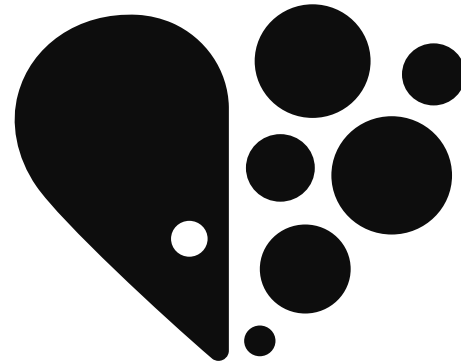


Dr.Reddy's



**DR. REDDY'S LABORATORIES S.A., AND
DR. REDDY'S LABORATORIES, INC.**

v.

EYE THERAPIES, LLC

May 13, 2025

IPR2024-00467 and IPR2024-00563

U.S. Patent Nos. 11,833,245 and 11,596,600

The Challenged Claims of the '245 and '600 Patents Are Unpatentable

Current Proceedings

[IPR2024-00467 \(U.S. Patent No. 11,833,245\)](#) and [IPR2024-00563 \(U.S. Patent No. 11,596,600\)](#)

GROUND 1

Claims 1, 2, 4-6, 7, 8, 9, 11-17, 20-22, 25, 27 of the '245 patent are obvious over Norden (Ex. 1006), Gil (Ex. 1004), Dean (Ex. 1007), the Alphagan Label (Ex. 1008), and Federal Register (Ex. 1009)

GROUND 1

Claims 1, 12, and 28 of the '600 patent are obvious over Norden (Ex. 1006), Gil (Ex. 1004), Dean (Ex. 1007), the Alphagan Label (Ex. 1008), and Federal Register (Ex. 1009)

Previously Decided

[IPR2022-00142 \(U.S. Patent No. 8,293,742\)](#)

GROUND 3

Claims 1-6 of the '742 patent are obvious over Gil (Ex. 1004) in combination with Norden (Ex. 1006), Dean (Ex. 1007), the Alphagan Label (Ex. 1008), and Federal Register (Ex. 1009)

'245 Petition (Paper 2), 33-35; '600 Petition (Paper 2), 33-36; '245 Reply (Paper 58), 27; '600 Reply (Paper 55) at 24-25; EX-1003 ('742 FWD), 35-61

Key Disputed Issues

1. Whether the -00142 FWD precludes Patent Owner from relitigating issues already decided by the Board?
2. Whether claim 1 of the '245 patent is limited to a “single drop” of brimonidine?
3. Whether the prior art motivated a POSA to use low concentrations of brimonidine with a reasonable expectation of success?
 - Whether the Alphagan Labels teach away from using low concentrations of brimonidine to reduce eye redness?
 - Whether Gil and Norden directed a POSA to use high “doses” of brimonidine?
4. Whether the result of reducing redness was taught by the prior art or otherwise inherent?
5. Whether the use of the preservative, benzalkonium chloride, was obvious?
6. Whether Gil is the closest prior art to the challenged claims?
7. Whether there is a nexus between the invention claimed and LUMIFY's sales?

Issue Preclusion Applies to IPR Proceedings



“It is well established that collateral estoppel applies to IPR proceedings.

It is well established that patent claims need not be identical for collateral estoppel to apply. Rather, collateral estoppel requires that the issues of patentability be identical. Thus, collateral estoppel may apply even if the patent claims use slightly different language to describe substantially the same invention, so long as **the differences between the unadjudicated patent claims and adjudicated patent claims do not materially alter the question of invalidity.”**

Google LLC v. Hammond Dev. Int’l, Inc., 54 F.4th 1377, 1381 (Fed. Cir. 2022) (internal citations and quotations omitted); ‘245 Petition and ‘600 Petition (Paper 2), 10-11; ‘245 Reply (Paper 58), 27; ‘600 Reply (Paper 55), 24-25

The Board Already Decided Identical Issues in the -00142 Final Written Decision

'742 Patent, Claim 3

3. A method for reducing eye redness

consisting essentially of topically administering to a patient having an ocular condition a composition **consisting essentially of** brimonidine into ocular tissue,

wherein pH of said composition is between about 5.5 and about 6.5,

wherein said brimonidine concentration is between about 0.001% and about 0.025% weight by volume and

wherein said composition is formulated as an ocular drop.

“Norden and Gil ... teach or suggest that brimonidine alone is effective in reducing eye redness.” EX-1003 ('742 FWD), 54 (citing EX-1006 (Norden), 4).

“Alphagan teaches brimonidine eye drops with a pH of 6.3 to 6.5, and that a POSA would, therefore, have been motivated to use a pH between about 5.5 and 6.5 with a reasonable expectation of success.” EX-1003 ('742 FWD), 53-54 (crediting Petitioners' expert Dr. Laskar).

Norden “teaches a method for reducing eye redness by administering prophylactic brimonidine to LASIK patients, which resulted in reducing ... hyperemia.” EX-1003 ('742 FWD), 53.

“Gil teaches administering 0.03% brimonidine ... and suggests that doing so will reduce eye redness in radial keratotomy patients....” EX-1003 ('742 FWD), 53.

“Gil teaches that vasodilation, increased vascular permeability, and redness are all signs of neurogenic inflammation, and that brimonidine ‘is effectively in reducing such neurogenic response.’” EX-1003 ('742 FWD), 53 (citing EX-1004 (Gil), 1:40-43, 5:38-40, 44-45).

'245 Petition (Paper 2), 33-35; '600 Petition (Paper 2), 33-36; '245 Reply (Paper 58), 27; '600 Reply (Paper 55), 24-25

The Board Made Several Material Factual Findings in the -00142 FWD

The Prior Art Taught Low Concentrations of Brimonidine Reduce Eye Redness

- Norden “teaches a method for reducing eye redness by administering prophylactic brimonidine to LASIK patients, which resulted in reducing ... hyperemia.” EX-1003 ('742 FWD), 53.
- “Gil teaches administering 0.03% brimonidine ... and suggests that doing so will reduce eye redness in radial keratotomy patients....” EX-1003 ('742 FWD), 53.
- “Gil teaches that vasodilation, increased vascular permeability, and redness are all signs of neurogenic inflammation, and that brimonidine ‘is effectively in reducing such neurogenic response.’” EX-1003 ('742 FWD), 53 (citing EX-1004 (Gil), 1:40-43, 5:38-40, 44-45).

The Prior Art Taught that Brimonidine Alone Is Effective in Reducing Eye Redness

- “Norden and Gil ... teach or suggest that brimonidine alone is effective in reducing eye redness.” EX-1003 ('742 FWD), 54 (citing EX-1006 (Norden), 4).

The Prior Art Directed a POSA to Use a pH between about 5.5 and about 6.5

- “Alphagan teaches brimonidine eye drops with a pH of 6.3 to 6.5, and that a POSA would, therefore, have been motivated to use a pH between about 5.5 and 6.5 with a reasonable expectation of success.” EX-1003 ('742 FWD), 53-54 (crediting Petitioners’ expert Dr. Laskar).

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4. Whether the result of reducing redness was taught by the prior art or otherwise inherent?
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6. Whether Gil is the closest prior art to the challenged claims?
7. Whether there is a nexus between the invention claimed and LUMIFY's sales?

Patent Owner's Narrow Construction of Claim 1 of the '245 Patent Is Unsupported

- Patent Owner argues claim 1 should be limited to “***a single drop of 0.025% brimonidine as the only active ingredient in a single step, where the single step is the only step taken to reduce eye redness.***”

'245 POR (Paper 25), 11

- + Patent Owner disregards the plain language of the term.
- + Patent Owner ignores the specification.
 - “ocular drop” describes the formulation, not the dose
 - Examples do not consistently use a single drop
- + Prosecution history does not address number of drops.
- + Patent Owner takes conflicting positions.

'245 Reply (Paper 58), 1-6; EX-1001 ('245 Patent), 22:37-39, 20:8-26, Figs. 5A-5C; '245 EX-1147 (Galanis Reply), ¶¶ 11-22

Claim 1 of the '245 Patent is Not Limited to Administration of a Single Drop

1. A method for reducing eye redness in a human subject having ocular hyperemia, consisting of topically administering to an eye of said human in need of said reduction of eye redness a composition in the form of an ocular drop consisting of 0.025% weight by volume brimonidine as the sole active ingredient, and one or more non-therapeutic components including benzalkonium chloride, wherein the ocular drop has a pH between 5.5 to 6.5, wherein the ocular hyperemia is reduced.

