IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

MEDA PHARMACEUTICALS INC. and CIPLA LTD.,	)	
Plaintiffs,	)	
	)	C.A. No. 15-785-LPS
v.	)	
TEVA PHARMACEUTICALS USA, INC.,	)	
Defendant.	)	

DEFENDANT TEVA PHARMACEUTICALS USA, INC.'S
OPENING CLAIM CONSTRUCTION BRIEF

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I. INTRODUCTION

Defendant Teva Pharmaceuticals USA, Inc. ("Teva") submits this Opening Claim Construction Brief pursuant to the Court's amended Scheduling Order (Dkt. 49). In this lawsuit, the Plaintiffs, Meda Pharmaceuticals Inc. and Cipla Ltd. (together, "Plaintiffs"), allege infringement of 40 claims of three patents, U.S. Patent Nos. 8,168,620 ("the '620 patent") (Ex. 2), 8,163,723 ("the '723 patent") (Ex. 3) and 9,259,428 ("the '428 patent") (Ex. 4) (collectively, the "patents-in-suit").[1]

According to Plaintiffs, the patents-in-suit cover Plaintiffs' DYMISTA® nasal spray, which contains a combination of a specific steroid (fluticasone propionate) and specific antihistamine (azelastine hydrochloride) for treatment of allergic rhinitis. However, the actual claim language is not so limited. Rather, the claims are ill-defined and uncommonly broad, and on their face cover treatment of *unspecified* conditions for which *unspecified* steroids or antihistamines might be useful, in *unspecified* amounts and in *any* mammal. *See, e.g.*, '723 patent, Claim 1.

In many instances, the claims of the patents-in-suit "fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention," and are therefore indefinite. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2124 (2014). And other claims were simply drafted poorly, such that they do not encompass certain preferred embodiments in the specification by their terms, or encompass new matter not present in the applications to which Plaintiffs contend the patents-in-suit claim priority.

Now, when confronted with the invalidity consequences of their claim drafting strategy, Plaintiffs look to the Court to fix them. However, Plaintiffs should not be permitted to alter the

[1] Unless otherwise noted, all Exhibits ("Ex.") referenced herein are attached to the Declaration of Justin A. MacLean, submitted concurrently herewith.

language of the claims, through claim construction, to preserve their validity. Rather, the constructions of the disputed terms should comport with the claim language itself, the specification, the prosecution history, and other evidence of those terms' plain and ordinary meaning. In this regard, Teva respectfully submits that Plaintiffs' proposed constructions should be rejected and Teva's positions should be adopted.

II. THE RELEVANT AND GOVERNING LEGAL PRINCIPLES

A. General Principles of Claim Construction

The words of a claim "are generally 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, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (*en banc*). However, the ordinary meaning of a term is not considered in a vacuum, but rather is interpreted in view of the intrinsic evidence, which includes the claim language, the specification and the prosecution history. *See id.* at 1312-17.

Indeed, "the specification is always highly relevant to the claim construction analysis. Usually it is dispositive; it is the single best guide to the meaning of a disputed term." *Id.* at 1315 (citations omitted). "Thus, claims must be construed so as to be consistent with the specification, of which they are a part." *Merck & Co. v. Teva Pharms. USA, Inc.*, 347 F.3d 1367, 1370 (Fed. Cir. 2003). Consistent with this principle, "a claim term will not receive its ordinary meaning if the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in either the specification or prosecution history." *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed.Cir. 2002); *see also Phillips*, 415 F.3d at 1316. This definition may be provided expressly or by implication in the specification. *Phillips*, 415 F.3d at

1320-21 ("[T]he specification acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication.") (citations omitted).

A court "should also consider the patent's prosecution history, if it is in evidence." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). The prosecution history "consists of the complete record of the proceedings before the PTO and includes the prior art cited during the examination of the patent." *Phillips*, 415 F.3d at 1317. "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.* at 1316. "When prior art that sheds light on the meaning of a term is cited by the patentee, it can have particular value as a guide to the proper construction of the term, because it may indicate not only the meaning of the term to persons skilled in the art, but also that the patentee intended to adopt that meaning." *Arthur A. Collins, Inc. v. Northern Telecom Ltd.*, 216 F.3d 1042, 1045 (Fed. Cir.2000).

B. Indefiniteness

"Indefiniteness under 35 U.S.C. § 112, ¶ 2 is an issue of claim construction and a question of law." *Cordis Corp. v. Boston Scientific Corp.*, 561 F.3d 1319, 1331 (Fed. Cir. 2009). "[A] patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus*, 134 S. Ct. at 2124. This "inquiry trains on the understanding of a skilled artisan at the time of the patent application, not that of a court viewing matters *post hoc*." *Id.* at 2130. A court may not rewrite indefinite claims to preserve their validity. *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1349 (Fed. Cir. 2008).

