CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-221

PHARMACOLOGY REVIEW(S)

Pharmacology/Toxicology Review
NDA 22-221 Akten™
Lidocaine HCl Ophthalmic Gel (3.5%)

Date:	October 16, 2007
To:	Jane Dean, RN Project Manager, DAIOP and File, NDA 22-221
From:	Maryam Rafie-Kolpin, Ph.D. Pharmacologist, DAIOP
Through:	Wendy Schmidt, Ph.D. Acting Pharmacology Team Leader, DAIOP
RE:	Pharmacology/Toxicology Review for Akten™ (NDA 22-221)

This NDA is for a new ophthalmic gel formulation of lidocaine hydrochloride (3.5%), Akten™ Ophthalmic Gel, for ocular surface anesthesia. The sponsor has requested that the Division would use its previous finding of safety from NDAs for lidocaine HCl to support the current NDA as permitted under section 505(b)(2) of the Federal food, Drug and Cosmetic Act. Lidocaine has been used as local anesthetic for labor/delivery, dental procedure, lumbar analgesia, surgical analgesia, obstetric procedures and postherpetic neuralgia. Lidocaine is available for intravenous and spinal injection as well as oral and topical administrations. Lidocaine is also available as ophthalmic drops. The recommended dose for lidocaine drops is 2 drops of 4% solution in both eyes, 6 times, 60 minutes prior to surgery. Assuming that roughly 100 uL of the lidocaine gel will be used, the human dose is roughly 60 ug/kg lidocaine.

The inactive ingredients used for Akten™ Ophthalmic Gel formulation are hydroxypropylmethyl Cellulose sterile (HPMC) at ——— sodium chloride and purified water. All the inactive ingredients in Akten™ Ophthalmic Gel have been used previously in other approved ophthalmic products at equal or higher concentrations. b(4)

No new nonclinical studies were requested by the Division or performed by the sponsor. The sponsor provided literature studies and a reference to the agency's previous findings for lidocaine to support the required labeling sections. There are no objections to approval of this NDA from the pharmacology/toxicology perspective based on the nonclinical information provided in this application. However, the nonclinical sections of the label should be harmonized with the most recent information available on the active ingredient. Labeling recommendations are below and are based on the package insert for xylocaine 2% Jelly, revised in January of 2006. Recommended additions are in bold and suggested deletions are in ~~strikethrough~~.

---

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

b(4)

2 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Pharm/Tox-1

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

/s/

Wendelyn Schmidt
3/12/2008 04:07:00 PM
PHARMACOLOGIST

PHARMACOLOGY/TOXICOLOGY NDA FILEABILITY CHECKLIST

NDA Number: 22-221
Drug Name: Akten™ (lidocaine hydrochloride) ophthalmic Gel, 3.5%
Applicant: Akron Inc.
Check Date: August 15, 2007

IS THE PHARM/TOX SECTION OF THE APPLICATION FILEABLE? YES

	Parameters	Yes	No	Comments
1	On its face, is the Pharmacology/Toxicology (P/T) section of the NDA organized in a manner to allow substantive review to begin?	√		
2	Is the P/T section of the NDA indexed and paginated in a manner to allow substantive review to begin?	√		
3	On its face, is the P/T section of the NDA legible so that substantive review can begin?	√		
4	Are ALL required and requested IND studies completed and submitted in this NDA (carcinogenicity, mutagenicity, teratogenicity, effects on fertility, juvenile studies, ocular toxicity studies, acute adult studies, chronic adult studies, maximum tolerated dosage determination, dermal irritancy, ocular irritancy, photocarcinogenicity, animal pharmacokinetic studies, etc)?	√		No nonclinical studies were requested since lidocaine is an approved drug and its safety profile with respect to nonclinical evaluation has been demonstrated.
5	If the formulation to be marketed is different from that used in the toxicology studies, has the sponsor made an appropriate effort to either repeat the studies with the to-be-marketed product or to explain why such repetition should not be required?	√		The safety of both the active and inactive ingredients have been established in a number of approved NDA/ANDAs. Therefore, no new nonclinical studies with the to-be-marketed product was requested.
6	Are the proposed labeling sections relative to pharmacology appropriate (including human dose multiples expressed in mg/m^2 or comparative serum/plasma levels) and in accordance with 201.57?	√		
7	Has the sponsor submitted all special studies/data requested by the Division during pre-submission discussions?	√		No special nonclinical studies were requested since lidocaine is an approved drug and its safety profile with respect to nonclinical evaluation has been demonstrated.
8	On its face, does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the sponsor submitted a rationale to justify the alternative route?	√		
9	Has the sponsor submitted a statement(s) that all of the pivotal P/T studies been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?		√	The sponsor provided cross references to previously approved lidocaine applications.
10	Has the sponsor submitted a statement(s) that the P/T studies have been performed using acceptable, state-of-the-art protocols which also reflect agency animal welfare concerns?			Not applicable
11	From a pharmacology perspective, is this NDA fileable?	√		

Reviewer's Signature: _____

Supervisor's Signature:
Concurrence: _____ _____

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

/s/

Maryam Rafie-Kolpin
8/21/2007 10:33:50 AM
PHARMACOLOGIST

Wendelyn Schmidt
8/21/2007 10:52:33 AM
PHARMACOLOGIST