Norian Does Not Support Patent Owner's Construction

Claim at issue in *Norian*:

A kit for preparing a calcium phosphate mineral, said kit **consisting of**:

at least one calcium source and at least one phosphoric acid source free of uncombined water as dry ingredients; and

a solution consisting of water and a sodium phosphate, where the concentration of said sodium phosphate in said water ranges from 0.01 to 2.0 M and said solution has a pH in the range of about 6 to 11.

Construed to be limited to a single type of sodium phosphate

- Specification only included examples where a single type of sodium phosphate was used
- Patentee surrendered broader interpretation during prosecution

'245 Reply (Paper 58), 1-4; *Norian Corp. v. Stryker Corp.*, 432 F.3d 1356, 1357-62 (Fed. Cir. 2005).

“An Ocular Drop” is a Type of Ophthalmic Formulation

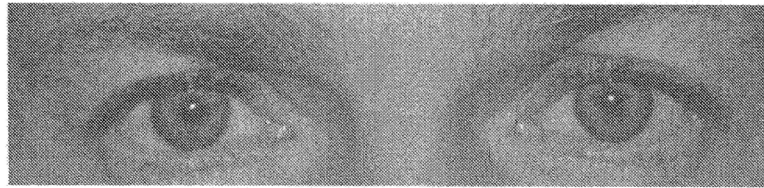
In one embodiment, the invention generally relates to a composition for inducing vasoconstriction consisting essentially of brimonidine, wherein said brimonidine concentration is from between about 0.01% to about 0.02% weight by volume, wherein pH of said composition is between about 5.5 and about 6.5, and wherein said composition is formulated as an ocular drop.

The topical compositions include, but are not limited to, ocular drops, ocular ointments, gels and creams. They may also include additional non-therapeutic components, which include, but are not limited to, preservatives, delivery vehicles, tonicity adjustors, buffers, pH adjustors, antioxidants, and water.

The Specification Does Not Support Limiting Claim 1 to a Single Drop

Baseline:

FIG. 5A



Right eye VISINE Original®

Left eye Brimonidine 0.012% x1

ii gtts tid, day 2 1st instillation

FIG. 5B

ii gtts tid, day 2 1st instillation



Note rebound hyperemia

Right eye Brimonidine 0.012% x1

Left eye Brimonidine 0.012% x1

ii gtts

FIG. 5C

ii gtts

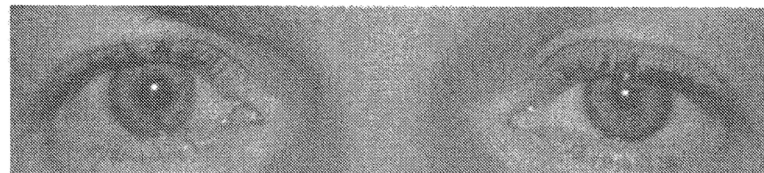


FIG. 5A is a baseline visual appearance of two eyes of a patient with an ocular condition of moderate hyperemia.

FIG. 5B depicts a visual appearance of the right eye of the patient after being treated with a prior art composition comprising VISINE Original® (tetrahydrozoline 0.05%) and the induction of rebound hyperemia, and the visual appearance of the left eye of the patient after being treated simultaneously with a composition of the present invention comprising brimonidine at 0.015%

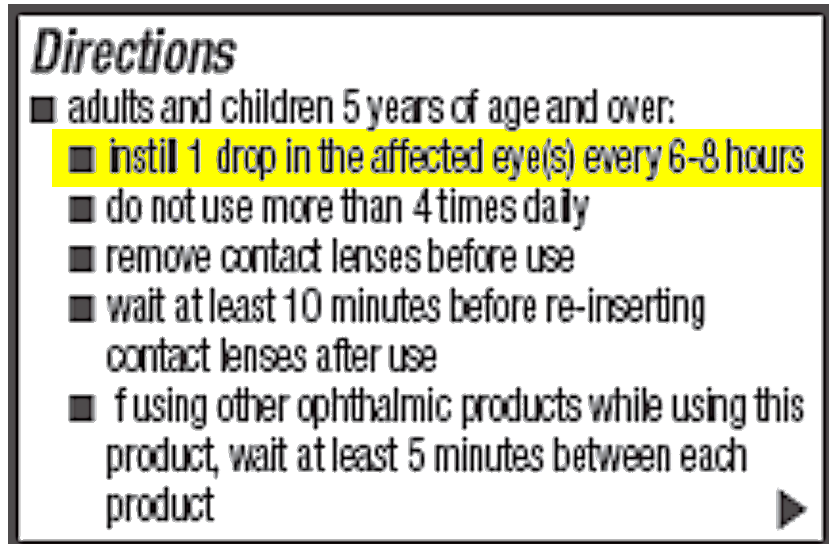
FIG. 5C depicts a visual appearance of the right eye of the patient after then being treated with the novel composition of the present invention comprising brimonidine at 0.015%, reversing the VISINE Original® induced rebound hyperemia, and a visual appearance of the left eye of the patient after being treated simultaneously with an additional drop of the composition of the present invention comprising brimonidine at 0.015%.

Prosecution History Does Not Address the Number of Drops

Moreover, the claim phrase “consisting of” has been introduced in claim 29. By consisting of, it is meant that brimonidine is the sole active ingredient administered in the method for reducing redness of claim 29, though inactive ingredients/excipients (such as benzalkonium chloride as recited in the claim) would not be excluded; however, it is clear that other active ingredients (such as steroids, anesthetics, carbonic anhydrase inhibitors, or NSAIDS, for example) would be excluded. Similarly, independent claim 36 requires brimonidine as the sole redness reducing active ingredient, precluding the use of additional active ingredients that may also cause vasoconstriction and reduction of hyperemia along with 0.025% brimonidine.

Patent Owner's Construction Is at Odds with Its Claim that Lumify Embodies the Claims

Patent Owner claims
Lumify practices
the challenged claims.



1 drop every 6–8 hours = up to 4 drops/day

Patent Owner claims prior art
administration does not fall within
the challenged claims.

EXAMPLE 1

A clinical study is performed to compare the analgesic effect of topically administered brimonidine and placebo following radial keratotomy surgery. One hundred and twenty-four male and female subjects, 21 to 45 years of age, undergo routine, elective, unilateral radial keratotomy for the correction of myopia and brimonidine is administered as a 0.03% ophthalmic solution.

Each subject receives one drop of the assigned study medication every four hours while awake one day prior to surgery and again every 20 minutes for the two hours just before surgery. Each subject then undergoes unilateral radial keratotomy. Following surgery, each subject receives one drop of the study medication in the operated eye every four hours while awake for 14 consecutive days. Postoperative examinations occur at days 1, 3, 7 and 14.

²⁴⁵ Reply (Paper 58), 5-6; EX-1004 (Gil), 4:45-5:2; EX-1147 (Galanis Reply), ¶ 18; EX-2050 (Lumify Label), 2; EX-1047 (Noecker Dep. Tr.), 69:18-74:21, 77:2-86:16, 87:8-94:20

Key Disputed Issues

1. Whether the -00142 FWD precludes Patent Owner from relitigating issues already decided by the Board?
2. Whether claim 1 of the '245 patent is limited to a “single drop” of brimonidine?
3. **Whether the prior art motivated a POSA to use low concentrations of brimonidine with a reasonable expectation of success?**
 - Whether the Alphagan Labels teach away from using low concentrations of brimonidine to reduce eye redness?
 - Whether Gil and Norden directed a POSA to use high “doses” of brimonidine?
4. Whether the result of reducing redness was taught by the prior art or otherwise inherent?
5. Whether the use of the preservative, benzalkonium chloride, was obvious?
6. Whether Gil is the closest prior art to the challenged claims?
7. Whether there is a nexus between the invention claimed and LUMIFY's sales?

