(19) DANMARK

(10) DK/EP 2667877 T3

(12) Oversættelse af europæisk patentskrift

Patent- og Varemærkestyrelsen

(51) Int.Cl.: *A 61 K 31/568 (2006.01)* *A 61 K 9/00 (2006.01)* *A 61 K 31/5685 (2006.01)*
A 61 K 31/569 (2006.01) *A 61 K 45/06 (2006.01)* *A 61 K 47/44 (2017.01)*
A 61 P 27/02 (2006.01)

(45) Oversættelsen bekendtgjort den: **2018-06-14**

(80) Dato for Den Europæiske Patentmyndigheds bekendtgørelse om meddelelse af patentet: **2018-03-07**

(86) Europæisk ansøgning nr.: **12702934.6**

(86) Europæisk indleveringsdag: **2012-01-25**

(87) Den europæiske ansøgnings publiceringsdag: **2013-12-04**

(86) International ansøgning nr.: **US2012022508**

(87) Internationalt publikationsnr.: **WO2012103186**

(30) Prioritet: **2011-01-26 US 201161436274 P**

(84) Designerede stater: **AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR**

(73) Patenthaver: **ALLERGAN, INC., 2525 Dupont Drive, Irvine CA 92612, USA**

(72) Opfinder: **TROGDEN, John T., 18671 Cerro Villa Drive, Villa Park, California 92861, USA**
SALAMEH, Adnan K., 23 Fairside, Irvine, California 92614, USA
PUJARA, Chetan P., 6 Wheeler, Irvine, California 92620, USA
GORE, Anuradha V., 8 Del Rey, Irvine, California 92612, USA
GIYANANI, Jaya, 25 Palatine, Apt 254, Irvine, California 92612, USA

(74) Fuldmægtig i Danmark: **Plougmann Vingtoft A/S, Rued Langgaards Vej 8, 2300 København S, Danmark**

(54) Benævnelse: **ANDROGENSAMMENSÆTNING TIL BEHANDLING AF OFTALMISK TILSTAND**

(56) Fremdragne publikationer:
WO-A1-94/20598
WO-A2-2008/070728
DE-A1- 3 514 724
US-A- 5 958 912
US-A- 6 093 706
US-A1- 2003 109 508
US-A1- 2003 144 635
US-A1- 2006 210 645
US-A1- 2008 045 486
Anonymous: "A Single-Center, Double-Masked, Randomized, VehicleControlled Study to Evaluate the Safety and Efficacy ofTestosterone 0.03% Ophthalmic Solution Compared toVehicle for the Treatment of Meibomian GlandDysfunction", INTERNET , 17 September 2008 (2008-09-17), XP055249568, Retrieved from the Internet: URL:https://clinicaltrials.gov/archive/NCT 00755183/2008_09_17 [retrieved on 2016-02-12]

Fortsættes ...

R M Schiffman: "IOVS | A Multi-Center, Double-Masked, Randomized, Vehicle-Controlled, Parallel Group Study to Evaluate the Safety and Efficacy of Testosterone Ophthalmic Solution in Patients With Meibomian Gland Dysfunction", INTERNET , May 2006 (2006-05), XP055249564, Retrieved from the Internet: URL:http://iovs.arvojournals.org/article.a spx?articleid=2395393 [retrieved on 2016-02-12]
Christopher Glenn: "New Thinking Spurs New Products", INTERNET , 15 February 2003 (2003-02-15), Retrieved from the Internet: URL:https://www.reviewofophthalmology.com/ article/new-thinking-spurs-new-products [retrieved on 2017-06-30]
Jennifer Byrne: "Dry eye treatment: a growing priority in the future of optpmetry", INTERNET , November 2004 (2004-11), Retrieved from the Internet: URL:https://www.healio.com/optometry/corne a-external-disease/news/print/primary-care -optometry-news/%7B1497ff3e-30f6-4c15-9594 -9af71a7364f2%7D/dry-eye-treatment-a-growi ng-priority-in-the-future-of-optometry [retrieved on 2017-06-30]

DESCRIPTION

BACKGROUND

[0001] Blepharitis is a disorder of the meibomian glands, which produce the lipid component of tear film. Both the upper and lower eye lids contain 30-40 glands, located beneath the skin. The glandular pores open just behind the base of the eye lashes on the eye lid margin. With blepharitis, the glands become inflamed and the pores become blocked. Symptoms of blepharitis include eye irritation, soreness, redness and an accumulation of matter on the eyelids. Patients may also experience dry eye as well. As a result of these symptoms, blepharitis is commonly misdiagnosed as conjunctivitis or dry eye.

