CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

21-073/S-001

Trade Name: Actos

Generic Name: (pioglitazone hydrochloride)

Sponsor: Takeda Pharmaceuticals America, Inc

Approval Date: February 25, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-001

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Approvable Letter	
Labeling	
Medical Review(s)	
Chemistry Review(s)	X
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-001

APPROVAL LETTER

NDA 21-073/S-001

FEB 25 2000

Takeda Pharmaceuticals America, Inc.
Attention: Robert M. Pilson, R.Ph.
Manager, Regulatory Compliance
475 Half Day Road, Suite 500
Lincolnshire, IL 60069

Dear Mr. Pilson:

Please refer to your supplemental new drug application dated December 20, 1999, received December 22, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Actos™ (pioglitazone hydrochloride) Tablets 15 mg, 30 mg and 45 mg.

This supplemental new drug application provides for the addition of [redacted] as a [redacted] facility for Actos.

We have completed the review of this supplemental application and it is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Ms. Jena Weber, Regulatory Project Manager, at (301) 827-6422.

Sincerely,

Stephen K. Moore 2/24/00

Stephen K. Moore, Ph.D.
Chemistry Team Leader I, for
Division of Metabolic and Endocrine Drug Products,
(HFD-510)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 21-073
HFD-510/Div. Files
HFD-511/JWeber
HFD-510/XYsern/DGWu/SMoore
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: jmw/February 14, 2000
Initialed by:XYsern 2/14/DGWu 2/14/EGalliers 2/18/00
final:JWeber 2/23/00
filename: N21073.001 2/23/00

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-001

CHEMISTRY REVIEW(S)

FEB 11 2000

CHEMIST'S REVIEW

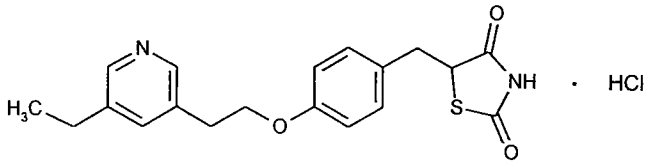
Organization CDER/HFD-510 Division of Metabolism and Endocrine Drug Products	**NDA # 21-073** Approved: 21-JUL-1999
Name and Address of Applicant: Takeda Pharmaceuticals America Inc. 101 Carnegie Center, Suite 207 Princeton, NJ 08540 Phone: (609) 452-1113 x-4409 Fax: (609) 452-1218	**Supplement** SCP-001 Doc. 20-DEC-1999 Rec. 22-DEC-1999 **Name Of The Drug** Actos™ Tablets **Nonproprietary Name** Pioglitazone Hydrochloride Tablets
Supplement provides for the [redacted] facility as [redacted] facility for Actos™ Tablets.	**New Correspondence** --

Pharmacological Category: Hypoglycemic Agent, treatment of NIDDM.	**How Dispensed** Oral Rx	**Supporting Documents** --
Dosage Form Tablets	**Potencies** 15-, 30- and 45-mg	

Chemical Name and Structure

Pioglitazone

$C_{19}H_{20}N_2O_3S \cdot HCl$
MW = 356.43 + 36.57 = 392.90



(±)-5[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-2,4-thiazolidinedione monohydrochloride

Comments: This Supplement –Changes Being Effected in 30 days- provides for an [redacted] The proposed [redacted], is currently approved as [redacted] for the drug product. The [redacted] site is located on [redacted] A letter from [redacted] dated September 17 1999, stating that their facility is in compliance with cGMP, is adequately provided. The [redacted] has been found acceptable [based on profile] by the Office of Compliance (EER summary report dated 09-FEB-2000 attached). The test methods and procedures to analyze the [redacted] at this [redacted] will be the test methods approved in NDA 21-073. The applicant commits to place the first production batch and annual batches on long-term stability studies using the approved protocol. Accordingly to the "Guidance for the Industry, Changes to an Approved NDA or ANDA, November 1999" document (page 8), this information [redacted] site- could be send as a Supplement or in the Annual Report with proper identification of the change. *Adequate information has been provided.*

Conclusions and Recommendations Satisfactory CMC information has been provided to support [redacted] as an [redacted] site for the product, Actos™ (Pioglitazone HCl) Tablets. From the chemistry point of view, this supplement can be approved. Issue approval letter.

Reviewer Name (and signature) Xavier Ysern

Xavier Ysern, PhD

Date Completed: 10-FEB-2000

R/D Init. Doug Nie for S. Moore 2-11-00

filename: /nda/21073s01.doc

DISTRIBUTION: Original: NDA 21-073 cc: HFD-510 Division File/ JWeber / SMoore/ XYsern

CBE-30 days
AP

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 21073/001**
Stamp: **22-DEC-1999** Regulatory Due: **22-APR-2000**
Applicant: **TAKEDA AMERICA**
101 CARNEGIE CENTER STE 207
PRINCETON, NJ 08540