It is not sufficient that "a court can ascribe some meaning to a patent's claims." *Nautilus*, 134 S. Ct. at 2130. A patent must afford clear notice of what is claimed, thereby "'appris[ing] the public of what is still open to them.'" *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 373 (1996). Otherwise there would be "[a] zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims." *United Carbon Co. v. Binney & Smith Co.*, 317 U.S. 228, 236 (1942).

III. CONSTRUCTION OF THE DISPUTED TERMS

1. "treatment…of [a] condition(s)" / "treatment of seasonal allergic rhinitis" ('723 Patent Claim 1, '428 Patent Claim 1, 28)

Teva's Proposed Construction	Plaintiffs' Proposed Construction
"curing or suppressing an underlying disease or illness or minimizing symptoms associated therewith" / "curing or suppressing seasonal allergic rhinitis or minimizing symptoms associated therewith"	Plain and ordinary meaning: "prevention or minimization of the symptoms of disease or illness" / Plain and ordinary meaning: "prevention or minimization of symptoms of seasonal allergic rhinitis"

Plaintiffs' proposed "plain and ordinary" meaning of "treatment"—the "prevention or minimization of the symptoms of a disease or illness"—is anything but, most notably because it omits any reference to combatting the underlying condition itself, let alone curing the disease or illness. It is a matter of common understanding that "treating" an illness entails more than merely managing the symptoms of the illness. In contrast, Teva's proposed construction comports with the plain and ordinary meaning of "treatment," the language of the claims themselves, as well as the intrinsic and extrinsic evidence.

As an initial matter, Plaintiffs' construction would improperly lead to a redundancy in Claim 1 of the '723 patent, which recites "[a] method for the *prophylaxis or treatment*[.]" Since

"prophylaxis" is synonymous with "prevention,"[2] Plaintiff's proposed construction would read "[a] method for the *prophylaxis* or *prophylaxis* or minimization of symptoms of disease or illness" (emphasis added). However, it is a "well-established rule that claims are interpreted with an eye toward giving effect to all terms in the claim." *Digital-Vending Servs. Int'l, LLC v. Univ. of Phoenix, Inc.*, 672 F.3d 1270, 1275 (Fed. Cir. 2012). Plaintiffs' construction of "treatment" would render superfluous the separate recitation of "prophylaxis" in the asserted claims. And, without "prevention," Plaintiffs' proposed construction reduces to "minimization of the symptoms of disease or illness," which is likewise at odds with the claims themselves. The *only* difference between Claims 1 and 14 of the '428 patent is that Claim 1 covers "[a] method for the *treatment*," (emphasis added), whereas Claim 14 covers "[a] method for *minimizing symptoms*" (emphasis added). Thus, construing "treatment" as merely the "minimization of the symptoms," as Plaintiffs urge, would not only render the term "treatment" superfluous, it would also improperly make Claims 1 and 14 *identical*. Of course, such a reading cannot be correct because the doctrine of claim differentiation "creates a presumption that each claim in a patent has a different scope." *Versa Corp. v. Ag–Bag Int'l Ltd.*, 392 F.3d 1325, 1330 (Fed. Cir. 2004); *Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, 438 F.3d 1374, 1381 (Fed. Cir. 2006). Thus, the language of the claims themselves dictates that "treatment" must have a meaning different from "minimization of symptoms" and "prevention."

Defendant's construction, on the other hand, is consistent with the plain and ordinary meaning of "treatment" in medicine, which, under well-established usage, encompasses "combatting a disease or disorder"—not just addressing symptoms. Ex. 5 (Miller-Keane

[2] See Ex. 41 (The American Heritage Medical Dictionary, Houghton Mifflin Co. (2007) (defining "prophylaxis" as "prevention of…disease")) and Ex. 5 (Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh Edition, Saunders (2003) (defining prophylaxis as "disease prevention.")).

Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh Edition, Saunders (2003)). The term "treatment" is understood by those of ordinary skill in the art to include so-called "active" treatment, which is directed to curing a disease, "causal" treatment, which is directed against the cause of a disease, and "expectant" treatment, which is directed at symptom management. *Id*. Consistent with this broad meaning, the intrinsic record indicates that both steroids and antihistamines are used to "cure" various conditions. For example, prior art patent EP0393658, titled "Novel Steroid Derivatives," which is cited on the face of the Patents-in-Suit, describes and claims steroid compositions "for *curing* or alleviating inflammation or rheumatism." Ex. 42 at 2:13-14; 20:18-19 (emphasis added). Similarly, Plaintiff Meda Pharmaceuticals Inc.'s own U.S. Patent No. 8,071,073, titled "Compositions comprising Azelastine and Methods of Use Thereof," which is cited on the face of the '428 patent, states that "a variety of physical disorders… may be delayed, prevented, *cured* or otherwise treated by the administration of azelastine or a pharmaceutically acceptable salt or ester thereof." Ex. 43 at 76:23-29 (emphasis added).[3]