[0002] In certain cases, a local androgen deficiency can cause blepharitis. Topical compositions containing an androgen would be desirable for the treatment of blepharitis.

[0003] In Investigative Ophthalmology & Visual Science May 2006, Vol.47, 5608, Schiffman et al. evaluated the safety and efficacy of a testosterone ophthalmic solution compared with a vehicle in patients with meibomian gland dysfunction. This study was a multicenter, randomized, double-masked, vehicle-controlled, parallel-group study. Patients with meibomian gland dysfunction and overall ocular discomfort score ≥ 1 and meibomian gland secretion quality score ≥ 2 at baseline were randomized to treatment with testosterone ophthalmic solution (0.01, 0.03, or 0.1%) or vehicle for 6 months. The authors conclude that treatment of meibomian gland dysfunction patients with 0.03% testosterone for 6 months is safe, and may improve the quality of meibomian gland secretions and reduce ocular discomfort.

[0004] Christopher Glenn: "New Thinking Spurs New Products", 15 February 2003 (2003-02-15), Retrieved from the Internet: URL:https:// www.reviewofophthalmology.com/article/new-thinking-spurs-new-products, discloses Refresh Endura, which contains castor oil, for the treatment of meibomian gland dysfunction, such as blepharitis.

BRIEF SUMMARY

[0005] The disclosure provides compositions for use in a method for treating one or more ocular conditions.

[0006] In one embodiment, a composition for use in a method for treating an ocular condition is provided comprising a physiologically effective amount of an androgen which is testosterone and castor oil, wherein said composition is suitable for topical administration to an eye.

[0007] In another embodiment, a composition for use in a method for treating an ocular condition resulting from an androgen deficiency is disclosed. The method 18591 PCT (AP)

comprises administering an effective amount of an ophthalmic composition comprising a physiologically effective amount of an androgen which is testosterone and castor oil, wherein said composition is suitable for topical administration to an eye, and wherein at least one symptom of the ocular condition is alleviated.

DETAILED DESCRIPTION

[0008] The disclosure provides an ophthalmic composition for use in a method for treating an ocular condition comprising a physiologically effective amount of an androgen which is testosterone and castor oil, wherein said composition is suitable for topical administration to an eye.

[0009] A composition for use in a method for treating an ocular condition associated with an androgen deficiency is also disclosed herein. The method comprises administering an effective amount of an ophthalmic composition comprising a physiologically effective amount of an androgen which is testosterone and castor oil, wherein said composition is suitable for topical administration to an eye, and wherein at least one symptom of the ocular condition is alleviated.

[0010] The compositions for use in a method for treating an ocular condition disclosed herein comprise an androgen which is testosterone. In some aspects, the term "androgen" includes all testosterone and testosterone containing moieties, endogenous and synthetic, as well as isomers, analogues, esters, and combinations thereof. The androgen can be an endogenously produced steroidal androgen, which includes testosterone (i.e., (17β)-17-hydroxyandrost-4-ene-3-one), dihydrotestosterone (DHT), dehydroepiandrosterone, androstenedione, androstenediol, and androsterone. Further included are testosterone-containing moieties, for example, esters of testosterone, such as the cypionate, propionate, phenylpropionate, cyclopentylpropionate, isocarporate, enanthate, phenylactate, acetate, buciclate, heptanoate, caprate, isocaprate, and decanoate esters, and other synthetic androgens such as oxymetholone, 17α-methylnortestosterone, and 7-methylnortestosterone and its acetate ester.

[0011] The ocular condition can be any condition of an eye, eye lid, gland, or skin surrounding the eye resulting from a local or systemic androgen deficiency. In certain embodiments, the ocular condition is blepharitis. Androgen deficiency can occur for a variety of reasons, for instance, during menopause or as a result of the natural aging process. Androgen deficiency can be due to a disease or condition, such as Sjögren's syndrome.

[0012] The patient to be treated can be any mammal of any age, or gender. The mammal can be a human, dog, cat, sheep, or cow in need of treatment. In certain embodiments, the patient to be treated is a human, male or female.