Norden, Gil, Dean, and the Federal Register Taught Low-Dose Brimonidine in a Method to Reduce Eye Redness



subconjunctival hemorrhage and reduce the amount of hyperemia.”). We find Norden’s disclosure, coupled with Gil’s teaching that low-dose brimonidine “is effective in reducing such neurogenic responses” like “redness,” and in view of Federal Register’s disclosure that ocular vasoconstrictors are eye-redness-reducers and Dean’s disclosure that topical brimonidine is an ocular vasoconstrictor, is sufficient motivation for a POSA to pursue low-dose brimonidine in a method to reduce eye redness with a reasonable expectation of success. See Ex. 1004, 1:40–43, 5:38–40, 44–45; Ex. 1006, 468; Ex. 1007, 2:35–36; Ex. 1009, 7082; Ex. 1049 ¶¶ 91–92.

EX-1003 ('742 FWD), 56

'245 Petition (Paper 2), 42-44; '600 Petition (Paper 2), 40-41; '245 Reply (Paper 58), 11; '600 Reply (Paper 55), 6

The Board's Conclusion in the -00142 IPR Is Correct

1. **Brimonidine was known to be a “strong” and “potent” vasoconstrictor.**
EX-1014 (Galanis Decl.), ¶¶ 76, 121, EX-1012 (Dana Decl.), ¶ 33.
2. **A POSA would have been motivated to use low concentrations of brimonidine.**
EX-1014 (Galanis Decl.), ¶¶ 85-89, 129-34.
 - Gil and Dean disclose the use of low concentrations of brimonidine to achieve vasoconstriction. *Id.*, ¶¶ 86-88, 129; EX-1004 (Gil), 3:63-66; EX-1007 (Dean), 5:20-24.
 - A POSA would have been motivated to lower concentration to reduce known side effects of high concentration brimonidine. EX-1014 (Galanis Decl.), ¶¶ 85-88; EX-1012 (Dana Decl.), ¶ 54.
3. **A POSA would have a reasonable expectation of success that low concentrations of brimonidine would reduce eye redness.** EX-1014 (Galanis Decl.), ¶¶ 75, 85-89
 - Gil discloses that low concentrations of brimonidine are “effective” in reducing “neurogenic responses,” including redness. *Id.*, ¶ 66; EX-1004 (Gil), 5:44-45.
 - The Federal Register taught that low concentrations of vasoconstrictors were redness reducers. EX-1014 (Galanis Decl.), ¶ 87; EX-1009 (Fed. Reg.), 9, 14
 - Determining the optimal concentration of brimonidine is “routine.” EX-1014 (Galanis Decl.), ¶ 85.

Brimonidine Was Known to be a “Strong” or “Potent” Vasoconstrictor of Vessels in the Front of the Eye

1998
Robin
(Ex. 70)

“[E]ven without $\alpha 1$ activation, $\alpha 2$ receptor activation can produce vasoconstriction. Locally in the eye, both **brimonidine** and apraclonidine produce anterior segment (*i.e.*, conjunctiva, iris, ciliary body) **vasoconstriction**.”

2001
Wikberg
(EX-1022)

(“The $\alpha 2$ -adrenoceptor agonists **brimonidine**, apraclonidine, and oxymetazoline are **potent vasoconstrictors** in the porcine ciliary artery.”)

2001
Gil
(EX-1004)

Brimonidine is **effective in reducing** “ocular responses characteristic of **neurogenic inflammation, including redness**.”

2001
Dean
(EX-1007)

“Brimonidine is a **potent** and relatively selective [alpha-2] agonist,” and “Upon topical ocular administration **brimonidine** causes **vasoconstriction in scleral vessels**.”

2002
Norden
(EX-1006)

“... **alpha-2 adrenergic agonist drugs** as a class are also considered to be **strong vasoconstrictors**.”

2005
Desco
(EX-1131)

“**Alpha-2 adrenergic agonist drugs**, as a class, are also considered to have a **strong effect as vasoconstrictors**.”

2007
Hong
(EX-1064)

“. . . [T]opical **brimonidine** administration before strabismus surgery reduced intraoperative bleeding and postoperative subconjunctival hemorrhage in adult patients, and is as **effective and as powerful** as the well-known **vasoconstrictor** phenylephrine.

'245 Petition (Paper 2), 36-39; '600 Petition (Paper 2), 37-41;
EX-1014 (Galanis Decl.), ¶ 44

Patent Owner and Patent Owner's Experts Admit Brimonidine Was a Known Vasoconstrictor

'245 Patent

category of a adrenergic receptor agonists. It is a known property of all a adrenergic receptor agonists, including brimonidine, to cause vasoconstriction. However, known

EX-1001 ('245 Patent), 2:7-9

PO's Expert: Dr. Donnenfeld

Q. Okay. And would you agree that as of 2002, brimonidine, this alpha-2 agonist, was known to be a strong vasoconstrictor?

A. Yes.

EX-2009 (PI Hearing Vol. 1), 80:24-81:1

'245 Reply (Paper 58), 7-10; '600 Reply (Paper 55), 2-5

A POSA Would Have Been Motivated to Use Low Concentrations of Brimonidine to Reduce Eye Redness

GIL (EX-1004)

For ophthalmic application, preferably solutions are prepared typically containing from about 0.01% to about 0.5% of active ingredient, and a physiological saline solution as a major vehicle. The pH of such ophthalmic solutions should

following radial keratotomy surgery. One hundred and twenty-four male and female subjects, 21 to 45 years of age, undergo routine, elective, unilateral radial keratotomy for the correction of myopia and brimonidine is administered as a 0.03% ophthalmic solution.

A dose range of an ophthalmic formulation of brimonidine (0.01% to 0.5% for instance) as well as a vehicle is filled into the chamber and the resultant nerve traffic from the cornea is recorded. In this way the effects of brimonidine on ocular

EX-1004 (Gil), 3:63–66, 4:48–52, 5:31–34

DEAN (EX-1007)

tor in vessels in the back of the eye. While brimonidine is a relatively safe compound it has been shown to cause the side effects of sedation and ocular hyperemia in an allergic like reaction in some patients. These side effects are thought to be due to the relatively high concentration of the drug administered topically. The sedation like side effects are believed to be caused by the drug crossing the blood brain barrier and triggering the sedative effects. The mechanism by which brimonidine causes hyperemia is not well understood. It is likely that the frequent instillation of relatively high drug concentrations causes this side effect. Thus, lowering the overall dose of brimonidine while maintaining IOP control would be advantageous.

1.0%–2.0% by weight, preferably 1.0% by weight. Brimonidine will normally be contained in the formulations at concentrations of 0.01%–0.2% by weight, preferably 0.05%–0.2% by weight. For these formulations 1–2 drops

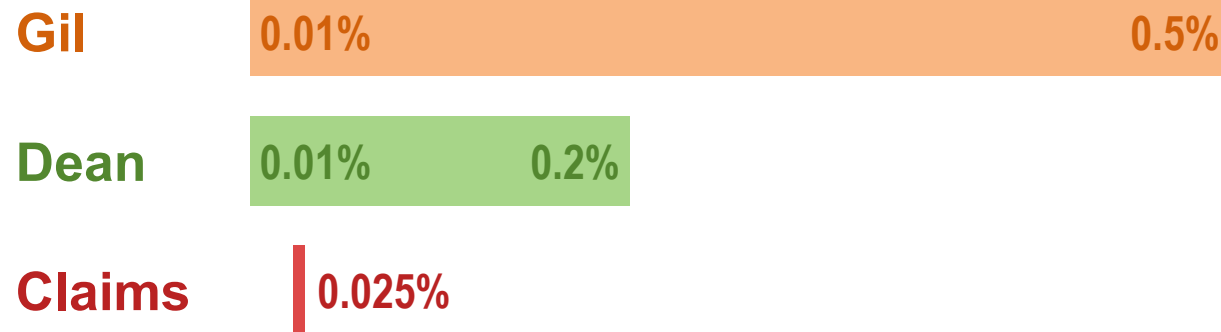
EX-1007 (Dean), 2:33–50, 5:20–23.

The Prior Art Disclosed Brimonidine Concentration Ranges that Overlap with Claims



“A presumption of obviousness applies where a claimed range overlaps with a range disclosed in the prior art.”