Teva's proposed construction is also consistent with the extrinsic evidence, which defines "treatment" as "[t]he use of an agent, procedure, or regimen, such as a drug, surgery, or exercise, in an attempt to *cure* or mitigate a disease, condition, or injury." *See* Ex. 41 (The American Heritage Medical Dictionary, Houghton Mifflin Co. (2007) (emphasis added)); Ex. 5 (Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh Edition (2003)) (defining "active treatment" as "treatment directed immediately to the *cure* of a disease or injury" and "causal treatment" as "treatment directed to the *cause* of the disease.") (emphasis added); Ex. 44 (The American Heritage Dictionary, Houghton Mifflin Co. (2001) (defining

[3] The foregoing patents were cited during prosecution of the Patents-in-Suit and are therefore intrinsic evidence. *See Phillips*, 415 F.3d at 1317.

"treatment" as "[t]he application of remedies to relieve or *cure* an underlying disorder.") (emphasis added)); Ex. 45 (Webster's II New College Dictionary, Houghton Mifflin Co. (2001) (defining "treatment" as "Medical application of remedies so as to effect a cure."). Thus, for the reasons above, Teva's proposed construction of "treatment," which is consistent with the patent claims, and the intrinsic and extrinsic record, should be adopted.

2. "one or more isotonization agents comprise from 2.3% (weight/weight) to 2.6% (weight/weight) of glycerine" ('428 Patent Claim 20)

Teva's Proposed Construction	Plaintiffs' Proposed Construction
"glycerine comprises from 2.3% to 2.6% (weight/weight) of the aggregate weight of all isotonization agents"	Plain and ordinary meaning: "one or more isotonization agents include glycerin[] at a concentration of 2.3% to 2.6% by weight of the formulation"

The language of Claim 20 of the '428 patent is clear on its face—it states that glycerine constitutes a certain percentage (i.e., 2.3-2.6%) *of the one or more isotonization agents*. Notwithstanding the clear language of the claims, Plaintiffs ask the Court to rewrite them to read that glycerine comprises a certain percentage "of the formulation"—not of the one or more of the isotonization agents, as the claims state. Even if that is what the patentee intended, Courts should not rewrite unambiguous claims. *See, e.g., Chef Am., Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1373 (Fed. Cir. 2004) (rejecting the argument that claim term "heating…dough to a temperature in the range of 400 to 850° F" means heating the air rather than the dough, even though, as written, the dough "would be burned to a crisp" (citing *Becton Dickinson & Co. v. C.R. Bard, Inc.,* 922 F.2d 792, 799 n.6 (Fed.Cir.1990) ("even 'a nonsensical result does not require the court to redraft the claims of the [] patent."))). Moreover, when intending to define ingredient amounts by reference to "the formulation" as a whole, the patentee clearly did so. *See, e.g.*, '428 patent at 11:51-61; 12:20-30; 12:31-44; 12:55-65; 13:24-34; 13:35-14:6; 14:15-18 ("wherein the *formulation* comprises from 0.65% (weight/weight) to 3% (weight/weight) of

microcrystalline cellulose…") (emphasis added); 14:19-34. This highlights that claims 7 and 20 of the '428 patent "mean exactly what they say." *Chef Am.,* 358 F.3d at 1373 ("[I]n accord with our settled practice we construe the claim as written, not as the patentees wish they had written it."). Accordingly, this court should adopt Teva's construction and reject Plaintiffs' attempt to contradict the unambiguous language of the claims.

3. "therapeutically effective amount" ('723 Patent Claim 1; '428 Patent Claims 1, 14, 28)

Teva's Proposed Construction	Plaintiffs' Proposed Construction
Indefinite	Plain and ordinary meaning "a therapeutically effective amount of a pharmaceutical composition" '723 Patent : "an amount of pharmaceutical composition that prevents or minimizes symptoms of a disease or illness" "a therapeutically effective amount of a nasal spray formulation" in the '428 patent: "an amount of the nasal spray formulation that prevents or minimizes symptoms of seasonal allergic rhinitis"

Claim 1 of the '723 patent calls for administration of a "*therapeutically effective amount*" of the pharmaceutical composition. However, the specification does not provide *any* dosing information—even for the exemplary rhinitis conditions—which one typically expects to find in pharmaceutical patents. That omission is far worse here than in a typical pharmaceutical patent because the '723 patent does not claim treatment of a specific condition, or even a set of identified conditions; rather, it claims treatment of *all* "conditions for which administration of one or more antihistamines and/or or more steroids is indicated." *See* Section IV.5., *infra*. Persons of ordinary skill in the art could not ascertain, with reasonable certainty, the "therapeutically effective amount[s]" required for treatment of this essentially unbounded and ill-defined range of diseases and illnesses.