[0013] A physiologically effective amount refers to an amount of a substance that is sufficient to achieve the intended purpose or effect. Various biological factors can influence the amount

required to be effective, for instance, age, gender, severity of the underlying condition, and overall health of the patient. As used herein, a dosage is considered effective if it prevents, reduces, or eliminates the symptoms associated with the ocular condition to be treated.

[0014] The androgen which is testosterone can be present in the ophthalmic compositions for use in a method for treating an ocular condition described herein in an amount of 0.001% to 5% by weight (w/w), or from 0.09% to 2% by weight, or from 0.01 % to 1.0% (w/w).

[0015] The disclosed compositions can be emulsions, solutions, suspensions, gels, ointments, occlusive films, or a sustained release films and they can be preserved or non-preserved formulations. The compositions can be formulated as eye drops, creams, ointments, and films that can be applied to an eye. The formulations can be administered to the eye, the upper eye lid, the lower eye lid, or a combination thereof. Topical administration of the compositions provides treatment at the site of the condition with minimal systemic levels of the medicament.

[0016] The present invention is defined in the appended claims. Subject matters which are not encompassed by the scope of the claims do not form part of the present invention. Listed in Table 1 are examples of formulation ingredients and exemplary concentrations. In the ophthalmic composition for use in a method for treating an ocular condition according to the invention, the lipophilic vehicle must comprise castor oil.

TABLE 1

Function	Ingredient	Composition (% w/w)
Active	testosterone	0.01 - 1.0
Thickener	carbomer, sodium carboxymethyl cellulose, methylcellulose, hydroxypropyl methylcellulose, polyvinyl alcohol, zanthan gum	0 - 3.0
Neutralizing Agent	sodium hydroxide, organic bases	0 - 2.0
Emulsifier	polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, POE-40-stearate, Pemulen ® and other polymeric emulsifiers.	0 - 2.0
Lipophilic Vehicle	castor oil, squalane, isostearyl isostearate, isopropyl myristate, , mineral oil, silicone oil, caprylic / capric triglycerides, cetyl alcohols, stearyl alcohols	0 - 80
Co-solvents	diethylene glycol monoethyl ether, propylene glycol, dipropylene glycol dimethyl ether, diethylene glycol, dipropylene glycol	0 - 80
Buffering Agent	sodium citrate dihydrate, boric acid, monosodium phosphate, monohydrate, sodium phosphate dibasic heptahydrate, sodium phosphate monobasic monohydrate	0 - 2
Tonicity Agent	Glycerin, erythritol, mannitol, potassium chloride, sodium chloride,	0 - 3

Function	Ingredient	Composition (% w/w)
Solubilizer	Cyclodextin, alpha-cyclodextrin, beta-cyclodextrin, gamma-cyclodextrin, hydroxypropyl-beta-cyclodextrin, Sulfobutyl ether-β-cyclodextrin (Captisol®)	0 - 10
Demulcent	carboxymethylcellulose sodium, hydroxypropyl methylcellulose hydroxyethyl cellulose, methylcellulose, polyvinyl alcohol, povidone, glycerin, propylene glycol, PEG 300, PEG 400	0 - 10
Preservative	benzalkonium chloride, PURITE®, and other ophthalmic preservatives	0 - 2.0
Plasticizer	Silicone oils, isostearyl alcohol, cetyl alcohol, glycerin	0 - 5.0
Occlusive Agent	silicone oils, petrolatum, waxes	0 - 80
Film Former	acrylate/octylacrylamide copolymer, poly(ethyl acrylate, methyl methacrylate), chitosan, polyvinyl alcohol, polyisobutylene, polyvinylpyrrolidone-vinyl acetate copolymer, silicon gum, polyvinylpyrrolidone, other sustained release polymeric films	0 - 10
Hydrophilic Vehicle	water	0 - 99

[0017] The emulsions of the disclosed compositions for use in a method for treating an ocular condition can be stabilized using one or more polyelectrolytes from the family of cross-linked polyacrylates, such as carbomers and PEMULEN® (Lubrizol). Pemulens are high molecular weight co-polymers of acrylic acid and a long chain alkyl methacrylate cross-linked with allyl ethers of pentaerythritol. They contain not less than about 52% and not more than about 62% of carboxylic acid groups. The viscosity of a neutralized 1.0% aqueous dispersion is between about 9,500 and about 26,500 centipoise. Additional emulsifiers include polysorbate-80, POE-40-Stearate, polysorbate-20, polysorbate 40, polysorbate-60, and a combination thereof in an amount of about 0% to about 4% or about 0.01 to about 2.0% by weight of the composition.