UCB, Inc. v. Actavis Labs. UT, Inc., 65 F.4th 679, 689-90 (Fed. Cir. 2023)
(internal quotation marks and citation omitted)



'245 Petition (Paper 2), 44-55; '600 Petition (Paper 2), 42-47; '245 Reply (Paper 58), 13-16; '600 Reply (Paper 55), 9-11; EX-1014 (Galanis Decl.), ¶¶ 85-87

Determining the Optimal Concentration Is Routine

PO's Expert: Dr. Stamer

“They take a drug and they expose humans to different doses and look at both the therapeutic effects and the off-target effects. So that’s pretty standard in drug development.”

EX-1045 (Stamer Depo. Tr.), 24:13-25:7

PO's Witness: Dr. Gil

Q. Now, that process, that dose study finding process, that’s a routine part of pharmacology, right?

A. Yes, correct.

EX-2016 (PI Vol. 2), 142:10-12

the pain. Exact dosing data have not been determined but it is anticipated that a topical formulation having between 0.01% and 0.5% (weight/volume) of a brimonidine will provide relief from ocular pain. The determination of the effective dose for any selected compound is well within the skill of an ordinary skilled physician.

EX-1004 (Gil), 3:46-51

Brimonidine is preferably formulated as a topical ophthalmic solution with a pH of about 4.5–7.8. It will normally be contained in the formulation at a concentration of 0.01%–0.2% by weight, preferably 0.1%–0.2% by weight. Thus, for topical presentation 1–3 drops of these formulations would be delivered to the surface of the eye 1–4 times a day according to the routine discretion of a skilled clinician.

EX-1007 (Dean), 5:20-27

'245 Petition (Paper 2), 47; '600 Petition (Paper 2), 44-45; '245 Reply (Paper 58), 17; '600 Reply (Paper 55), 13; EX-1014 (Galanis Decl.), ¶ 85

A POSA Would Reasonably Expect Low Concentrations of Brimonidine to Reduce Redness

GIL (EX-1004)

the pain. Exact dosing data have not been determined but it is anticipated that a topical formulation having between 0.01% and 0.5% (weight/volume) of a brimonidine will provide relief from ocular pain. The determination of the effective dose for any selected compound is well within the skill of an ordinary skilled physician.

EX-1004 (Gil), 3:46-51

Efficacy is assessed by evaluation of pain intensity, pain relief, subjective global analgesic efficacy. Symptoms of ocular inflammation (burning/stinging, tearing, etc.) are also recorded.

EX-1004 (Gil), 4:62-65

Ocular responses characteristic of neurogenic inflammation, including redness and pupillary constriction, are also observed in rabbits following external stimuli. The ability of an ophthalmic solution of brimonidine at concentrations ranging from 0.01% to 0.5% to reduce the neurogenic response at 5, 10, 15, 30 and 60 minutes following administration is determined. Brimonidine is effective in reducing such neurogenic responses.

EX-1004 (Gil), 5:38-46

Federal Register (EX-1009)

minor eye irritation, that of redness. In its general discussion of ocular vasoconstrictors, the Panel stated that redness resulting from minor ocular irritation may be relieved by aqueous eye drops containing low concentrations of an ocular vasoconstrictor, which functions by constricting blood vessels underlying the surface of the eye that have dilated in response to noxious or irritating agents (45 FR 30033). The

EX-1009 (Federal Register), 9

'245 Petition (Paper 2), 44-46; '600 Petition (Paper 2), 42-44;
EX-1014 (Galanis Decl.), ¶¶ 75, 85-89

The Alphagan Labels Do Not Teach Away from Low Concentrations of Brimonidine

- Patent Owner argues “[t]he prior art taught that the minimum effective dose to reduce eye redness was about 0.2% brimonidine, which emanates From the FDA-approved Alphagan clinical studies.”

'600 & '245 PO Sur-Reply (Paper 68), 1

- + Patent Owner ignores the express teaching of Gil and Dean.
- + Patent Owner ignores that the Alphagan labels do not define conjunctival blanching, how it was measured, or who measured it.
- + Patent Owner ignores Hong.

'245 Petition (Paper 2), 44-50; '600 Petition (Paper 2), 42-47; '245 Reply (Paper 58), 13-20; '600 Reply (Paper 55), 9-16; EX-1064 (Hong), 1-2

Patent Owner Again Ignores the Express Teaching of Norden, Dean, and Gil



“Again, Patent Owner attempts to disregard the express teachings of Norden and Gil to assert that the art teaches away from using low-dose brimonidine. We are not persuaded that the Alphagan data rises to the level of teaching away.

Even considering the Alphagan data, however, Norden and Gill are still prior art for all that they teach. And, as explained above, we find that Norden and Gil teach the use of low-dose brimonidine to reduce eye redness.”

EX-1003 ('742 FWD), 59

'245 Petition (Paper 2), 44-50; '600 Petition (Paper 2), 42-47; '245 Reply (Paper 58), 9-16; '600 Reply (Paper 55), 6-11

The Alphagan Labels Provide Virtually No Information on Conjunctival Blanching

Alphagan 0.5%

ADVERSE REACTIONS

The most common adverse events reported in association with the use of ALPHAGAN® 0.5% in conjunction with ALT was transient conjunctival blanching in 50% of patients and upper lid retraction in 30% of patients.

EX-1067 (Alphagan 2001 Label), 4

Alphagan 0.2%

ADVERSE REACTIONS

Events occurring in approximately 3-9% of the subjects, in descending order included corneal staining/erosion, photophobia, eyelid erythema, ocular ache/pain, ocular dryness, tearing, upper respiratory symptoms, eyelid edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival blanching, abnormal vision and muscular pain.

EX-1067 (Alphagan 2001 Label), 9

Alphagan P

ADVERSE EVENTS

Adverse events occurring in approximately 10-20% of the subjects included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritis.

EX-1075 (Alphagan P), 17

The Alphagan Labels Provide Virtually No Information on Conjunctival Blanching

	Alphagan 0.5%	Alphagan 0.2%	Alphagan P (0.15%)
Condition	Post-operative IOP after ALT	Open-angle glaucoma or ocular hypertension	Open-angle glaucoma or ocular hypertension
Dosing	Single drop	Twice daily	Three times daily
Duration of Study	Three hours	Up to one year	Undisclosed
Terminology used	“Transient conjunctival blanching”	“Conjunctival blanching”	N/A
Blanching Defined?	No	No	No
Grading Scale	Not disclosed	Not disclosed	Not disclosed
Grading Scores	Not disclosed	Not disclosed	Not disclosed

²⁴⁵ Reply (Paper 58), 17-20; ⁶⁰⁰ Reply (Paper 55), 13-16; EX-1067 (Alphagan Label); Ex-1075 (Alphagan P Label)

Hong: A Single Drop of 0.15% Brimonidine “Is as Effective and As Powerful as the Well-Known Vasoconstrictor Phenylephrine.”

Brimonidine-purite 0.15% is a selective α 2-adrenergic agonist that has been widely used to lower intraocular pressure in glaucoma patients.⁴ It is also considered to have a vasoconstrictive property. There are some reports that the preoperative use of topical brimonidine can help reduce bleeding-related problems during laser in situ keratomileusis (LASIK) and cataract surgery.^{5,6} We determined whether the preoperative use of topical brimonidine reduces intraoperative bleeding and postoperative subconjunctival hemorrhage during strabismus surgery in adult patients, and compared its effect with the well-known strong vasoconstrictor phenylephrine.

EX-1064 (Hong), 1

A drop of brimonidine-purite 0.15% (42 eyes), phenylephrine 1% (38 eyes), or sodium hyaluronate 0.1% (38 eyes) was applied randomly to the eye(s) of each patient 15 minutes prior to strabismus surgery. All procedures were

EX-1064 (Hong), 1

In conclusion, topical brimonidine administration before strabismus surgery reduced intraoperative bleeding and postoperative subconjunctival hemorrhage in adult patients, and is as effective and as powerful as the well-known vasoconstrictor phenylephrine.

EX-1064 (Hong), 2

Patent Owner's Focus on Absolute Dosage Ignores the Claims, Specification, and Expert Testimony

- Patent Owner argues that a POSA would focus on the “amount” or “dose” of brimonidine administered, not the concentration.