Plaintiffs acknowledge, in their own proposed construction, that whatever the claimed "amount" is, it must actually prevent or treat the disease or illness. The "therapeutically effective amount" to prevent or treat the disease or illness will, of course, depend on which disease or illness is being treated.[4] And, the range of "conditions" for which steroid or antihistamine treatment is indicated is myriad and diverse. Notably, Claim 1 does *not* recite "treatment in a mammal of a condition for which administration of *a pharmaceutically acceptable ester of fluticasone* is indicated," nor does it recite "treatment in a mammal of a condition for which administration of *azelastine, or a pharmaceutically acceptable salt thereof* is indicated." Instead, by patentee's own choice, it expansively claims "treatment in a mammal of a condition for which administration of one or more antihistamines and/or one or more steroids is indicated."

However, persons of ordinary skill in the art understand that "pharmaceutically acceptable esters of fluticasone" are not simply interchangeable with any "steroid."[5] Fluticasone is a glucocorticoid, meaning that it exerts its activity on the glucocorticoid receptors. But, the claims embrace treatment of "conditions" which require mineralocorticoids (*e.g.*, aldosterone or fludrocortisone)—*not* glucocorticoids—or worse still, conditions which require steroids that are not even corticosteroids, such as estradiols, progesterone, testosterone and their analogs. It would be difficult enough to ascertain whether fluticasone esters could even treat those

[4] *See* Ex. 46 (DEXPAK® (Dexamethasone) Label) ("The initial dosage of dexamethasone varies from 0.75 to 9 mg a day depending on the disease being treated."); Ex. 47 (RAYOS Label) ("It should be emphasized that dosage requirements are variable and must be individualized on the basis of the disease under treatment and the response of the patient"). Claim 1 of the '723 patent is also not limited to treatment of humans, but instead includes treatment of all mammals, and thus a "pharmaceutically effective amount" would naturally depend on *which mammal* is being treated.

[5] Indeed, even different esters of fluticasone have dramatically different anti-inflammatory and pharmacological properties. *See* Section IV.4., *infra*.

conditions, let alone to identify, with reasonable certainty, suitable dosage amounts for doing so. Similarly, azelastine is not simply interchangeable with any "antihistamine." Azelastine exerts its activity at the H1 histamine receptor, but other histamine receptors (*i.e.*, H2, H3, and H4) are also important therapeutic targets of other antihistamines. For example, the H2 histamine receptor is involved in gastric acid secretion, and consequently antihistamines that are antagonists at the H2 receptor, such as ranitidine (Zantac®) are indicated for treatment of active duodenal ulcer. Not only would there be no expectation that azelastine (an H1 receptor antagonist) would be suitable for treating *any* condition involving H2 histamine receptor, including active duodenal ulcer, but the "therapeutically effective amounts" for doing so would be virtually indeterminate and, in any event, could not be ascertained with reasonable certainty.

Complicating matters further is the fact that Claim 1 calls for "intranasal administration" of the azelastine/fluticasone pharmaceutical composition, but the "conditions" are not similarly restricted to those for which "*intranasal* administration" of one or more antihistamines and/or one or more steroids is indicated. Instead, by patentee's deliberate drafting, they cover "conditions" for which any "administration" of one or more antihistamines and/or one or more steroids is indicated.[6] Thus, the range of conditions includes those for which steroids or antihistamines are indicated for intranasal, topical, oral, intravenous, or subcutaneous

[6] "General descriptive terms will ordinarily be given their full meaning; modifiers will nto be added to broad terms standing alone." *Johnson Worldwide Assoc's, Inc. v. Zebco Corp.*, 175 F.3d 985, 989 (Fed. Cir. 1999). This is especially true in this case, where the patent claim itself draws a distinction between the term "administration" and "intranasal administration," implying that the broader term "administration" as it first appears in the claim was not intended to be limited to intranasal application. *See Takeda Pharm. Co. v. Zydus Pharms. USA, Inc.*, 743 F.3d 1359, 1363-64 (Fed. Cir. 2014) (construing "400 μm or less" to mean "precisely 400 μm or less" and not allowing for a degree of imprecision, because "the remainder of claim 1 demonstrates that the inventors knew how to express ambiguity in claim language when they so desired [by use of the term '*about*' in other areas of the claim] …. [H]ad the inventors desired the average particle diameter to include a margin of error, they could easily have included the word 'about' in the claim language." (citations omitted)).

administration. As an example, the corticosteroid budesonide is indicated for treatment of inflammatory bowel disease (IBD) as an oral dosage form. The patents provide no guidance as to how much fluticasone would be required to treat IBD, let alone, how much *intranasally* administered fluticasone would be effective to treat IBD. While intranasal drug delivery is, in principle, capable of achieving systemic levels of the drug, it was known in the prior art that fluticasone propionate and fluticasone furorate, in fact, had very low systemic availability when delivered intranasally. *See* Ex. 37 (FLONASE® Label); Ex. 38 (Biggadike). Accordingly, persons of ordinary skill in the art would not have understood, with reasonable certainty, how much intranasally administered fluticasone ester would constitute a "therapeutically effective amount" against conditions requiring systemic levels of steroids.