[0018] The composition for use in a method for treating an ocular condition comprises the lipophilic vehicle castor oil. Further lipophilic vehicles may also be comprised in the composition, such as, for example, squalane, diethylene glycol monoethyl ether, propylene glycol, isostearyl isostearate, isopropyl myristate, dipropylene glycol dimethyl ether, diethylene glycol, dipropylene glycol, mineral oil, silicone oil, caprylic/capric triglycerides, cetyl alcohols, stearyl alcohols, and a combination thereof. The lipophilic vehicle can be present in an amount of up to about 85%, or about 1% to about 50%, or about 2% to about 15% of the composition by weight.

[0019] The disclosed compositions for use in a method for treating an ocular condition can comprise a neutralizing agent such as sodium hydroxide and organic bases in an amount of

about 0 to about 2.5% by weight of the composition.

[0020] In certain embodiments, the composition for use in a method for treating an ocular condition may include a demulcent such as carboxymethylcellulose sodium, hydroxypropyl methylcellulose, hydroxyethyl cellulose, methylcellulose, polyvinyl alcohol, povidone, glycerin, propylene glycol, PEG 300, PEG 400, and a combination thereof. The demulcent can be present in an amount of about 0 to about 10%, or about 2%, 5%, 7%, or 9%, by weight of the composition.

[0021] In some embodiments, the composition for use in a method for treating an ocular condition comprises a tonicity agent such as sodium chloride, glycerin, mannitol, potassium chloride, erythritol, and a combination thereof, in an amount of about 0 to about 4% or about 0.01% to about 3% by weight of the composition.

[0022] In some embodiments, the composition for use in a method for treating an ocular condition may include one or more buffering agents. Suitable buffering agents include phosphates, citrates, acetates, borates, and combinations thereof. The amount of buffer component employed is sufficient to maintain the pH of the composition in a range of about 6 to about 8, or from about 6.5 to about 7.5. In certain embodiments, the buffer is present in an amount of about 0 to about 2.0% by weight of the composition.

[0023] In certain embodiments, the composition for use in a method for treating an ocular condition includes a thickener or viscosity agent. The viscosity agent can be selected from the group consisting of carbomer, sodium carboxymethyl cellulose, methyl cellulose, hydroxypropyl methyl cellulose, polyvinyl alcohol, zanthan gum, and a combination thereof. The viscosity agent can be present in an amount of about 0% to about 4% or about 0.01% to about 3.0% by weight of the composition.

[0024] In certain embodiments, the composition for use in a method for treating an ocular condition includes a solubilizer or solubility enhancing agent. The solubilizer or solubility enhancing agent can be selected from the group consisting of Cyclodextin, alpha-cyclodextrin, beta-cyclodextrin, gamma-cyclodextrin, hydroxypropyl-beta-cyclodextrin, Sulfobutyl ether-β-cyclodextrin (Captisol®) and a combination thereof. The solubilizer or solubility enhancing agent can be present in an amount of about 0% to about 10%. In some embodiments, the solubilizer or solubility enhancing agent can be present in an amount of about 0.01% to about 7.0%. In some embodiments, the solubilizer or solubility enhancing agent can be present in an amount of about 0.1 to about 4% by weight of the composition.

[0025] The composition for use in a method for treating an ocular condition can be administered topically in the form of a solution (i.e., drops), cream, ointment, or film. The composition can be administered to a left eye, a right eye, or both eyes. When the composition is administered as a solution, a drop of solution should disperse readily upon contact with a tear solution.

[0026] The compositions for use in a method for treating an ocular condition according to the present disclosure may include one or more other components in amounts effective to provide one or more useful properties and/or benefits. For example, although the present compositions may be substantially free of added preservative components, in other embodiments, the present compositions include effective amounts of preservative components. Examples of such preservative components include, without limitation, PURITE® (Allergan, Irvine, CA), quaternary ammonium preservatives such as benzalkonium chloride ("BAC" or "BAK") and polyoxamer; biguanidebigunanide preservatives such as polyhexamethylene biguanidebiguandide (PHMB); methyl and ethyl parabens; hexetidine; chlorite components, such as stabilized chlorine dioxide or metal chlorites; other ophthalmically acceptable preservatives and mixtures thereof. The concentration of the preservative component, if any, in the present compositions is a concentration effective to preserve the composition, and (depending on the nature of the particular preservative used) is often and generally used in a range of about 0% to about 4.0% by volume or about 0.1% to about 2.0% by volume of the composition.