'245 PO Sur-Reply (Paper 72) at 17-18

- + Patent Owner ignores that the claims and specification are silent on “amount” or “dose” of brimonidine administered.
See EX-1147 (Galanis Reply), ¶ 8-9
- + Patent Owner ignores that the prior art always discloses concentration, sometimes discloses number of drops, and never discloses drop volume. See EX-1147 (Galanis Reply), ¶ 57
- + Patent Owner ignores that there is variability in drop volume that impacts absolute dosage.
See EX-1147 (Galanis Reply), ¶ 56; EX-1069 (Sklubalova 2005); EX-1070 (Sklubalova 2006)

'245 Reply (Paper 58), 1-5, 16-17

Key Disputed Issues

1. Whether the -00142 FWD precludes Patent Owner from relitigating issues already decided by the Board?
2. Whether claim 1 of the '245 patent is limited to a “single drop” of brimonidine?
3. Whether the prior art motivated a POSA to use low concentrations of brimonidine with a reasonable expectation of success?
 - Whether the Alphagan Labels teach away from using low concentrations of brimonidine to reduce eye redness?
 - Whether Gil and Norden directed a POSA to use high “doses” of brimonidine?
- 4. Whether the result of reducing redness was taught by the prior art or otherwise inherent?**
5. Whether the use of the preservative, benzalkonium chloride, was obvious?
6. Whether Gil is the closest prior art to the challenged claims?
7. Whether there is a nexus between the invention claimed and LUMIFY's sales?

The Result of Reduced Eye Redness Was Taught by the Prior Art and Is Inherent

- The '245 patent admits that the invention was the “discovery” that low concentrations of brimonidine “achieve vasoconstriction with significantly reduced hyperemia”:

and methods for inducing vasoconstriction. One of the key discoveries of the present invention lies in using low doses of highly selective α -2 adrenergic receptor agonists to achieve vasoconstriction with significantly reduced hyperemia.

EX-1001
(’245 Patent), 2:52-55

- In any event, the prior art taught low concentrations of brimonidine would be effective in reducing hyperemia:

We find Norden and Gil also teach a composition “consisting essentially of brimonidine,” as the references teach or suggest that brimonidine alone is effective in reducing eye redness. *Id.*; Ex. 1006, 4;

EX-1003
(’742 FWD), 54

’245 Petition (Paper 2), 37-39; ’600 Petition (Paper 2), 37-39; ’245 Reply (Paper 58), 11-17, 20; ’600 Reply (Paper 55), 6-12

Key Disputed Issues

1. Whether the -00142 FWD precludes Patent Owner from relitigating issues already decided by the Board?
2. Whether the claims are limited to the administration of a “single drop” of brimonidine?
3. Whether the prior art motivated a POSA to use low concentrations of brimonidine with a reasonable expectation of success?
 - Whether the Alphagan Labels teach away from using low concentrations of brimonidine to reduce eye redness?
 - Whether Gil and Norden directed a POSA to use high “doses” of brimonidine?
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6. Whether Gil is the closest prior art to the challenged claims?
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BAK Was and Remains a Widely Used Preservative in Over-the-Counter Eye Drops

APPROVED BEFORE 2008

	Over-the-Counter Ophthalmic Solution	Company
1	Zaditor (ketotifen, ketotifen fumerate)	Alcon
2	Naphcon-A (naphazoline hydrochloride, pheniramine maleate)	Alcon
3	Alaway (ketotifen)	Bausch & Lomb
4	Opcon (naphazoline, pheniramine maleate)	Bausch & Lomb
5	Advanced Eye Relief Dry Eye Lubricant Eye Drops (glycerine, propylene glycol)	Bausch & Lomb
6	Visine Dry Eye Relief (polyethylene glycol)	Johnson & Johnson
7	Clear Eyes Redness Relief (glycerine, naphazoline hydrochloride)	Preferred Pharmaceuticals Inc.
8	Clear Eyes Maximum Redness Relief (glycerine, naphazoline hydrochloride)	Prestige Consumer Health Care
9	Clear Eyes Maximum Itchy Eye Relief (glycerine, naphazoline hydrochloride, zinc sulfate)	Prestige Consumer Health Care
10	Clear Eyes Triple Action (polyvinyl alcohol, povidone, tetrahydrozoline hydrochloride)	Prestige Consumer Health Care
11	Clear Eyes Cooling Redness Relief (glycerin, naphazoline hydrochloride)	Prestige Consumer Health Care
12	Clear Eyes Cooling Comfort Itchy Eye Relief (glycerin, naphazoline hydrochloride, zinc sulfate)	Health Consumer Health Care
13	Rohto Cool Max (naphazoline hydrochloride, polysorbate 80)	The Mentholatum Company
14	Rohto Cool (naphazoline hydrochloride, polysorbate 80)	The Mentholatum Company
15	Rohto Digi-Eye (hypromellose, tetrahydrozoline hydrochloride)	The Mentholatum Company

APPROVED AFTER 2008

	Ophthalmic Product	Preservative	Year of Approval
1	Xiidra	Not preserved	2016
2	Rhopressa	BAK; 150 ppm	2017
3	Vyzulta	BAK; 200 ppm	2017
4	Oxervate	Not preserved	2018
5	Rocklatan	BAK; 200 ppm	2019
6	Zerviate	BAK; 100 ppm	2019
7	Eysuvis	BAK, 100 ppm	2020
8	Lastacraft	BAK; 50 ppm	2021
9	Verkazia	Cetalkonium chloride	2021
10	Vuity	BAK; 75 ppm	2021
11	Iheezo Gel	Not preserved	2022
12	Omlonti	BAK; 50 ppm	2022
13	Mydcombi	BAK; 100 ppm	2023
14	Xdemvy	Potassium sorbate	2023

'245 EX-1077-EX-1083; EX-1013 (Laskar Decl.), ¶¶ 54-58

Key Disputed Issues

1. Whether the -00142 FWD precludes Patent Owner from relitigating issues already decided by the Board?
2. Whether claim 1 of the '245 patent is limited to a “single drop” of brimonidine?
3. Whether the prior art motivated a POSA to use low concentrations of brimonidine with a reasonable expectation of success?
 - Whether the Alphagan Labels teach away from using low concentrations of brimonidine to reduce eye redness?
 - Whether Gil and Norden directed a POSA to use high “doses” of brimonidine?
4. Whether the result of reducing redness was taught by the prior art or otherwise inherent?
5. Whether the use of the preservative, benzalkonium chloride, was obvious?
- 6. Whether Gil is the closest prior art to the challenged claims?**
7. Whether there is a nexus between the invention claimed and LUMIFY's sales?

Gil Is the Closest Prior Art



“Contrary to Patent Owner’s assertion, we are not persuaded that the closest prior art is Visine and the prior commercial redness relievers, which do not contain brimonidine at all.

As explained above, Gil discloses the use of low-dose 0.03% brimonidine and that low-dose brimonidine is effective in reducing ocular responses characteristic of neurogenic inflammation, such as redness.”

EX-1003 ('742 FWD), 59

'245 Reply (Paper 58), 22-24; '600 Reply (Paper 55), 20

Gil Is the Closest Prior Art Because It Teaches the Use of Low Concentrations of Brimonidine



In cases where the patent claims the use of a chemical compound for a method of treatment, the closest prior art is not simply “another . . . drug on the market” for the same treatment, but is instead the most “structurally similar compound.”

Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc., 752 F.3d 967, 976-78 (Fed. Cir. 2014)

Key Disputed Issues

1. Whether the -00142 FWD precludes Patent Owner from relitigating issues already decided by the Board?
2. Whether claim 1 of the '245 patent is limited to a “single drop” of brimonidine?
3. Whether the prior art motivated a POSA to use low concentrations of brimonidine with a reasonable expectation of success?
 - Whether the Alphagan Labels teach away from using low concentrations of brimonidine to reduce eye redness?
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4. Whether the result of reducing redness was taught by the prior art or otherwise inherent?
5. Whether the use of the preservative, benzalkonium chloride, was obvious?
6. Whether Gil is the closest prior art to the challenged claims?
- 7. Whether there is a nexus between the invention claimed and LUMIFY's sales?**

There Is No Nexus Between the Claimed Invention and Lumify's Success

The '245 patented methods differ materially from how the Board construed the '742 patented invention. Neither party disputes that the '245 patent claims are

'245 POR (Paper 25), 5

The '600 patented methods differ materially from how the Board construed the '742 patented invention. Neither party disputes that the '600 patent claims are

'600 POR (Paper 27), 6

Lumify's success directly ties to the claimed invention: redness reduction generated by using a single drop of only 0.025% brimonidine. Lumify's clear and consistent messaging focuses on its approved redness-relieving indication using this specific concentration. Jarosz ¶¶137; Ferris ¶¶11-13. And market research substantiates that its success is both directly and indirectly tied to the invention of the '245 patent. Ferris ¶¶14-20.

