a patient's body."

3. <u>"an effective amount"</u>

Claim Term/Phrase	Lilly's Proposed Construction	Apotex's Proposed Construction
"an effective amount"	This term will necessarily be construed as part of the term "an effective amount of pemetrexed disodium" and "an effective amount of folic acid and an effective amount of methylmalonic acid lowering agent." The construction of this term separate and apart from that phrase is neither efficient nor proper here.	"an amount that is capable of performing the intended result"

Lilly asserts that the phrase "an effective amount" should not be construed in isolation and out of context, and Apotex asserts that the specification clearly defines "an effective amount" as "an amount that is capable of performing the intended result."

Apotex argues that the Court previously found in the Teva case that the '209 patent defines "effective amount," and thus, Apotex proposes that the term does not require construction. But if any construction of the term is necessary, Apotex proposes that the Court apply the express definition in the '209 patent at column 3, line 53 as "an amount that is capable of performing the intended result." (Filing No. 88-1 at 4.)

Lilly contends that the phrase "an effective amount" must be construed in conjunction with the substances to be administered as well as the particular intended result of the substance. Lilly asserts that the specification makes clear that each part of the regimen has a particular intended result, and a person of ordinary skill in the art would understand the purpose of pemetrexed disodium, folic acid, and the methylmalonic acid lowering agent. Therefore, truncating the construction of the term "effective amount" to "an amount that is capable of performing the intended result" would leave the construction incomplete.

Lilly further asserts that, in all other previous cases addressing the '209 patent, all parties either agreed with Lilly's construction or did not challenge it. Lilly also points out that, in a different proceeding, Apotex's expert previously submitted sworn testimony before the Patent Trial and Appeal Board that Lilly's proposed construction is correct (Filing No. 88-16 at 4, 22–23).

In *Teva*, this Court explained,

> [T]he Federal Circuit concluded that a term definition within a patent's specification that contained words such as "means" or "as used herein" could be interpreted as redefinitions of those terms from their ordinary and customary

> meanings. *Id.* at 1210. Like the patent at issue in *Abbott*, the '209 patent provides for definitions of certain terms by using particular words, such as "means" or "as used herein," in the process of defining the term. *See, e.g.*, Dkt. 1-1, col. 3, ll. 53-55 ("As used herein, the term 'effective amount' refers to . . ."), ...

Eli Lilly & Co. v. Teva Parenteral Meds., Inc., 2012 U.S. Dist. LEXIS 85369, at *31 (S.D. Ind. June 20, 2012 (first ellipses in original)). Thus, while the Court acknowledged in *Teva* that the specification provides a definition for the term "effective amount," the Court did not actually identify or discuss the definition and whether further construction was necessary.

Standing alone, the term "effective amount," is adequately defined by the specification as "an amount of a compound or drug, which is capable of performing the intended result." (Filing No. 88-1 at 4.) However, this definition and the other language in the specification make clear that "effective amount" must be considered in conjunction with "a compound or drug". Every reference to "effective amount" in the specification couples the term with "antifolate". Importantly, the language in the claim does not use the term "effective amount" in isolation. The term "effective amount" appears only in claim 1, and the three times the term is used, it is used in conjunction with "pemetrexed disodium," "folic acid," and "a methylmalonic acid lowering agent." Notably, Apotex's proposed construction—"an amount that is capable of performing the intended result"—omits the specification's language "a compound or drug" from its definition. The Court declines to adopt Apotex's construction of "an effective amount" and further declines to construe the term "an effective amount" in isolation.

4. "an effective amount of folic acid and an effective amount of a methylmalonic acid lowering agent," "an effective amount of pemetrexed disodium"

Claim Term/Phrase	Lilly's Proposed Construction	Apotex's Proposed Construction
"an effective amount of folic acid and an effective amount of a methylmalonic acid lowering agent"	"amounts of folic acid and a methylmalonic acid lowering agent that are capable of reducing the prevalence or	"an amount of folic acid that is capable of performing the intended result and an amount of methylmalonic acid

	severity of one or more toxicities associated with the administration of pemetrexed disodium"	lowering agent that is capable of performing the intended result"
"an effective amount of pemetrexed disodium"	"an amount of pemetrexed disodium that is capable of providing a therapeutic benefit to the patient in need thereof"	"an amount of pemetrexed disodium that is capable of performing the intended result"

The only difference between the parties' proposed construction of these phrases is that Apotex suggests using the definitional language from the specification "an amount that is capable of performing the intended result" with the addition of identifying the substance, whereas Lilly suggests identifying the substance as well as identifying the intended result of the substance.

Apotex offers no argument for its position other than that noted in the previous section of this Order. It asserts that the definitional language of the specification is sufficient.

Lilly argues that the specification and claims clearly delineate the intended results of pemetrexed disodium, folic acid, and the methylmalonic acid lowering agent, and a person of ordinary skill in the art would understand what those intended results are and apply them to the claims. Lilly asserts that the specification makes clear that the purpose of administering folic acid and a methylmalonic acid lowering agent is to reduce the prevalence or severity of one or more toxicities associated with the administration of pemetrexed disodium, and the purpose of administering pemetrexed disodium is to provide a therapeutic benefit to the patient in need thereof. The specification explains that there was a known toxicity problem with using antifolates and that the invention of the '209 patent was the discovery that administering a methylmalonic acid lowering agent and folic acid synergistically reduced the toxic events associated with administering antifolate drugs.