The Federal Circuit has explained that "'effective amount' is a common and generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without undue experimentation." *Geneva Pharmaceuticals v. GlaxoSmithKline PLC*, 349 F. 3d 1373, 1384 (2003) (citing *In re Halleck*, 57 C.C.P.A. 954, 422 F.2d 911, 914 (1970)). If ever there were a case in which a person of ordinary skill in the art could *not* determine the specific amounts without undue experimentation, it is here. As Dr. Philpot explains, it would take nearly all of the efforts of a major pharmaceutical company to determine "therapeutically effective amount[s]" for just a handful of conditions. *See* Declaration of Edward E. Philpot, M.D., M.B.A. ("Philpot Decl.") ¶ 28. Determining the "therapeutically effective amount[s]" for the full scope of the claimed conditions would be, as a practical matter, impossible. *Id*.

When read in light of the claim language, Plaintiffs' proposed construction is a tautology—a "therapeutically effective amount" is simply whatever amount works. Such a

reading does nothing to clarify the meaning and would only serve to further undermine the notice function of the claims. Plaintiffs' construction should not be adopted.

4. "pharmaceutically acceptable ester of fluticasone" ('723 Patent)

Teva's Proposed Construction	Plaintiffs' Proposed Construction
Indefinite	Plain and ordinary meaning: "ester of fluticasone that can be incorporated into a dosage form for human or mammalian use"

The patents-in-suit do not define what is meant by "pharmaceutically acceptable ester of fluticasone." And, there is no art-recognized meaning for "pharmaceutically acceptable ester." The prior art provides multiple definitions of "pharmaceutically acceptable ester," including: ester forms that are substantially non-toxic (*see, e.g.*, Ex. 48 (U.S. Patent No. 5,908,830) at 10:47-48; Ex. 49 (U.S. Patent No. 5,994,343) at 7:4-8); esters in which the parent compound's carboxyl functions are replaced with specific alkoxycarbonyl functions (*see, e.g.*, Ex. 50 (U.S. Patent No. 6,323,180) at 8:20-36); and esters that hydrolyze *in vivo*, leaving only the active parent compound. (*See, e.g.*, Ex. 51 (U.S. Patent No. 5,985,911) at 9:9-12; Ex. 52 (U.S. Patent No. 5,925,630) at 4:29-34.). *See* Declaration of Dr. Edmund Elder ("Elder Decl.") ¶ 15. The Patents-in-Suit fail to inform which, if any, of these multiple definitions apply.

Further, fluticasone propionate and fluticasone valerate—the only "pharmaceutically acceptable esters of fluticasone" disclosed in the Patents-in-Suit (*see, e.g.*, '723 patent at 6:54-57)—*do not* both hydrolyze *in vivo*, unlike other "pharmaceutically acceptable esters" of steroids disclosed in the prior art. *See, e.g.*, Ex. 38 (MEDA_TEVA_00025501); Ex. 37 (FLONASE Label); Elder Decl. ¶ 15. The intrinsic evidence further explains that "a number of topical glucocorticoid esters are indeed ester prodrugs releasing the active parent glucocorticoid in the body. However, fluticasone 17α esters are remarkably stable and remain attached to the fluticasone backbone even during metabolism." Ex. 38 (MEDA_TEVA_00025501). And, "[t]he

ester group also contributes to the physicochemical characteristics of the molecule," affecting the drug substance's "pharmacokinetic and pharmacodynamics properties." *Id.*

Since fluticasone esters, including fluticasone propionate, do not hydrolyze *in vivo*, they differ from the traditional understanding of "pharmaceutically acceptable esters" as "pro-drugs," and are instead distinct active agents. The patent fails to inform a person of ordinary skill in the art, with reasonable certainty, what constitutes "a pharmaceutically acceptable ester of fluticasone." Accordingly, the term is indefinite.