[0027] In certain embodiments, the composition for use in a method for treating an ocular condition can be in the form of a film, such as an occlusive film or a sustained release film. Also contemplated are liquids that dry to form films. Where films are employed, the films will be in the range of at least about 0.5 mm × 0.5 mm, usually about 3-10 mm × 5-10 mm with a thickness of about 0.1-1.0 mm for ease of handling. The size and form of the film can be used to control the rate of release. Such compositions can comprise one or more film forming agents such as acrylate/octylacrylamide copolymer, poly(ethyl acrylate, methyl methacrylate), chitosan, polyvinyl alcohol, polyisobutylene, polyvinylpyrrolidone-vinyl acetate copolymer, silicon gum, polyvinylpyrrolidone, other sustained release polymeric films, and a combination thereof. The film forming agent can be present in an amount of about 0% to about 10% by weight of the composition.

[0028] The frequency, duration, and dosage of the administration are determined by the prescribing physician. The dosage can vary depending on the dosage form. When the composition for use in a method for treating an ocular condition is a solution, for example, 1, 2, 3, or more drops can be administered per eye per administration. Frequency of administration can be one or more times daily (such as once, twice, three, or four or more times daily), bi-weekly, and/or monthly. Duration of administration can continue until the condition to be treated is resolved, that is, until one or more symptoms of the ocular condition are reduced or eliminated. Accordingly, the composition can be administered for hours, days, weeks, months, and years.

[0029] A symptom is considered to be alleviated if it is prevented, reduced or eliminated. A symptom is prevented in a patient that typically experiences a particular symptom with the ocular condition (or if patients similarly situated typically experience a particular symptom) and the patient does not experience the onset of the symptom following administration of the disclosed composition. A reduction of a symptom is considered achieved if there is a 5%, 10%, 20%, 50%, 75%, 90% or more reduction in the severity or duration of one or more symptom

associated with the ocular condition, in a patient. An elimination of one or more symptoms associated with the ocular condition is achieved when it ceases to be present or substantially present in a patient.

[0030] Certain embodiments of the disclosed compositions for use in a method for treating an ocular condition incorporate a local anesthetic, which can be selected from the group of ambucaine, amolanone, amylocaine, benoxinate, benzocaine, betoxycaine, biphenamine, bupivacaine, butacaine, butamben, butanilicaine, butethamine, butoxycaine, carticaine, chloroprocaine, cocaethylene, cocaine, cyclomethycaine, dibucaine, dimethysoquin, dimethocaine, diperodon, dycyclonine, ecgonidine, ecgonine, ethyl chloride, etidocaine, beta-eucaine, euprocin, fenalcomine, formocaine, hexylcaine, hydroxytetracaine, isobutyl p-aminobenzoate, leucinocaine mesylate, levoxadrol, lidocaine, mepivacaine, meprylcaine, metabutoxycaine, methyl chloride, myrtecaine, naepaine, octacaine, orthocaine, oxethazaine, parethoxycaine, phenacaine, phenol, piperocaine, piridocaine, polidocanol, pramoxine, prilocaine, procaine, propanocaine, proparacaine, propipocaine, propoxycaine, psuedococaine, pyrrocaine, ropivacaine, salicyl alcohol, tetracaine, tolycaine, trimecaine, zolamine, and salts thereof. The concentration of the local anesthetic in the compositions described herein can be therapeutically effective, meaning the concentration is adequate to provide a therapeutic benefit without inflicting harm to the patient.

[0031] The compositions for use in a method for treating an ocular condition can further comprise an opthalmologically acceptable anti-inflammatory agent, such as any non-steroidal anti-inflammatory drug (NSAID) in an amount effective to reduce inflammation in an eye. Non-limiting examples include agents that inhibit the cycloxygenase (COX)-1 and/or -2 enzyme, including propionic acids such as naproxen, flurbiprofen, oxaprozin, ibuprofen, ketoprofen, fenoprofen; ketorolac tromethamine; acetic acid derivatives such as sulindac, indomethacin, and etodolac; phenylacetic acids such as diclofenac, bromfenac, and suprofen; arylacetic prodrugs such as nepafenac, and amfenac; salicyclic acids, such as aspirin, salsalate, diflunisal, choline magnesium trisalicylate (CMT); para-aminophenol derivatives such as acetaminophen; naphthylalkanones such as nabumetone; enolic acid derivatives such as piroxicam and meloxicam; femanates such as mefenamic acid, meclofenamate and flufenamic acid; pyrroleacetic acids such as tolmetin; and pyrazolones such as phenylbutazone; COX-2 selective inhibitors such as celecoxib, valdecoxib, parecoxib, etoricoxib, and luaricoxib; including all esters and pharmaceutically acceptable salts thereof. A steroidal anti-inflammatory agent can also be incorporated, in certain embodiments, and can include hydrocortisone, cortisone, prednisolone, and prednisone.