Furthermore, Lilly explains, the claims specify that pemetrexed disodium is administered to a patient in need thereof or a patient in need of chemotherapeutic treatment. Thus, Lilly argues, to provide a complete construction of the phrases "an effective amount of folic acid and an effective amount of a methylmalonic acid lowering agent" and "an effective amount of pemetrexed disodium," it is appropriate for the Court to include the known intended results in the construction of the phrases. Additionally, as noted above, Lilly points out that, in a different proceeding, Apotex's expert previously submitted sworn testimony before the Patent Trial and Appeal Board that Lilly's proposed construction is correct (Filing No. 88-16 at 4, 22–23).

Lilly's position is well taken concerning the construction of these phrases. The purpose or intended result of folic acid and a methylmalonic acid lowering agent is clearly delineated in the specification; they are to reduce the prevalence or severity of one or more toxicities associated with the administration of pemetrexed disodium. The purpose or intended result of pemetrexed disodium is clearly delineated in the specification and claims; it is to provide a therapeutic benefit to a patient in need thereof. Including the known intended result in the claim construction of these phrases is supported by the language of the specification. Immediately following the specification's definitional language for "effective amount," the specification explains, "For example, an effective amount of an antifolate drug that is administered in an effort to reduce tumor growth is that amount which is required to reduce tumor growth." (Filing No. 88-1 at 4.) The specification's example provides the known intended result.

Therefore, the Court will adopt Lilly's proposed construction of these phrases. "An effective amount of folic acid and an effective amount of a methylmalonic acid lowering agent" means "amounts of folic acid and a methylmalonic acid lowering agent that are capable of reducing the prevalence or severity of one or more toxicities associated with the administration of

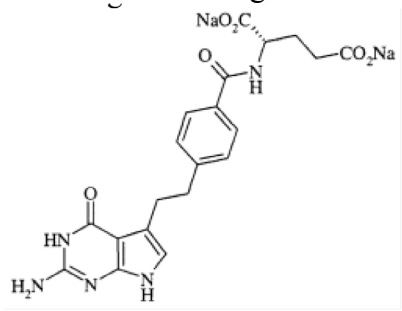
pemetrexed disodium." "An effective amount of pemetrexed disodium" means "an amount of pemetrexed disodium that is capable of providing a therapeutic benefit to the patient in need thereof."

5. "<u>disodium</u>"

Claim Term/Phrase	Lilly's Proposed Construction	Apotex's Proposed Construction
"disodium"	This term will necessarily be construed as part of the term "administering pemetrexed disodium," administration of pemetrexed disodium," or "administering an effective amount of pemetrexed disodium." The construction of this term separate and apart from those phrases is neither efficient nor proper here. To the extent a construction is required, however, it is: "two sodiums"	"containing two sodium atoms"

Lilly argues that the term "disodium" should not be construed in isolation or out of context. When pressed by Apotex, Lilly provided "two sodiums" as the construction of "disodium" if the Court was to determine the construction of the term on its own. Apotex asserts that the ordinary and customary meaning of "disodium" is "containing two sodium atoms." The Court declines to construe the term "disodium" on its own because the term "disodium" is not found anywhere in the '209 patent claims or specification divorced from "pemetrexed". In every use of "disodium" in the '209 patent, it is coupled with "pemetrexed". Therefore, the Court turns its consideration to the term "pemetrexed disodium".

6. <u>"pemetrexed disodium"</u>

Claim Term/Phrase	Lilly's Proposed Construction	Apotex's Proposed Construction
"pemetrexed disodium"	This term will necessarily be construed as part of the term "administering pemetrexed disodium," administration of pemetrexed disodium," or "administering an effective amount of pemetrexed disodium." The construction of this term separate and apart from those phrases is neither efficient nor proper here. To the extent a construction is required, however, it is: "pemetrexed and two sodiums"	"any solid form of the drug substance that has the chemical name L-glutamic acid, N-[4-[2-(2-amino-4,7-dihydro-4-oxo-1H-pyrrolo[2,3-d]pyrimidin-5yl)ethyl]benzoyl]-, disodium salt, and a structural formula including:  "

Lilly asserts that, if "pemetrexed disodium" is to be construed on its own, it should be construed as "pemetrexed and two sodiums." Apotex argues that "pemetrexed disodium" should be construed as "any solid form of the drug substance that has the chemical name L-glutamic acid, N-[4-[2-(2-amino-4,7-dihydro-4-oxo-1H-pyrrolo[2,3-d]pyrimidin-5yl)ethyl]benzoyl]-, disodium salt, and a structural formula including [the figure depicted above]."