5. "condition[s] for which administration of one or more antihistamine and/or one or more steroid is indicated" ('723 Patent)

Teva's Proposed Construction	Plaintiffs' Proposed Construction
Indefinite	Plain and ordinary meaning: "disease[s] or illness[es] where the symptoms may be prevented or minimized by application of one or more antihistamine and/or one or more steroid"

Independent Claim 1 of the '723 patent recites a "method for the prophylaxis or treatment in a mammal of a condition for which administration of one or more antihistamines and/or one or more steroids is indicated." The Court has already construed "condition" as meaning "disease[s] or illness[es]." *See Meda Pharms. Inc. et al. v. Apotex Inc. et al.*, No. 1:14-cv-01453-LPS (D. Del.) ("Apotex Litigation"), D.I. 114. The '723 patent does not identify the set of "conditions," except for the preferred rhinitis embodiments. Therefore, whether a "disease[s] or illness[es]" is within the scope of the claims turns on whether steroid or antihistamine treatment was "indicated."

However, the term "indicated" is far from concrete. For example, Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh Edition, Saunders (2003), defines "indication" as "a sign or circumstance that *points to* or shows the cause, treatment, or some other aspect of a disease." Ex.6 (emphasis added). Whether a

treatment is "indicated" is often highly subjective—it may depend on a physician's opinion, which source or study one is relying on, the time frame, the geographical location, or a physician's particular assessment of the patent in question. *See, e.g.*, Ex. 54 (Bonnie Snow, Drug Information: A Guide to Current Resources, Scarecrow Press (1999)) at 70 ("[Q]uestions about unapproved uses originate not only from consumers, but also from health science professionals, who may need to verify acceptable dosage for unlabeled indications or may ask for authoritative references to alternative therapies… The status quo regarding correct or legal drug use is undoubtedly confusing."). To the extent the claim covers the subjective beliefs of a prescribing physician or the patients themselves, the claim is fatally indefinite because what may be "indicated" in the view of one physician or patient, may not be to others. *See Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1350 (Fed. Cir. 2005) (claim term is indefinite where its scope "would depend on the unpredictable vagaries of any one person's opinion.").

The term "indicated" is generally understood to include "off-label" uses, in addition to approved used. As explained by the US Pharmacopeia:

> "*Indications* of use stated in manufacturers' labeling and approved by the U.S. Food and Drug Administration (FDA) or Health Canada's Therapeutic Products Directorate are generally included, as well as additional *off-label indications* selected as appropriate by USP Advisory Panels. These *two types of indications* are included under an Accepted subheading. An Unaccepted indications section identifies uses of a drug that are considered by USP Advisory Panels to be inappropriate, obsolete, or unproven."

Ex. 15 (USPDI: Drug Information for the Health Care Professional, 21st Rev. Edition (2001)) at viii (emphasis added). This raises the question of whether a drug must be approved by a regulatory body for a particular treatment to constitute an "indication," and, if so, which regulatory body? Is a treatment that is approved in Canada (or elsewhere), but not the United States an "indication"? And, are off-label "indications" covered by the claims? As explained by

the US Pharmacopeia, off-label "indications" may be based on mere "opinions" of "respected" authorities. *See* Ex. 15.

Whether treatment of a given disease is covered by the claims, depends on whether other, unidentified antihistamines or steroids were "indicated" for the disease. The patent fails to identify those other steroids or antihistamines, and provides not guidance whatsoever as to whether a given condition is indicated for treatment. Due to the inherent ambiguity of the term "indicated," and the lack of guidance in the Patents-in-Suit, the public is not apprised of the metes and bounds of the claim with reasonable certainty. *Nautilus*, 134 S. Ct. at 2124.

6. "from 0.001% (weight/weight) % (weight/weight) of azelastine hydrochloride" ('428 Patent, Claims 28, 29, 30)

Teva's Proposed Construction	Plaintiffs' Proposed Construction
Indefinite	Plain and ordinary meaning: "from 0.001% (weight/weight) to 1% (weight/weight) of azelastine hydrochloride"

Claim 28 contains an error on its face, leaving the amount of azelastine hydrochloride undefined. Consequently, one of ordinary skill in the art would not be informed of the scope of the claim with reasonable certainty, rendering Claim 28 (and the claims which depend on it) indefinite. *See Nautilus*, 134 S. Ct. at 2124. While a certificate of correction was issued on May 3, 2016, that certificate is not applicable to this action[7] because it issued after the cause of action arose. *See* 35 U.S.C. § 254 ("Every such patent, together with such certificate, shall have the same effect and operation in law on the trial of actions for *causes thereafter arising* as if the same had been originally issued in such corrected form") (emphasis added); *Southwest Software,*

[7] Plaintiffs have not amended their Complaint to add the corrected version of the '428 patent. For this reason alone, the Certificate of Correction is not properly at issue in this case. Moreover, given the advanced stage of discovery and claim construction proceedings in this case, and in view of Plaintiffs' failure to amend the Complaint in the several months since the Certificate of Correction issued, and the consequent prejudice to Defendant, Plaintiffs should not be permitted to bring the Certificate of Correction into this case.

