CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

21-073/S-005

Trade Name: Actos

Generic Name: (pioglitazone hydrochloride)

Sponsor: Takeda Pharmaceuticals America, Inc

Approval Date: July 26, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-005

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

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APPLICATION NUMBER:

21-073/S-005

APPROVAL LETTER

JUL 26 2000

NDA 21-073/S-005

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

Dear Mr. Pilson:

Please refer to your supplemental new drug application dated June 23, 2000, received June 26, 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 "Special Supplement - Changes Being Effected in 30 Days"application provides for the addition of [redacted] located in [redacted] as an [redacted] facility for the the drug product, 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 Health Project Manager, at 301-827-6422.

Sincerely,

Stephen K. Moore 7-26-00

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-510/XYsern/SMoore
HFD-511/JWeber 7/25/00
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: jmw/July 25, 2000
Initialed by:XYsern 7/25/SMoore 7/25/EGalliers 7/25/00
final: Jweber 7/26/00
filename: N21073AP.005

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-005

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW

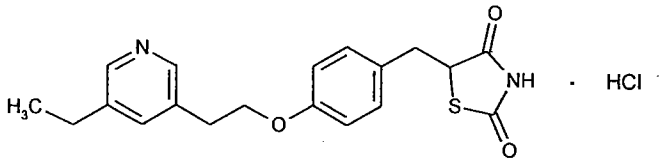
Organization CDER/HFD-510 Division of Metabolism and Endocrine Drug Products	**NDA # 21-073** Approved: 21-JUL-1999
Name and Address of Applicant: JUL 24 2000 Takeda Pharmaceuticals America Inc. 101 Carnegie Center, Suite 207 Princeton, NJ 08540 Phone: (609) 452-1113 x-4409 Fax: (609) 452-1218	**Supplement** SCM-005 Doc. 23-JUN-2000 Rec. 26-JUN-2000 **Name Of The Drug** Actos™ Tablets **Nonproprietary Name** Pioglitazone Hydrochloride Tablets
Supplement provides for the addition of [redacted] site 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 addition of [redacted] facility at [redacted] as an additional [redacted] for Actos™ Tablets. In support of this submission the applicant, Takeda Pharmaceuticals, certifies that the tests methods approved in NDA 21-073 have been transferred to [redacted] utilizing an Approved Transfer Protocol. Relating to [redacted] the applicant, has made no postapproval commitments [redacted] has the capability to perform the intended [redacted] is in compliance with current Good Manufacturing Practices. The [redacted] facility at [redacted] has been found acceptable (based on profile) as an [redacted] facility by the District Office. A copy of the EER summary report, dated 24-JUL-2000, is attached. *Adequate information has been provided, and all regulatory requirements have been fulfilled.*

Conclusions and Recommendations The [redacted] has been found acceptable for [redacted] of the 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:** 24-JUL-2000

Xavier Ysern, PhD

R/D Init.

filename: /nda/21073s05.doc

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

CBE-30 days
AP

Stephen Moore 7/24/2000

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 21073/005**
Stamp: **26-JUN-2000** Regulatory Due: **26-DEC-2000**
Applicant: **TAKEDA PHARMS**
475 HALF DAY RD STE 500
LINCOLNSHIRE, IL 60069

Priority: **1P** Org Code: **510**
Action Goal: District Goal: **21-NOV-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 24-JUL-2000 by S. FERGUSON (HFD-324) 301-827-0062

Establishment: [redacted]
DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **24-JUL-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: 1 X 1

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-073/S-005

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-073/S-005 JUL - 6 2000

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

Attention: Robert M. Pilson
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-005

Date of Supplement: June 23, 2000

Date of Receipt: June 26, 2000

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on August 25, 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-005
HFD-510/Div. Files
HFD-510/CSO/Weber

filename:

SUPPLEMENT ACKNOWLEDGEMENT

ORIGINAL

NDA NO. 21,073 REF NO. 005

NDA SUPPL FOR SCM

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

TAKEDA PHARMACEUTICALS AMERICA, INC.

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUN 26 2000
HFD-510

June 23, 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
THIS SUPPLEMENT IS BEING FILED UNDER
"SUPPLEMENT-CHANGES BEING EFFECTED IN 30 DAYS

Dear Dr. Jenkins:

This "Supplement-Changes Being Effected in 30 Days", is being submitted to add

to the above referenced New Drug Application. This supplement is based on 21CFR§314.70 (g)(2), *Changes requiring supplement submission at least 30 days prior to distribution of the product made using the change;* Guidance for Industry, Stability Testing of Drug Substances and Drug Products, Draft Guidance, June 1998, p. 89, and Guidance for Industry Postapproval Changes April 1998. Currently, being performed by the site approved in the New Drug Application, and

In compliance with Takeda Pharmaceuticals America, Inc. certifies that approved in NDA 21-073 have been transferred to utilizing an approved Transfer Protocol. No postapproval commitments have been made by the applicant relating to the has the capability to perform the intended has certified (enclosed) that their facility is in compliance with current Good Manufacturing Practices.

CFN

TAKEDA PHARMACEUTICALS AMERICA, INC.

The documentation supporting the addition of [redacted] includes:

1. CGMP Certification by [redacted]
2. A statement indicating why a [redacted] supplement is appropriate (i.e., the four circumstances above exist)
3. The name and address of the new [redacted]

Additionally [redacted] will perform on an as needed basis [redacted] 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 7/100 DATE