[0032] Antimicrobial agents suitable for use in the disclosed compositions for use in a method for treating an ocular condition include antibiotics such as aminoglycosides such as gentamycin, kanamycin, neomycin, and vancomycin; amphenicols such as chloramphenicol; cephalosporins, such as cefazolin HCl; penicillins such as ampicillin, penicillin, carbenicillin, oxycillin, methicillin; lincosamides such as lincomycin; polypeptide antibiotics such as polymixin and bacitracin; tetracyclines such as tetracycline; quinolones such as ciproflaxin; sulfonamides such as chloramine T; and sulfones such as sulfanilic acid as the hydrophilic entity; as well as

anti-viral drugs, e.g. acyclovir, gancyclovir, vidarabine, azidothymidine, dideoxyinosine, and dideoxycytosine. Antifungal agents and any other opthalmically suitable antimicrobials are contemplated herein as well.

[0033] Table 2, 3, and 4 provide exemplary eye drop, cream, and film formulations for use in a method for treating an ocular condition, respectively. The formulations in tables 3 and 4 do not form part of the invention and are provided for information purposes only.

TABLE 2

Ingredient	Function	% w/w
testosterone	active	0.03
castor oil	lipophilic vehicle	2.0
Pemulen TR-1	emulsifier	0.15
polysorbate 80	emulsifier	0.1
sodium hydroxide	neutralizing Agent	QS pH 7.3
Glycerin	demulcent/ tonicty agent	1.0
mannitol	tonicity	2.0
PURITE®	preservative	0.01
Water	hydrophilic vehicle	QS 100

TABLE 3

Ingredient	Function	% w/w
testosterone	active	0.05
squalane	lipophilic vehicle	12.0
diethylene glycol monoethyl ether	lipophilic vehicle	3.0
Pemulen TR-1	emulsifier	0.1
Polsorbate 80	emulsifier	0.1
Carbomer	thickener	0.1
Sodium hydroxide	neutralizing Agent	QS pH 6.5
PURITE®	preservative	0.01
Water	hydrophilic vehicle	QS 100

TABLE 4

Ingredient	Function	% w/w
testosterone	active	0.05
squalane	lipophilic vehicle	10
diethylene glycol monoethyl ether	lipophilic vehicle	10
Pemulen TR-2	emulsifier	0.2
Glycerin	plasticizer	4.0
Isostearyl alcohol	plasticizer	1.0

Ingredient	Function	% w/w
acrylate/octylacrylamide copolymer	film former	2.5
Carbomer	thickener	0.1
Sodium hydroxide	neutralizing agent	QS pH 6.5
PURITE®	preservative	0.01
Water	hydrophilic vehicle	QS 100

[0034] Tables 5 and 6 set forth additional formulations for use in a method for treating an ocular condition contemplated by the practice of the invention.

Table 5

Ingredient	Grade	Formulation A	Formulation B
Testosterone	USP, PhEur	0.02	0.03
Castor oil	USP, PhEur	0.25	0.5
Polyoxyl 40 stearate	NF, PhEur	0.25	0.5
Polysorbate 80	USP, PhEur	0.25	0.5
Sulfobutyl ether-β-cyclodextrin (Captisol®)		0.25	0.3
Glycerin	USP, PhEur	1.5	1.5
Carbomer copolymer type A (Pemulen TR2)	NF	0.1	0.1
Boric acid	NF	0.6	0.6
Sodium hydroxide	USP, PhEur	q.s to pH 7.4	q.s to pH 7.4
Purified water	USP, PhEur	qs	qs