Inc. v. Harlequin Inc., 226 F.3d 1280, 1297 (Fed. Cir. 2000) ("Southwest's cause of action against Harlequin and ECRM arose before the certificate of correction was issued. Because the certificate of correction is not effective for purposes of this action…claim 1 of the '257 patent is invalid"); *Nautilus Neurosciences, Inc. v. Wockhardt USA LLC*, No. CIV.A. 11-1997 ES, 2013 WL 775750, at *16 (D.N.J. Feb. 27, 2013) (holding, in the context of an ANDA case, that "any certificate of correction that may issue from the PTO would not apply to this action because Plaintiffs brought this action before the issuance of any such certificate").

In this case, the Amended Complaint alleges that "Teva's submission of ANDA No. 208436 infringes one or more claims of the '428 patent under 35 U.S.C. § 271(e)(2)(A)." See DI 24, ¶ 52. Thus, Plaintiffs' cause of action against Teva arose when Teva filed its ANDA. *See AstraZeneca Pharmaceuticals LP v. Apotex Corp.*, 669 F.3d 1370, 1377 (Fed. Cir. 2012) ("We have further explained that § 271(e)(2) provided a new cause of action so that courts could promptly resolve infringement and validity disputes before the ANDA applicant had engaged in the traditional statutorily defined acts of infringement."). The certificate of correction issued *after* Defendants' ANDA filing and *after* the Plaintiffs' Amended Complaint, and therefore it is ineffective for the purposes of this action. Accordingly, the error in Claim 28, as issued, renders Claims 28-30 of the '428 patent indefinite.

7. "% (weight/weight)" ('620, '723 and '428 Patents)

Teva's Proposed Construction	Plaintiffs' Proposed Construction
"% (weight/weight), in a solid or semi-solid formulation" / Indefinite as to claims reciting a liquid formulation (*e.g.*, nasal spray, solution, or suspension)	Plain and ordinary meaning: "% (weight/weight) of the formulation"

The meaning of the phrase "% (weight/weight)" is altered by the patents-in-suit to be limited to "solid or semi-solid formulations," and is expressly described as *not* including solutions or suspensions. Even if the phrase "% (weight/weight)" would have a plain and

ordinary meaning in other contexts, the meaning was altered by the patentee to be expressly limited to "solid or semi-solid formulations" in the Patents-in-Suit. The "inventor's lexicography governs" in this case because the specifications "reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess." *Phillips*, 415 F.3d at 1316. Specifically, the patents-in-suit state that:

> In the case of solutions/suspensions reference is ***always*** made to percent by weight/volume, in the case of solid or semi-solid formulations to percent by weight/weight of the formulation.

'723 patent at 3:4-7; '620 patent at 3:3-6; '428 patent at 3:26-29; Ex. 12 (GB 2,389,530) at 3 (the "Priority Application") (emphasis added). The suitable ranges for the constituents of the formulations were defined strictly according to this distinction. For instance, the amount of the claimed preservatives, including benzalkonium chloride, is defined as follows: "Each of these compounds may be used in a concentration of 0.002 to 0.05%, for example 0.02% (*weight/volume in liquid formulations*, *otherwise weight/weight*)."[8] Accordingly, the patents "exhibit a clear intent to distinguish" the defined amounts of preservatives used in liquids (*e.g.*, solutions/suspensions) from the amounts used in solid/semi-solid formulations. *SkinMedica, Inc. v. Histogen Inc.*, 727 F.3d 1187, 1197 (Fed. Cir. 2013). Therefore, Teva submits that the proper construction of the phrase "% (weight/weight)" should be restricted, as per the explicit lexicography in the Patents-in-Suit, to mean "% (weight/weight), in a solid or semi-solid formulation."

Because of the patentee's deliberate choice to limit "% (weight/weight)" to solid/semi-solid formulations, several asserted claims are indefinite as contradicted by the specification. Specifically, certain claims recite both "% (weight/weight)" and "nasal spray" or "aqueous

[8] '723 patent at 2:44-47; '620 patent at 2:43-46; '428 patent at 2:67-3:3 (emphasis added).

suspension,"[9] even though the patents state that "reference is ***always*** made to percent by weight/volume" for suspensions and "percent by weight/weight" for solid/semi-solid formulations.[10] In view of the contradiction between the claims and the specification, a person of ordinary skill in the art would not understand the scope of the invention with reasonable certainty. *See Allen Eng'g*, 299 F.3d at 1349 (claims reciting "perpendicular" pivoting of component indefinite where specification stated that component was incapable of such pivoting); *Application of Cohn*, 438 F.2d 989, 993 (C.C.P.A. 1971) (claims requiring the use of an "alkali silicate" to create an "opaque finish" held indefinite where specification stated that an "opaque finish" is not obtained when an alkali metal silicate is used). Therefore, claims reciting "% (weight/weight)" in an aqueous suspension or nasal spray are indefinite.