Priority: **1P** Org Code: **510**
Action Goal: District Goal: **18-MAR-2000**
Brand Name: **ACTOS (PIOGLITAZONE HCL)15/30/45MG TABS**
Established Name:
Generic Name: **PIOGLITAZONE HCL**
Dosage Form: **TAB (TABLET)**
Strength: **15-, 30- AND 45-MG**

FDA Contacts:

J. WEBER	**(HFD-510)**	**301-827-6422**	**, Project Manager**
X. YSERN	**(HFD-510)**	**301-827-6420**	**, Review Chemist**
S. MOORE	**(HFD-510)**	**301-827-6430**	**, Team Leader**

Overall Recommendation:

ACCEPTABLE on 09-FEB-2000 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment:

DMF No:
AADA No:

Profile: **TCM** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **09-FEB-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities:

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-001

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-073/S-001

Takeda Pharmaceuticals America, Inc.
475 Half Day Road Suite 500
Lincolnshire, Illinois 60069

JAN - 7 2000

Attention: Robert M. Pilson
Manager, Regulatory Compliance

Dear Mr. Polson:

We acknowledge receipt of your supplemental application for the following:

Name of Drug:	Actos™ (pigoglitazone hydrochloride) 15mg, 30mg, 45mg
NDA Number:	21-073
Supplement Number:	S-001
Date of Supplement:	December 20, 1999
Date of Receipt:	December 22, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on February 20, 2000, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Attention: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine
Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 21-073/S-001
HFD-510/Div. Files
HFD-510/CSO/Weber

filename: C:\WPWIN61\WPDOCS\21073.WPD

SUPPLEMENT ACKNOWLEDGEMENT

ORIGINAL

475 Half Day Road • Suite 500
Lincolnshire, Illinois 60069
p/ 847.383.3000

TAKEDA PHARMACEUTICALS AMERICA, INC.

NDA NO. 21-073 SEE NO. 001
NDA SUPPL FOR SCP

December 20, 1999

Solomon Sobel, M.D., Director
Division of Metabolic & Endocrine Drug Products (HFD-510)
Center for Drug Evaluation & Research
Document Control Room #14B-19
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

CENTER FOR DRUG REC'D DEC 22 1999 HFD-510 EVALUATION AND RESEARCH

Re: ACTOS™ (pioglitazone hydrochloride) 15mg, 30mg, 45mg
NDA No. 21-073
CHEMISTRY, MANUFACTURING AND CONTROLS

"SUPPLEMENT--CHANGES BEING EFFECTED IN 30 DAYS"

see review #1

Dear Dr. Sobel:

This "Supplement--Changes Being Effected in 30 Days", is being submitted to add [redacted] as a [redacted] to the above referenced New Drug Application. This is based on 21CFR§(g)(2), Guidance for Industry, Stability Testing of Drug Substances and Drug Products, Draft Guidance, June, 1998, p. 88, and Guidance for Industry, Changes to an Approved NDA or ANDA, November, 1999, VI (C), p. 10. [redacted] currently approved [redacted] NDA 21-073. The documentation supporting the addition of [redacted] includes:

1. a Reference Letter for Drug Master File [redacted]
2. a cGMP certification signed by the [redacted]

XY 2/9/00

In compliance with 21CFR§(g)(1)(iii)(A) through §(g)(1)(iii)(G), a description and location of the proposed change as well as the affected products is provided above and in the supporting documentation. The test methods that will be utilized to analyze the [redacted] will be the test methods approved in NDA 21-073. All Standard Operating Procedures related to this proposed change are contained in [redacted] Takeda Pharmaceuticals America, Inc. also commits to place the first production batch and annual batches on long-term stability studies using the approved protocol in the application.

AP

REVIEWS COMPLETED
CSO ACTION: ☐ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS 2/23/00 DATE

TAKEDA PHARMACEUTICALS AMERICA, INC.

We feel that the documentation provided in this "Supplement--Changes Being Effected in 30 days" adequately supports the [redacted] as a [redacted] for NDA 21-073. Please call me if you need further information regarding this submission.

This submission is also being provided concurrently to the Chicago District Office.

Sincerely,

Robert M. Pilson

Robert M. Pilson, RPh
Manager, Regulatory Compliance
(847) 383-3023
(847) 383-3143 FAX

cc: Raymond Mlecko, District Director, Chicago District Office, 300 S. Riverside Plaza, Ste 550S, Chicago, IL 60606

NDA 21-073 SUPPL. SCM-001

SUPPLEMENT SUBMITTED AS A *CHANGE BEING EFFECTED* (CBE)

Please determine whether this submission qualifies as a CBE by (date) ~~2.28.99~~ 1/11/99

All *required* primary reviewers:

Qualifies as CBE: (Signed) Lanie Isern (10-FEB-2000) XY 10-FEB-2000

Does not qualify: (Signed) _____

(If CMC, **Chemistry Team Leader** must also sign.)

Qualifies: _____ Does not qualify: _____

(If *in vivo* biopharmaceutics data are included, evaluation by **Biopharm reviewer** may be needed.)

Qualifies: _____ Does not qualify: _____

Return completed form to PM _____

(Name)

n:\dmedps1\egallier\form.cbe