'245 POR (Paper 25), 60

Lumify's success directly ties to the claimed invention: redness reduction generated by using a low dose of only brimonidine, applied as a single eyedrop with a concentration of 0.025%. Lumify's clear and consistent messaging focuses on its approved redness-relieving indication using this specific low dose of brimonidine. Jarosz ¶¶138; Ferris ¶¶11-13. And market research substantiates that its success is both directly and indirectly tied to the invention of the '600 patent. Ferris ¶¶14-20.

'600 POR (Paper 25), 56

'245 Reply (Paper 58), 25-26; '600 Reply (Paper 55), 20-24

Patent Owner Has Already Tried to Establish a Nexus Through the Use of Low Concentration Brimonidine

Here, Patent Owner repeatedly relies on the use of “low-concentration brimonidine” as the reason for Lumify’s success. Patent Owner claims “[Lumify’s] success is directly tied to . . . redness reduction using low-dose brimonidine.” PO Resp. 68. And Patent Owner contends that “the claimed use of low-concentration brimonidine has led to a cascade of real-world benefits for Lumify users,” which has resulted in industry praise and licensing of the product. *Id.* at 68–69; *see also id.* at 70 (asserting successful licensing is “attributable to the patented invention”).

EX-1003 ('742 FWD), 66

Despite Patent Owner’s assertions to the contrary, we agree with Petitioner that the use of low-dose brimonidine was known in the art. Namely, we find Gil discloses low-dose 0.03% brimonidine and teaches that low-dose brimonidine is effective in reducing ocular responses characteristic of neurogenic inflammation, such as vasodilation and redness. Ex. 1004, 1:11–13, 40–43, 5:38–45. Thus, we find that Patent Owner’s evidence of industry praise, commercial success, licensing, and copying is not probative of nonobviousness (or at best carry little weight), as Lumify’s success was not the result of the novel features of the claim. *See Ormco*, 463 F.3d at

EX-1003 ('742 FWD), 66

'245 Reply (Paper 58), 25-26; '600 Reply (Paper 55), 20-23

Other Disputed Issues

Prior Art Need Not Be Directed to Specific Subject Matter of Challenged Claims



“To the extent arriving at the claimed shapes would require a combination of elements, the motivation to combine analysis does not require the Board to seek out precise teachings directed to the specific subject matter of the challenged claim, because the Board can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.”

Laitram, LLC v. Ashworth Bros., Inc., 2023 WL 3449148, at *8 (Fed. Cir. May 15, 2023)
(quotation marks omitted)

'245 Reply (Paper 58), 7-10; '600 Reply (Paper 55), 2-5; EX-1147 (Galanis Reply) ¶¶ 30-33

Prior Art Need Not Be Directed to Specific Subject Matter of Challenged Claims



“Courts generally take an expansive view of what constitutes analogous art... It is enough that the prior art reference falls within the relevant field of endeavor of the patent-in-suit.”

Netflix, Inc. v. DivX, LLC, 80 F.4th 1352, 1359 (Fed. Cir. 2023) (cleaned up)

A reference that “is from the same field of endeavor” counts as relevant prior art “regardless of the problem addressed.”

Corephotonics, Ltd. v. Apple Inc., 84 F.4th 990, 1004 (Fed. Cir. 2023)

'245 Reply (Paper 58), 7-10; '600 Reply (Paper 55), 2-5; EX-1147 (Galanis Reply) ¶¶ 30-33

Norden Established that Brimonidine Was Effective in Reducing Eye Redness

- Norden discloses data from a clinical study in which brimonidine was administered prophylactically to patients undergoing LASIK
 - Brimonidine reduced hyperemia compared to placebo

Although two independent clinical studies have shown that topical brimonidine does not significantly alter posterior segment hemodynamics^{2,3}, the alpha-2 adrenergic agonist drugs as a class are also considered to be strong vasoconstrictors.⁴ There are many anecdotal reports that the use of topical brimonidine before laser in situ keratomileusis (LASIK) can help prevent bleeding-related problems in the anterior segment, and some refractive surgeons now administer it prophylactically to reduce subconjunctival hemorrhage and improve the post-operative appearance.

EX-1006 (Norden), 468

RESULTS: Subconjunctival hemorrhage was observed in 22 of 61 eyes (36.1%). Three of these 22 eyes (13.6%) received prophylactic brimonidine; the remaining 19 eyes with subconjunctival hemorrhage (86.3%) did not receive brimonidine ($P<.0001$). All but three eyes had some hyperemia; however, the amount of hyperemia was lower in the brimonidine group ($P<.0001$). Bleeding from the superior micropapilla occurred in four of 61 eyes (6.6%). One of these four eyes received brimonidine. There was one case of flap slippage in a non-brimonidine eye with a nasal hinge; no flap striae were observed after repositioning.

CONCLUSION: This study suggests that brimonidine administered before LASIK may significantly reduce subconjunctival hemorrhage and reduce the amount of hyperemia. [*J Refract Surg* 2002;18:468-471]

EX-1006 (Norden), 468

The Board Should Reject Patent Owner's Criticisms of Norden

- Patent Owner argues that Norden is a “trauma model” and meant “micro-vessel hemorrhage” when it referred to “hyperemia.”

'245 POR (Paper 25), 6-7, 15-17, 21-22;

'600 POR (Paper 27), 16-19, 20

- + The specification of the '245 patent contradicts Patent Owner that a POSA would not be motivated by LASIK results.
- + Patent Owner fails to address that Norden observed patients under high magnification using “slit-lamp microscopy.”
- + Patent Owner fails to substantiate its expert's opinion that “hyperemia” is Norden refers to “micro-vessel hemorrhage.”

'245 Reply (Paper 58), 9; '600 Reply (Paper 55), 4; EX-1147 (Galanis Reply), ¶¶ 32, 35-41; EX-1001 ('245 Patent), 7:42-44, 10:36-38; 12:11-41; 13:5-8; 21:39-40

The Claims and Specification of the '245 Patent Confirm that the Cause of Eye Redness Is Irrelevant

The “Present Invention” Includes Use of Brimonidine in Ocular Surgery

Methods of Treatment and Compositions Thereto

The surprising and unexpected discoveries of the present invention potentially have application in treating a nasal congestion and a variety of ocular and pulmonary conditions.

b) Ocular Conditions

Ocular conditions include, but are not limited to, red eye, including chronic red eye; ocular vascular congestion after Lasik surgery; prophylactic intraoperative and postoperative reduction of hemorrhage and hyperemia after Lasik surgery; preoperative hemorrhage and hyperemia prophylaxis prior to Lasik surgery; prophylactic diabetic retinopathy; macular

EX-1001 ('245 Patent), 12:11-41

redness of an eye. The methods and compositions of the present invention can be used with other ocular procedures, particularly cataract surgery, retinal surgery, pterygiae removal, and motility surgery. At the concentration range

EX-1001 ('245 Patent), 13:5-9

The '245 Claims Cover Ocular Hyperemia Caused by “Trauma”

1. A method for reducing eye redness in a human subject having ocular hyperemia, consisting of topically administering to an eye of said human in need of said reduction of eye redness a composition in the form of an ocular drop consisting of 0.025% weight by volume brimonidine as the sole active ingredient, and one or more non-therapeutic components including benzalkonium chloride, wherein the ocular drop has a pH between 5.5 to 6.5, wherein the ocular hyperemia is reduced.

