

STRADLING YOCCA CARLSON & RAUTH

A PROFESSIONAL CORPORATION
ATTORNEYS AT LAW

660 NEWPORT CENTER DRIVE, SUITE 1600
NEWPORT BEACH, CA 92660-6422
TELEPHONE (949) 725-4000
FACSIMILE (949) 725-4100

SAN FRANCISCO OFFICE
44 MONTGOMERY STREET, SUITE 4200
SAN FRANCISCO, CALIFORNIA 94104
TELEPHONE (415) 283-2240
FACSIMILE (415) 283-2255

SANTA BARBARA OFFICE
302 OLIVE STREET
SANTA BARBARA, CALIFORNIA 93101
TELEPHONE (805) 564-0065
FACSIMILE (805) 564-1044

LOUIS C. CULLMAN
DIRECT DIAL (949) 725-4154
LCULLMAN@SYCR.COM

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CITIZEN PETITION

Stradling Yocca Carlson and Rauth ("petitioner") on behalf of a pharmaceutical client, hereby submits this citizen's petition ("petition") pursuant to 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act ("the Act"), and its implementing regulations 21 U.S.C. §§ 355(j)(2)(C) 1999; 21 CFR §§ 10.25, 40.30, 314.93 (2003). This petition requests that the Commissioner of Foods and Drugs ("the Commissioner") permit the filing of an abbreviated new drug application (ANDA) for a preservative-free Ciprofloxacin HCL (3.5 mg/mL equivalent to 3.0 mg/mL base) ophthalmic solution in unit dose containers (0.4 mL).

A. Action Requested

The petitioner requests authorization from the Commissioner to submit and ANDA for a preservative-free Ciprofloxacin HCL (3.5 mg/mL equivalent to 3.0 mg/mL base) ophthalmic solution, unit dose containers (0.4 mL). The proposed drug product differs from the reference listed drug (RLD), Alcon Ciloxan® Ophthalmic Solution (ciprofloxacin HCL (3.5 mg/mL equivalent to 3.0 mg base supplied in 2.5 mL, 5 mL and 10 mL plastic dropper dispensers) in dosage form (unit dose versus the RLD multi-dose form) and the elimination of benzalkonium chloride (0.006%) as permitted by section 505(j)(2)(C) of the Act. 21 USC §§ 355(j)(2)(C).

B. Statement of Grounds

The Act provides, in relevant part, that any person may file an ANDA for the approval of a new drug that is the "same" as a listed drug. 21 U.S.C. §§ 355(j)(2)(A), (j)(2); 21 CFR § 314.92(a)(1). Abbreviated applications may also be submitted for a new drug, which differed from a listed drug in one or more specified aspects, provided that FDA has declared

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the product suitable for ANDA submission through the ANDA process 21 U.S.C. §§ 355(j)(2)(A), (j)(2)(C); 21 CFR § 314.92(a)(3). Permitted product changes include, among other things, a different route of administration, dosage form, or strength from that of a listed drug. *Id.* FDA must approve a petition seeking one or more of these product changes, unless the proposed product change(s) presents questions of safety or effectiveness. 21 U.S.C. §355 (j)(2)(C)(i); 21 CFR §314.93.

This petition accordingly seeks FDA authorization to submit an ANDA for a preservative-free Ciprofloxacin HCL (3.5 mg/mL equivalent to 3.0 mg/mL base) ophthalmic solution in unit dose containers (0.4 mL) product. The proposed ANDA will reference RLD, Alcon Ciloxan® Ophthalmic Solution (ciprofloxacin HCL (3.5 mg/mL equivalent to 3.0 mg/mL base supplied in 2.5 mL, 5 mL and 10 mL multi-dose plastic dropper dispensers)). The proposed drug product will differ from the listed drug in fill volume and elimination of benzalkonium chloride from the formulation, changes permitted by the Act. Specifically, the proposed drug product will contain the same active ingredient for the same labeled use as the RLD, but in unit dose containers instead of multi-dose containers.

Item	Ciprofloxacin HCl Ophthalmic Solution in Unit Dose Container	Alcon's Ciloxan® (Ciprofloxacin HCl) Ophthalmic Solution
<u>Dosage Form</u>	<u>Sterile Liquid</u>	<u>Sterile Liquid</u>
<u>Route of Administration</u>	<u>Ophthalmic</u>	<u>Ophthalmic</u>
<u>Ciprofloxacin HCl Concentration</u>	<u>3.5 mg/mL (equivalent to 3.0 mg/mL base)</u>	<u>3.5 mg/mL (equivalent to 3.0 mg/mL base)</u>
<u>Inactive Ingredients</u>	<u>Sodium Acetate, Acetic Acid, Mannitol, Edetate Disodium, Hydrochloric Acid and/or Sodium Hydroxide (to adjust pH) and Purified Water</u>	<u>Sodium Acetate, Acetic Acid, Mannitol, Edetate Disodium, Hydrochloric Acid and/or Sodium Hydroxide (to adjust pH) and Purified Water</u>
<u>Preservatives</u>	<u>N/A</u>	<u>Bezalkonium Chloride</u>
<u>How Supplied</u>	<u>0.4 mL in a single-dose container</u>	<u>2.5 mL, 5 mL and 10 mL in multi-dose containers</u>

The availability in unit dose form may improve product sterility, patient compliance, convenience and reduce the likelihood of administering excess drug. Moreover, the unique unit dose form will reduce the likelihood of multiple persons using the same applicator and thus reduce the likelihood of disease transmission. Thus the proposed drug product will provide physicians with an additional dosage form option for ease of administration, while providing the same therapeutic and safety benefits as that of the listed drug.

Additionally, the unit-dose form eliminates the need for a preservative, specifically 0.006% benzalkonium chloride. Preservatives are necessary when the medicament is packaged in multi-dose form where contamination of the opened container is possible during storage. The proposed unit dose form will be used once immediately after opening and then discarded. The product will be sterile packaged and thus there is no risk of microbial contamination during the product life cycle. Consequently preservatives are not necessary for the proposed unit-dose ciprofloxacin product.

The labeling of the proposed drug product will be the same as the currently approved labeling for the listed drug, with a few minor changes which are required because of the differences approved under this petition. See attachments.

C. Environmental Impact

Petitioner claims a categorical exclusion under 21 CFR §25.31 (2003)

D. Economic Impact

Information under this section will be submitted upon request by the Commissioner.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views which the petition relies, and that includes representative data and information known to the petitioner which is unfavorable to the petition.

Respectfully Submitted,



Louis C. Cullman

Stradling Yocca Carlson and Rauth

Attachments

1. Electronic Orange Book, Approved Drug Products with Therapeutic Equivalence Evaluations, update as of March 2004, Alcon Ciloxan® Ophthalmic Solution.
2. Copy of Package Insert from Ciloxan® Ophthalmic Solution.
3. Proposed package insert for Ciprofloxacin HCL (3.5 mg/mL equivalent to 3.0 mg base) ophthalmic solution, unidose containers (0.4 mL)