CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-918

PHARMACOLOGY REVIEW(S)

INTEROFFICE MEMORANDUM

DATE: 2/10/06

TO: Susmita Samanta, M.D.
Project Manager, DAIOP
and
File, NDA 21-918

FROM: Amy L. Ellis, Ph.D.
Pharmacologist, DAIOP

THROUGH: Terry S. Peters, DVM
Acting Pharmacology Team Leader, DAIOP

RE: Pharmacology/Toxicology Review for Ciprofloxacin Otic Solution 0.2%, NDA 21-918

This NDA is for a new otic formulation of ciprofloxacin that does not contain a steroid, in contrast to two other marketed otic products (Cipro® HC and Ciprodex®) containing ciprofloxacin. It is administered twice daily into an affected ear at a volume of 0.25 ml, for a total dose of up to 2 mg of ciprofloxacin per day if bilateral treatment is necessary. The sponsor, Laboratorios SALVAT, S.A., Barcelona, Spain (U.S. representative, PAREXEL International, Durham, NC) is requesting approval of this new formulation for the treatment of acute otitis externa in adult and pediatric patients ≥ 1 year of age.

The ingredients of Ciprofloxacin Otic Solution 0.2% are as follows: 0.233% ciprofloxacin hydrochloride (0.2% as base), — , povidone [—], — , glycerin, lactic acid and sodium hydroxide as needed for pH adjustment to (—), and water for injection (qs). Although povidone and lactic acid are not present in any other otic preparations marketed in the US, both are present in other topical products at concentrations that exceed those in Ciprofloxacin Otic Solution 2%. Their use in a topical otic product indicated for otitis externa is expected to be safe. b(4

The sponsor has requested that the Division rely on its findings of safety for previously approved otic ciprofloxacin products to support the current NDA, as described in Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. There are 2 approved otic products containing ciprofloxacin that are marketed in the U.S. They are Cipro® HC Otic Suspension (0.2% ciprofloxacin and 1% hydrocortisone, approved for acute otitis externa) and Ciprodex® Otic Suspension (0.3% ciprofloxacin and 0.1% dexamethasone, approved for acute otitis externa and acute otitis media with tympanostomy tubes). The label for the current product would be consistent with those for the 2 approved products. SALVAT has also submitted an annotated summary of ciprofloxacin toxicity and pharmacokinetic data from the literature and reports from studies of similar, but not identical, otic products that the sponsor markets in Europe. The sponsor's product Cetraxal Otico® contains 0.3% ciprofloxacin in a vehicle different from Ciprofloxacin Otic Solution 0.2% and Cetraxal Plus® contains 0.349% ciprofloxacin and 0.025% fluocinolone, also in a different vehicle. In short, ciprofloxacin is not ototoxic following

topical otic or intratympanic exposure, and none of the topical ciprofloxacin products is a primary irritant. Additionally, ciprofloxacin products are not considered potent sensitizers.

There is no objection to the approval of this NDA based on the nonclinical information submitted in this application and the Division's findings of safety for other ciprofloxacin products. The sponsor has proposed a label that is based upon those for Cipro® HC Otic Suspension and Ciprodex® Otic Suspension. This is appropriate. When the Division and Sponsor finalize the label, we will request a minor editorial change to harmonize the proposed label for this product with the others.

APPEARS THIS WAY
ON ORIGINAL

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Amy Ellis
2/10/2006 02:11:37 PM
PHARMACOLOGIST
There is no objection to the approval of the NDA based on the nonclinical information submitted in the application.
Terry- You signed the paper copy of this review memo on 2/10/06.

Terry Peters
2/13/2006 09:19:06 AM
PHARMACOLOGIST