EX-1001 ('245 Patent), 22:36-44

'245 Reply (Paper 58), 9; '600 Reply (Paper 55), 4;
EX-1147 (Galanis Reply) ¶¶ 32, 35-41

A POSA Would Understand that Norden Assessed Hyperemia Under Magnification 5 Minutes Postoperatively

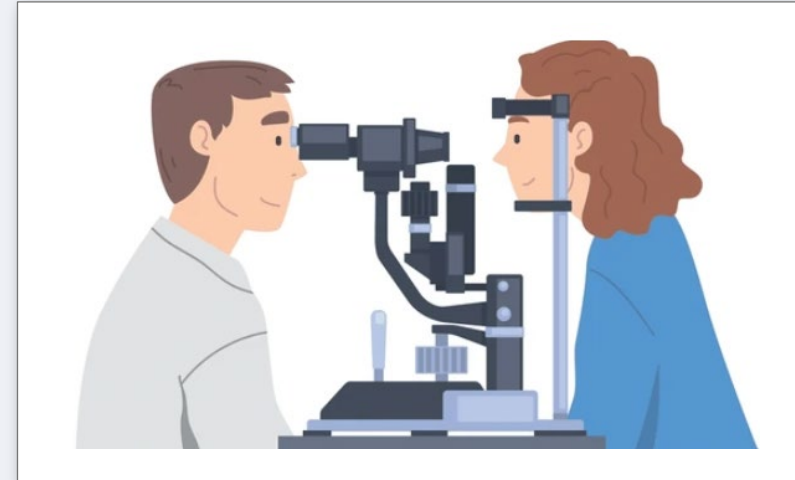
Norden (EX-1006)

Slit-lamp microscopy was performed 5 minutes postoperatively. All patients then received a copious

remained in place until the next day. For purposes of this study, eyes were examined again the next morning. The postoperative medication regimen

The operating surgeon (R.N.) performed the post-operative examinations and recorded the amount of subconjunctival hemorrhage, hyperemia, bleeding from the micropannus, and flap slippage/wrinkling.

Slit Lamp Microscopy



PO's Expert: Dr. Noecker ('742 IPR)

170. First, Norden 2002 measured redness only once, five minutes after the LASIK surgery. See EX-1006 (Norden 2002) at 5. At least two measurements,

EX-1129,
¶ 170

'245 Reply (Paper 58), 9, 11-13; '600 Reply (Paper 55) 4, 6-9; EX-1147 (Galanis Reply), ¶¶ 35-44

There Is No Support that “Hyperemia” Refers to “Micro-Vessel Hemorrhage” in Norden

PO's Expert: Dr. Donnenfeld

Q. Have you cited any references in your declaration to support that clinicians performing LASIK used the term hyperemia in the way you've described?

A. I'm not aware of any articles that describe this.

EX-1054 (Donnenfeld PI Dep. Tr.), 113:13-1824:13-25:7.

PO's Expert: Dr. Noecker

Q. Were you aware that microvessel hemorrhage was caused by Lasik surgery prior to be told that by Dr. Donnenfeld?

A. He kind of clarified that.

EX-1047 (Noecker Dep. Tr.), 96:1-4

'245 Reply (Paper 58), 9, 11-13; '600 Reply (Paper 55) 4, 6-9; EX-1147 (Galanis Reply), ¶¶ 35-44

The Literature Accepted that Norden Evaluated Hyperemia or “Ocular Redness”



Aslanides
2005

Norden⁵ conducted a double-masked study and concluded that α -agonists applied topically may decrease hyperemia and subconjunctival hemorrhage after LASIK surgery significantly, without increasing the risk of flap slippage.

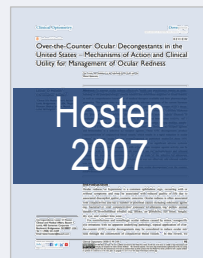
Aslanides 2005 (EX-1103), 1;
Aslanides 2006 (EX-1063), 4



Desco
2005

monidine on flap adherence in LASIK patients and Norden (6) concluded that brimonidine administered before LASIK may significantly reduce the amount of hyperemia and improve the postoperative appearance without inducing flap slippage. Nowadays many refractive

Desco (EX-1131), 1



Hosten
2007

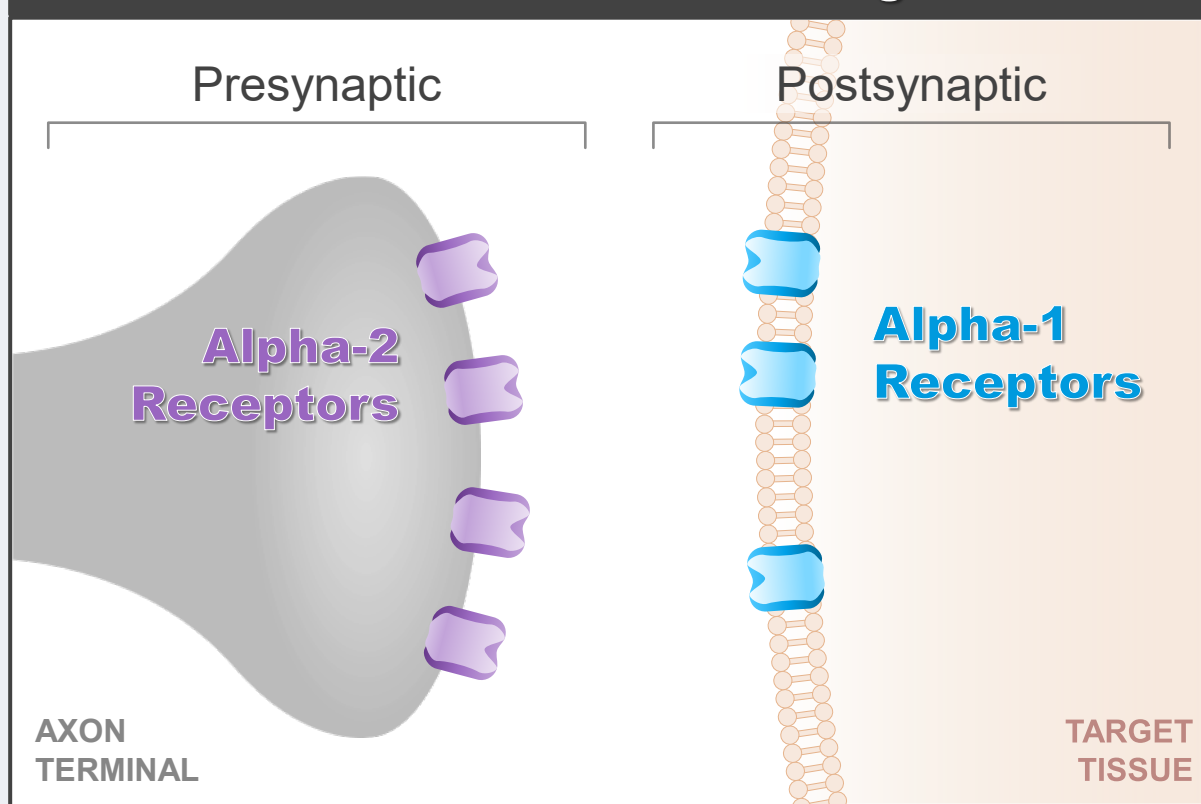
facial erythema of rosacea. Off-label use of brimonidine prior to laser in situ keratomileusis (LASIK) and pterygium surgery demonstrated that brimonidine was effective at reducing subconjunctival hemorrhage and ocular redness at prescription ophthalmic strength and lower

Hosten
(EX-1144), 3

'245 Reply (Paper 58), 9, 11-13; '600 Reply (Paper 55) 4, 6-9;
EX-1147 (Galanis Reply), ¶ 38