Lilly argues that Apotex's attempt to construe "pemetrexed disodium" by limiting it to "any solid form of the drug substance . . ." is improper because pemetrexed disodium is actually administered to patients in a liquid form solution. Lilly asserts that the '209 patent concerns methods of administering pemetrexed disodium, not the chemical compound itself, so the construction of "pemetrexed disodium" should be in context of its administration as a liquid.

Lilly asserts that, out of context, "pemetrexed disodium" can refer to a solid salt, but it certainly is not limited to the solid form alone. Apotex pointed to the language in the specification

that states "pemetrexed disodium (Alimta®, Eli Lilly and Company, Indianapolis, Ind.) has demonstrated thymidylate synthase, dihydrofolate reductase, and glycinamide ribonucleotide formyltransferase inhibition." (Filing No. 88-1 at 3.) But Lilly's expert explained that only dissociated pemetrexed dissolved in aqueous solution is capable of these types of "inhibition" and the resulting anti-cancer effects and toxicities that are the subject of the patent (Filing No. 88-3 at 42–43, 77). Solid pemetrexed disodium has no such effect, so a person of ordinary skill in the art would understand that pemetrexed disodium in the context of the claims cannot mean the solid form alone.

Lilly further argues that Apotex's reliance on Lilly's prescribing information is unavailing and actually supports Lilly's position that the term "pemetrexed disodium" should not be limited to the solid form. Lilly asserts that the solid substance it distributes as Alimta® is referred to as "pemetrexed disodium". However, its prescribing information describes the way that pemetrexed disodium is to be used in a liquid form, administered through intravenous infusion. The solid powder must be completely dissolved before administration, and if any particulate matter remains, it is not to be administered to the patient. Thus, the prescribing information would inform a person of ordinary skill in the art that pemetrexed disodium is in both a solid form and a liquid solution form. Lilly argues Apotex's attempt to limit "pemetrexed disodium" to "any solid form of the drug substance" is not supported by the evidence and should not be adopted by the Court.

Apotex advances its expert's opinion that a person of ordinary skill in the art would understand the claims and specification as describing "pemetrexed disodium" as "any solid form of the drug substance pemetrexed disodium." Apotex asserts that a person of ordinary skill in the art would understand "pemetrexed disodium" to be the solid form of the drug because the FDA-

approved product label that Lilly submitted to the patent examiner describes "pemetrexed disodium" as a white to almost-white solid.

The Court agrees with Lilly that Apotex's attempt to limit "pemetrexed disodium" to only any solid form of the drug is inappropriate and not supported by the evidence. While the evidence supports the conclusion that pemetrexed disodium can be in a solid form, it does not support the conclusion that pemetrexed disodium is limited to a solid form. Therefore, the Court declines to adopt Apotex's construction of "pemetrexed disodium". However, the Court also declines to adopt Lilly's construction of "pemetrexed disodium" as "pemetrexed and two sodiums." Lilly advanced this same construction for the term "pemetrexed disodium" based on what appears to be the same or very similar arguments and evidence in the case of *Eli Lilly & Co. v. Eagle Pharmaceuticals* (D. Del., No. 17-1293-MSG).

The court in *Eagle Pharmaceuticals* construed the term "pemetrexed disodium" for the '209 patent. This Court has carefully reviewed the *Eagle Pharmaceuticals* opinion and agrees with that court's well-reasoned analysis and conclusion regarding the construction of the term "pemetrexed disodium". For the reasons explained in the *Eagle Pharmaceuticals* opinion (*see Eli Lilly & Co. v. Eagle Pharm., Inc.*, 2019 U.S. Dist. LEXIS 46853, at *6–10 (D. Del. Mar. 21, 2019)), this Court declines to adopt Lilly's proposed construction of "pemetrexed disodium" as "pemetrexed and two sodiums" and instead construes the term "pemetrexed disodium" to mean "the chemical compound pemetrexed disodium." The Court notes that this construction of "pemetrexed disodium" in conjunction with its construction of "administration" and "administering" "would cover administration of a compound or drug by an injection." *Eagle Pharm.*, 2019 U.S. Dist. LEXIS 46853, at *9.

IV. CONCLUSION

For these reasons set forth above, the disputed claim terms and phrases have the following meanings:

Claim Term/Phrase	Meaning
administration of pemetrexed disodium administering pemetrexed disodium	administration of pemetrexed disodium administering pemetrexed disodium
administering administration	prescribing that results in a patient receiving, directing that results in a patient receiving, or writing orders that results in a patient receiving, or putting on or in a patient's body
an effective amount of folic acid and an effective amount of a methylmalonic acid lowering agent an effective amount of pemetrexed disodium	amounts of folic acid and a methylmalonic acid lowering agent that are capable of reducing the prevalence or severity of one or more toxicities associated with the administration of pemetrexed disodium an amount of pemetrexed disodium that is capable of providing a therapeutic benefit to the patient in need thereof
pemetrexed disodium	the chemical compound pemetrexed disodium

The clerk is **directed** to terminate the gavel at dkt. 132.

SO ORDERED.

Date: 12/23/2019

TANYA WALTON PRATT, JUDGE
United States District Court
Southern District of Indiana

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