CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

21-073/S-003

Trade Name: Actos

Generic Name: (pioglitazone hydrochloride)

Sponsor: Takeda Pharmaceuticals America, Inc

Approval Date: April 11, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-003

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-003

APPROVAL LETTER

NDA 21-073/S-003

APR 11 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 March 21, 2000, received March 22, 2000, 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 "Changes Being Effected in 30 days" supplemental new drug application provides for the addition of the [redacted] as an [redacted] facility for Actos Tablets.

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 4/10/2000

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

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

Drafted by: jmw/April 5, 2000
Initialed by:XYsern 4/5/SMoore 4/5/EGalliers 4/8/00
final:JWeber 4/10/00
filename: N21073.003

4/10/00

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-003

CHEMISTRY REVIEW(S)

APR - 5 2000

CHEMIST'S REVIEW

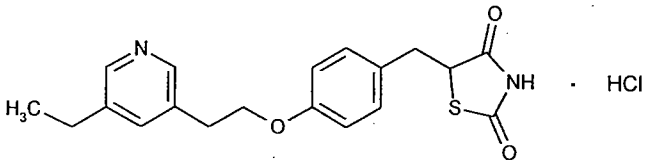
Organization CDER/HFD-510 Division of Metabolism and Endocrine Drug Products	**NDA # 21-073** Approved: 21-JUL-1999
Name and Address of Applicant: Takeda Pharmaceuticals America Inc. 101 Carnegie Center, Suite 207 Princeton, NJ 08540 Phone: (609) 452-1113 x-4409 Fax: (609) 452-1218	**Supplement** SCS-003 Doc. 21-MAR-2000 Rec. 22-MAR-2000 **Name Of The Drug** Actos™ Tablets **Nonproprietary Name** Pioglitazone Hydrochloride Tablets
Supplement provides for the addition of the [redacted] facility at [redacted] as an [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 the [redacted] facility at [redacted] as an [redacted] for Actos™ Tablets. This facility is currently approved as [redacted] facility for the drug product. The [redacted] at [redacted], has been found acceptable [based on profile] as a packaging facility by the District Office. A copy of the EER summary report, dated 05-APR-2000, is attached. *Adequate information has been provided.*

Conclusions and Recommendations The [redacted] has been found acceptable for [redacted] drug 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 **Date Completed:** 05-APR-2000

Xavier Ysern, PhD

R/D Init.

filename: /nda/21073s03.doc

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

CBE-30 days
AP

Stephen Moore 4/5/2000

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 21073/003**
Priority: **1P** Org Code: **510**
Stamp: **22-MAR-2000** Regulatory Due: **22-SEP-2000**
Action Goal: District Goal: **18-AUG-2000**
Applicant: **TAKEDA PHARMS**
475 HALF DAY RD STE 500
LINCOLNSHIRE, IL 60069
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 05-APR-2000 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: [redacted]
DMF No:
AADA No:

Profile: **TCM** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **05-APR-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: [redacted]

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 21073/003**
Stamp: **22-MAR-2000** Regulatory Due: **22-SEP-2000**
Applicant: **TAKEDA PHARMS**
475 HALF DAY RD STE 500
LINCOLNSHIRE, IL 60069

Priority: **1P** Org Code: **510**
Action Goal: District Goal: **18-AUG-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:

Establishment: [redacted]

DMF No:
AADA No:

Profile: **TCM** OAI Status: **NONE**
Last Milestone: **SUBMITTED TO OC**
Milestone Date: **05-APR-2000**

Responsibilities: [redacted]

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-003

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MAR 29 2000

NDA 21-073/S-003

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

Attention: Robert M. Pilson, R. Ph.
Manager, Regulatory Compliance

Dear Mr. Pilson:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: ACTOS® (pioglitazone hydrochloride) 15 mg, 30 mg, 45 mg

NDA Number: 21-073

Supplement Number: S-003

Date of Supplement: March 21, 2000

Date of Receipt: March 22,2000

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on May 21, 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-003
HFD-510/Div. Files
HFD-510/CSO/Weber

filename:

SUPPLEMENT ACKNOWLEDGEMENT

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

TAKEDA PHARMACEUTICALS AMERICA, INC.

NDA NO. 21073 REF NO. 003
NDA SUPPL FOR SCM

March 21, 2000

John K. Jenkins, M.D., F.C.C.P.
Acting 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

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

"SUPPLEMENT-CHANGES BEING EFFECTED IN 30 DAYS

Dear Dr. Jenkins:

This "Supplement-Changes Being Effected in 30 Days", is being submitted to add [redacted] as a [redacted] the above referenced New Drug Application. This is based on 21CFR§314.70 (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] is currently approved as [redacted] in NDA 21-073. The documentation supporting the addition of [redacted] includes:

1. a cGMP certification signed by the [redacted]
2. Name and Address of the [redacted] site
3. [redacted]

In compliance with 21CFR§314.70 (g)(1)(iii)(A) through 21CFR§314.70 (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 documention. 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 located on site [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.

TAKEDA PHARMACEUTICALS AMERICA, INC.

We feel that the documentation provided in this "Supplement-Changes Being Effected in 30 Days" adequately supports the addition of [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, R.Ph.
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

REVIEWS COMPLETED

CSO ACTION

☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS

4/7/00

DATE