Table 6

	C	D	E	F	G
Ingredient	% (w/w)	% (w/w)	% (w/w)	% (w/w)	% (w/w)
Testosterone	0.01	0.02	0.03	0.1	0.3
Castor oil	0.25	0.25	0.25	0.25	0.25
Polyoxyl 40 stearate	0.25	0.25	0.25	0.25	0.25
Polysorbate 80	0.25	0.25	0.25	0.25	0.25
Sulfobutyl ether-β-cyclodextrin (Captisol®)	0.12	0.25	0.36	1.25	3.75
Glycerin	1.5	1.5	1.5	1.5	1.0
Carbomer copolymer type A (Pemulen ™ TR2)	0.1	0.1	0.1	0.1	0.1
Boric acid	0.6	0.6	0.6	0.6	0.6

	C	D	E	F	G
Sodium hydroxide	Q.S to pH 7.4	Q.S to pH 7.4	Q.S to pH 7.4	Q.S to pH 7.4	Q.S to pH 7.4
Purified water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

EXAMPLE 1

Treatment Example

[0035] A 50 year old male presents with bilateral redness, inflammation and irritation of the eye. He is diagnosed with blepharitis and treated with the composition disclosed in Table 2. After 3 days of treatment the symptoms are diminished and after 1 week of treatment, the symptoms are eliminated.

EXAMPLE 2

Alternate Treatment Example

[0036] A 55 year old post-menopausal female presents with ongoing irritation, redness and matter accumulation in both eyes. She is diagnosed with blepharitis and treated with the composition disclosed in Table 3. After 2 days she experiences a reduction in irritation and redness and within 1 week experiences a complete cessation of symptoms. This example does not form part of the invention and is provided for information purposes only.

EXAMPLE 3

Alternate Treatment Example

[0037] A 47 year old man is diagnosed with blepharitis. He is treated with the composition disclosed in Table 4 for 2 weeks and experiences an elimination of all symptoms associated with the condition. This example does not form part of the invention and is provided for information purposes only.

[0038] Unless otherwise indicated, all numbers expressing quantities of ingredients, properties

such as molecular weight, reaction conditions, and so forth used in the specification and claims are to be understood as being modified in all instances by the term "about."

[0039] The terms "a," "an," "the" and similar referents used in the context of describing the invention (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context.

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Non-patent literature cited in the description

- **SCHIFFMAN**Investigative Ophthalmology & Visual Science, 2006, vol. 47, 5608- [0003]
- **CHRISTOPHER GLENN**New Thinking Spurs New Products, 2003, [0004]

Patentkrav

1. Oftalmisk sammensætning til anvendelse i en fremgangsmåde til behandling af en okulær tilstand omfattende en fysiologisk effektiv mængde af et androgen, der er testosteron og ricinusolie.

2. Sammensætning til anvendelse ifølge krav 1, hvor testosteron er til stede i sammensætningen fra 0,01 vægt/vægt-% til 0,05 vægt/vægt-%.

3. Sammensætning til anvendelse ifølge krav 1, hvor sammensætningen er udvalgt fra gruppen bestående af en opløsning, emulsion, suspension, gel, salve, okklusiv film og en depotfilm.

4. Sammensætning til anvendelse ifølge krav 1, hvor sammensætningen omfatter en supplerende bestanddel, der er udvalgt fra gruppen bestående af et fortykningsmiddel, neutraliseringsmiddel, emulgeringsmiddel, buffermiddel, tonicitetsmiddel, lindrende middel, konserveringsmiddel, plastificeringsmiddel, okklusivt middel, en filmdanner og en kombination deraf.

5. Sammensætning til anvendelse ifølge krav 1, der endvidere omfatter et middel, der er udvalgt fra gruppen bestående af et antiinflammatorisk middel, antimikrobielt middel, analgetikum, anæstetikum, smøremiddel og en kombination deraf.

6. Sammensætning til anvendelse ifølge krav 1, der endvidere omfatter et middel til forbedring af opløselighed.

7. Sammensætning til anvendelse ifølge krav 1, hvor den okulære tilstand er følgen af en androgen deficiens.

8. Sammensætning til anvendelse ifølge krav 7, hvor den okulære tilstand er blefaritis.

9. Sammensætning til anvendelse ifølge krav 1, hvor symptomer forbundet med den okulære tilstand forhindres, reduceres eller elimineres.

10. Sammensætning til anvendelse ifølge krav 1, hvor administrationen gentages, indtil ét eller flere symptomer på den okulære tilstand er reduceret eller elimineret.

11. Sammensætning til anvendelse ifølge krav 1, hvor sammensætningen administreres til øjet, det øvre øjenlåg, det nedre øjenlåg og en kombination deraf.