Alternatively, should the claims be found definite, many, if not all, of the claims of the '428 patent would be entitled to an effective filing date of March 18, 2015. This would directly bear on claim construction issues,[11] because the "ordinary and customary meaning of a claim term 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, i.e., *as of the effective filing date of the patent application.*" *Phillips*, 415 F.3d at 1313 (emphasis added). It would also result in the claims being invalid over the publication of the earlier applications in the priority chain.[12]

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[9] *See, e.g.*, '723 patent at Claim 12; '620 patent at Claim 5; '428 patent at Claim 3.

[10] *See* '723 patent, col. 3, ll. 4-7; '620 patent, col. 3, ll. 4-7; '428 patent, col. 3, ll. 26-29.

[11] As discussed above, Plaintiffs' own U.S. Patent No. 8,071,073, titled "Compositions comprising Azelastine and Methods of Use Thereof," which issued in 2011 and is cited in the file history of the '428 patent, directly contradicts Plaintiffs' construction of the term "treatment" as discussed in Section IV.1., *supra*, as it discloses that azelastine "treatment" includes "curing." Even though this patent issued after the earliest *claimed* priority date, it is "intrinsic evidence" to the '428 patent because it is "prior art cited in a patent or cited in the prosecution history of the patent." *Powell v. Home Depot U.S.A., Inc.*, 663 F.3d 1221, 1231 (Fed. Cir. 2011).

[12] *See, e.g.*, PCT/GB03/02557, which published as WO03/105856 on December 24, 2003.

The effective filing date of any claims reciting "0.002% (weight/weight) to 0.05% (weight/weight) of benzalkonium chloride" in a nasal spray formulation (or aqueous suspension) should be the *actual* March 18, 2015 filing date of U.S. Application No. 14/661,720 ("the '720 application") from which the '428 patent issued. This is because the first disclosure of that range in a liquid formulation was in the claims as filed on March 18, 2015, in the '720 application. *See Lucent Technologies, Inc. v. Gateway, Inc.,* 543 F.3d 710, 718-19 (Fed.Cir.2008) (to claim priority based on the filing date of an earlier application, the earlier application must support the claims of the later-filed application). While the specifications disclose the *numerical* range, they specifically distinguish the *units* depending on whether the formulation is a liquid or solid. (*See, e.g.*, '428 patent at 3:1-3 ("0.002 to 0.05%, for example 0.02% (weight/volume in liquid formulations, otherwise weight/weight)"). Further, as explained in the Declaration of Dr. Edmund Elder, 0.002% (weight/***volume***) is *not* equal to 0.002% (weight/***weight***), and 0.05% (weight/***volume***) is *not* equal to 0.05% (weight/***weight***), in the claimed formulations. *See* Elder Decl. ¶¶ 18-20. Therefore, Teva respectfully submits that a determination of the effective filing date of the claim limitation "0.002% (weight/weight) to 0.05% (weight/weight) of benzalkonium chloride" is appropriate at this time.

8. "wherein said pharmaceutical formulation is in a dosage form suitable for nasal administration" / "suitable for nasal administration" / "wherein said dosage form suitable for nasal administration comprises [nasal drops or] a nasal spray" ('620 Patent Claim 29, 47)

Teva's Proposed Construction	Plaintiffs' Proposed Construction
"applied onto the nasal mucosa"	"applied onto the nasal mucosa and that is tolerable to patients"

The parties are in agreement that a pharmaceutical formulation which is "in a dosage form suitable for nasal administration" is one which "can be applied onto the nasal mucosa." The only dispute lies with Plaintiffs' attempt to import "tolerable" into the claim. The patents-

in-suit never describe a pharmaceutical formulation "suitable for nasal administration" as one which is "tolerable to patients." Plaintiffs point to only a single instance of the term "tolerated" within the patents-in-suit, but the term is not used in connection with "intranasal administration." *See* '428 patent at 1:55-59. While tolerability may be a desirable feature of pharmaceutical formulation, there surely exist many other desirable features, although there is similarly no basis for reading them into the claims.

Plaintiffs' proposed construction should be rejected because there is no basis for importing the term "tolerated" into the patent claims.[13] Moreover, what is "tolerated" by one patient may not be "tolerated" by another patient, and this level of subjectivity would add ambiguity, rather than certainty, to the claim.

IV. CONCLUSION

For all of the foregoing reasons, Teva requests that the Court adopt its proposed constructions.

Respectfully submitted,

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[13] It is notable that Plaintiff Meda Pharmaceuticals Inc.'s own contemporaneous U.S. Patent No. 8,071,073, which also relates to azelastine nasal sprays, defines "intranasal administration" as meaning "administered directly to the nasal mucosa," without any tolerability requirement. Exhibit 43 at 12:2-14.