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(71) Applicant *(for all designated States except US)*: **ALCON UNIVERSAL LTD.** [CH/CH]; Bosch 69, P.O. Box 62, CH-6331 Hunenberg (CH).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **YANNI, John, M.** [US/US]; 2821 Donnybrook Drive, Burleson, TX 76028 (US).

(74) Agents: **RYAN, Patrick, M.** et al.; R & D Counsel Q-148, 6201 South Freeway, Fort Worth, TX 76134-2099 (US).

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(54) Title: OPHTHALMIC ANTI-ALLERGY COMPOSITIONS SUITABLE FOR USE WITH CONTACT LENSES

(57) Abstract: Topically administrable anti-allergy compositions comprising olopatadine and a polymeric quaternary ammonium preservative are suitable for use by patients wearing contact lenses.

OPHTHALMIC ANTI-ALLERGY COMPOSITIONS SUITABLE FOR USE WITH CONTACT LENSES

BACKGROUND OF THE INVENTION

The present invention relates generally to ophthalmic anti-allergy compositions. In particular, the present invention relates to topical anti-allergy compositions that can be safely applied by a patient wearing contact lenses.

Ophthalmic formulations generally contain one or more active compounds along with excipients such as surfactants, comforting agents, complexing agents, stabilizers, buffering systems, chelating agents, viscosity agents or gelling polymers and anti-oxidants. Ophthalmic formulations which are intended for multidose use require a preservative. Benzalkonium chloride ("BAC") is the most widely used ophthalmic preservative.

Topically administrable multidose ophthalmic products are generally not suitable for use with contact lenses because the active or the preservative may bind to or accumulate in the contact lenses, causing irritation or toxic effects.

Olopatadine is a known anti-allergy drug. See U.S. Patent No. 5,641,805 (Yanni, et al.). PATANOL® brand of olopatadine hydrochloride ophthalmic solution is marketed as a topical anti-allergy composition. Emedastine is a known anti-histamine drug. EMADINE® brand of emedastine difumarate solution is marketed as a topical anti-allergy composition. Like other topically administrable anti-allergy products, these compositions are preserved with BAC. BAC is known to bind to or accumulate in contact lenses. Thus, like other topically administrable ophthalmic pharmaceutical products containing BAC, PATANOL® brand of olopatadine hydrochloride ophthalmic solution and EMADINE® brand of emedastine difumarate ophthalmic solution contain in their labelling information precautionary

instructions to remove contact lenses before use and to wait ten minutes after administering the product before replacing the lenses. The dosing regimen for anti-allergy products typically calls for two to four applications a day, making it inconvenient for contact lens wearers to treat ophthalmic allergy symptoms.

Polyquaternium-1, which is used under the trade name Polyquad®, is one preservative known to be compatible with contact lenses. Polyquaternium-1 and other polymeric quaternary ammonium compounds are used as disinfectants and preservatives in contact lens care and artificial tear solutions. See, for example, U.S. Patent Nos. 5,037,647; 4,525,346; and 4,407, 791. The currently marketed Opti-Free® brand of contact lens care products, including multi-purpose solutions and cleaning solutions, contains polyquaternium-1 as a disinfectant and preservative.

In addition to contact lens care products, polyquaternium-1 can also be used as a preservative in certain topically administrable ophthalmic drug products. U.S. Patent No. 5,603,929 discloses the use of polyquaternium-1 in combination with boric acid to preserve topically administrable ophthalmic compositions of acidic drugs, such as non-steroidal anti-inflammatory drugs. Although the '929 patent defines suitable ophthalmic drug compounds for use with the polyquaternium-1 and boric acid preservative system to include ophthalmically acceptable salts, amides, esters and prodrugs of the many types of acidic drugs, it does not mention anti- allergy drugs or olopatadine in particular. See Col. 3, lines 12 -30 of the '929 patent.

SUMMARY OF THE INVENTION

It has now been discovered that compositions of olopatadine and emedastine that comprise polyquaternium-1 as a preservative are suitable for use with contact lenses. The present invention relates to multi-dose, topically administrable compositions of olopatadine and emedastine containing a polymeric quaternary ammonium compound, such as polyquaternium-1, as a preservative. The compositions of the present invention do not contain BAC.

The present invention also relates to a method for treating or controlling ocular allergies in patients wearing contact lenses which comprises topically administering a composition comprising olopatadine or emedastine and a polymeric quaternary ammonium compound as a preservative, where the composition is applied without removing the contact lenses.

DETAILED DESCRIPTION OF THE INVENTION

Olopatadine is (Z)-11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]- oxepin-2-acetic acid. Olopatadine can be made using the methods disclosed in U.S. Patent No. 5, 116,863, the entire contents of which are hereby incorporated by reference. The concentration of olopatadine in the compositions of the present invention will range from about 0.0001 to 5 %(w/v), preferably from about 0.001 to 0.25 %(w/v), and most preferably from about 0.1 to 0.25 %(w/v), based on the sterilized purified water. The olopatadine ingredient may be present in the form of a pharmaceutically acceptable salt. Unless indicated otherwise, "olopatadine" as used herein refers to both olopatadine and its pharmaceutically acceptable salts. The most preferred form of olopatadine is olopatadine hydrochloride. The most preferred concentration of olopatadine hydrochloride is from about 0.111 to 0.222 %(w/v), which is equivalent to 0.1 to 0.2 %(w/v) olopatadine.

Emedastine's chemical name is 1-(2-ethoxyethyl)-2-(4-methyl-1-homopiper-azinyl)-benzimidazole. The ophthalmic use of emedastine is

disclosed in U.S. Patent No. 5,441,958. Emedastine can be made using the methods disclosed in U.S. Patent No. 4,430,343, the entire contents of which are hereby incorporated by reference. The concentration of emedastine in the compositions of the present invention will range from about 0.0001 to 1 %(w/v), preferably from about 0.005 to 0.1 %(w/v), and most preferably about 0.05 %(w/v). The emedastine ingredient may be present in the form of a pharmaceutically acceptable salt. Unless indicated otherwise, "emedastine" as used herein refers to both emedastine and its pharmaceutically acceptable salts. The most preferred form of emedastine is emedastine difumarate. The most preferred concentration of emedastine difumarate is about 0.0884 %(w/v), which is equivalent to 0.05 %(w/v) emedastine.

In addition to olopatadine or emedastine, or a pharmaceutically acceptable salt thereof, the compositions of the present invention contain a polymeric quaternary ammonium compound as a preservative. The polymeric quaternary ammonium compounds useful in the compositions of the present invention are those which have an antimicrobial effect and which are ophthalmically acceptable. Preferred compounds of this type are described in US Patents Nos. 3,931,319; 4,027,020; 4,407,791; 4,525,346; 4,836,986; 5,037,647 and 5,300,287; and PCT application WO 91/09523 (Dziabo et al.). The most preferred polymeric ammonium compound is polyquaternium-1 , otherwise known as Polyquad® or Onamer M®, with a number average molecular weight between 2,000 to 30,000. Preferably, the number average molecular weight is between 3,000 to 14,000.

The polymeric quaternary ammonium compounds are generally used in the compositions of the present invention in an amount from about 0.00001 to about 3 %(w/v), preferably from about 0.001 to about 0.1 %(w/v). Most preferably, the compositions of the present invention contain from about 0.001 to about 0.05 %(w/v) of polymeric quaternary ammonium compounds.

It may be necessary or desirable to add boric acid to the compositions to achieve desired levels of preservative efficacy. See U.S. Patent No.

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