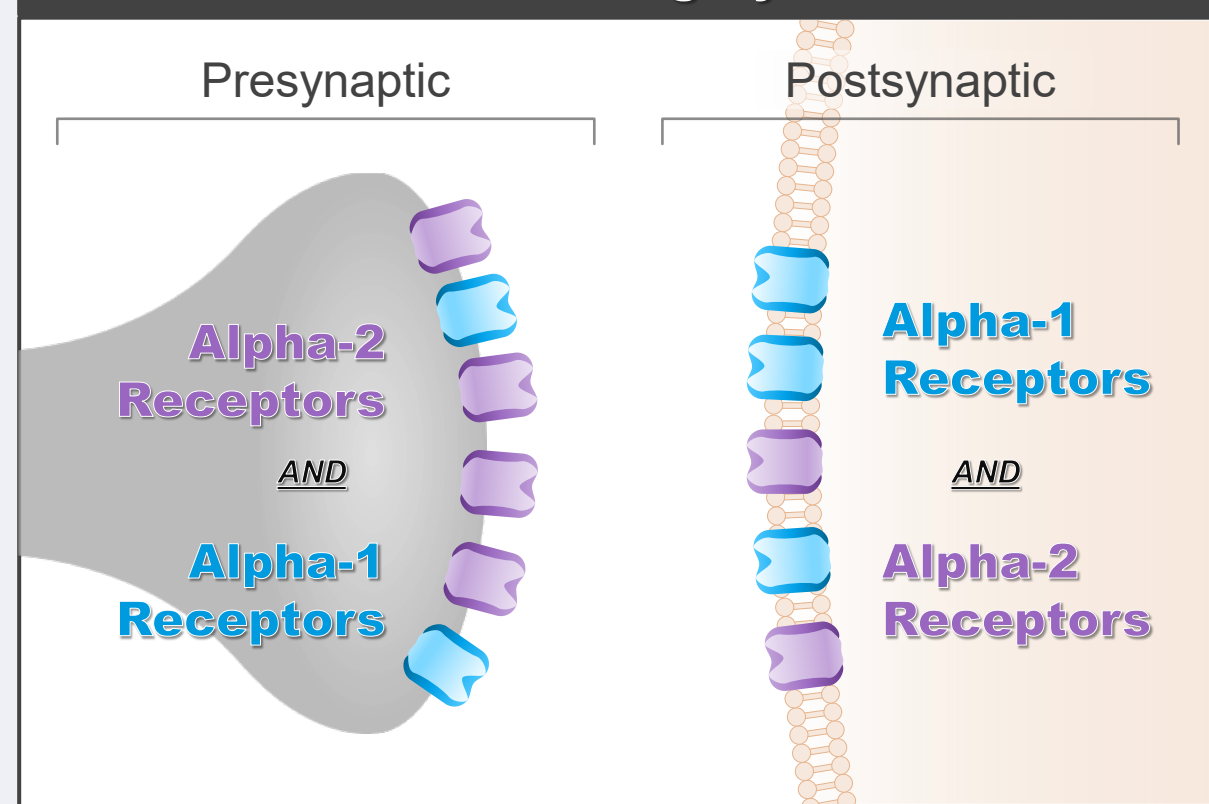
Patent Owner's Alpha-1 Argument Depends on Outdated Science

The Old Understanding



DIRECTION OF SIGNAL

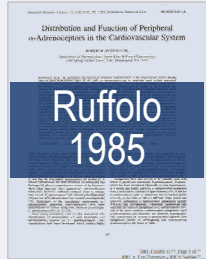
Understanding By 2008



DIRECTION OF SIGNAL

'245 Petition (Paper 2), 21-24;
'600 Petition (Paper 2), 22-25;
EX-1012 (Dana Decl.), ¶ 38-45

A POSA Would Have Understood that Vasoconstriction Could Be Mediated by Both Alpha-1 and Alpha-2 Receptors

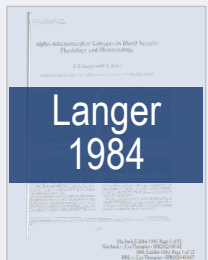


holds true. However, sufficient evidence exists to indicate that not all α_1 -adrenoceptors are located postsynaptically [34] and not all α_2 -adrenoceptors are located presynaptically [73]. Particularly in the vasculature, postsynaptic α_2 -adrenoceptors mediating vasoconstriction have been demonstrated to coexist along with 'classical' postsynaptic α_1 -adrenoceptors [15, 16, 21, 72].

EX-1157
(Ruffolo), 1

Postsynaptically, in the vascular smooth muscle, the α_1 -adrenoreceptor is the predominant receptor mediating vasoconstriction, but there are also postsynaptic α_2 -adrenoreceptors which mediate vasoconstriction in arterial as well as in venous vascular smooth muscle (Fig. 1, Tables 3,4).

Langer (EX-1050), 3



'245 Petition (Paper 2), 21-24; '600 Petition (Paper 2) 22-25; EX-1012 (Dana Decl.), ¶¶ 38-45; see also EX-1051 (Duka), 1; EX-1158 (Khan); EX-1052 (Phillip), 6

The Board Should Reject Patent Owner's pH Arguments

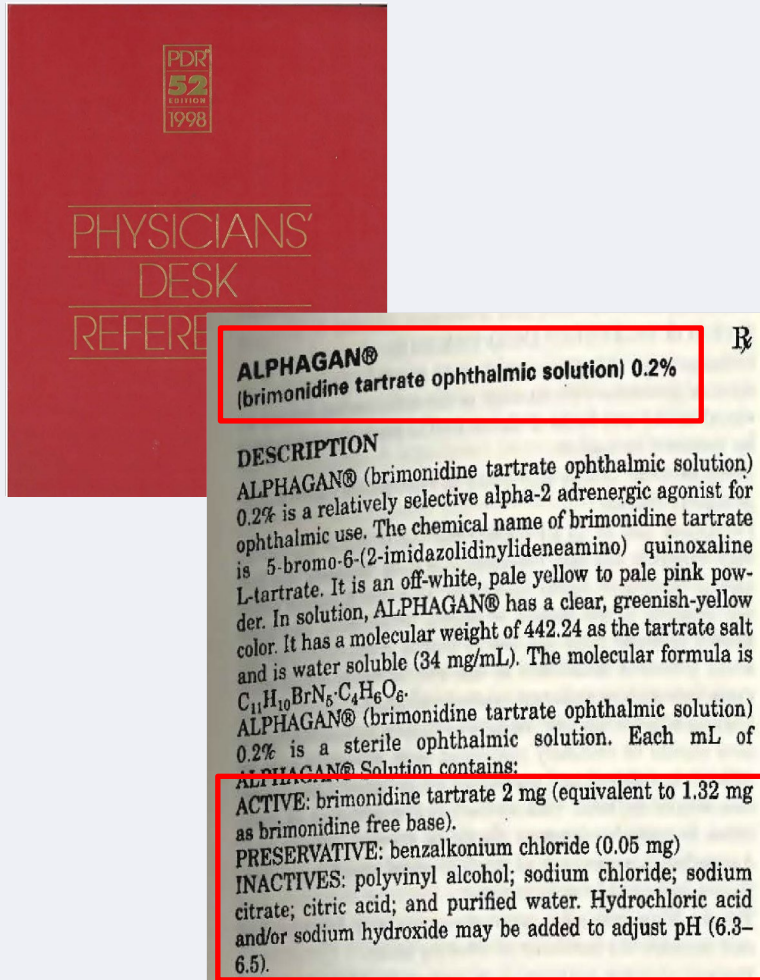
- Patent Owner argues that a POSA would not have used BAK or the claimed pH when creating an ophthalmic brimonidine product.

'245 POR (Paper 25), 38-39;
'600 POR (Paper 27), 43-44

- + Brimonidine had been successfully formulated with BAK, and BAK continues to be used as a preservative.
- + Brimonidine had been successfully formulated at the claimed pH.
- + A POSA would have looked to Alphagan as a reference.

'245 Petition (Paper 2), 51-53; '600 Petition (Paper 2), 22-25; EX-1013 (Laskar Decl.) ¶¶ 36-50; EX-1014 (Galanis Decl.), ¶¶ 92-96

Alphagan Was Formulated with BAK and pH 5.5-6.5



ALPHAGAN®
(brimonidine tartrate ophthalmic solution) 0.2%

ACTIVE: brimonidine tartrate 2 mg (equivalent to 1.32 mg as brimonidine free base).
PRESERVATIVE: benzalkonium chloride (0.05 mg)
INACTIVES: polyvinyl alcohol; sodium chloride; sodium citrate; citric acid; and purified water. Hydrochloric acid and/or sodium hydroxide may be added to adjust pH (6.3–6.5).

EX-1008 (Alphagan PDR), 3

