CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 21-073/S015

Trade Name: Actos Tablets

Generic Name: pioglitazone HCL

Sponsor: Takeda Pharmaceuticals North America, Inc.

Approval Date: February 2, 2002

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APPLICATION NUMBER:
NDA 21-073/S015

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Reviews / Information Included in this NDA Review.

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Chemistry Review(s)	**X**
Pharmacology Review(s)	
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APPLICATION NUMBER:

NDA 21-073/S015

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-073/S-015

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

Dear Mr. Pilson:

Please refer to your supplemental new drug application dated October 4, 2001, received October 5, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Actos® (pioglitazone HCl) Tablets 15 mg, 30 mg, and 45 mg.

We acknowledge receipt of your submission dated October 30, 2001.

This "Changes Being Effected in 30 days" supplemental new drug application provides for the addition of the [redacted], as an additional site for the [redacted] of pioglitazone HCl drug substance.

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,

{See appended electronic signature page}

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

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/s/

Stephen Moore
2/28/02 04:03:20 PM

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APPLICATION NUMBER:

NDA 21-073/S015

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW

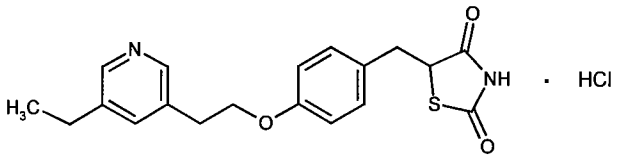
Organization CDER/HFD-510 Division of Metabolism and Endocrine Drug Products	**NDA # 21-073** Approved: 21-JUL-1999
Name and Address of Applicant: Takeda Pharmaceuticals North America, Inc. 475 Half Day Road, Suite 500 Lincolnshire, IL 60069 Phone: (847) 383-3023 Fax: (847) 383-3143	**Supplement** SCM-015 Doc. 04-OCT-2001 Rec. 05-OCT-2001 **Name Of The Drug** Actos™ Tablets **Nonproprietary Name** Pioglitazone Hydrochloride Tablets
Supplement provides for the [redacted] as an additional site for the [redacted] of the drug substance, pioglitazone hydrochloride.	**Amendment(s)** Doc. 30-OCT-2001 Rec. 31-OCT-2001

Pharmacological Category:	**How Dispensed**	**Supporting Documents**
Hypoglycemic Agent, treatment of NIDDM.	Oral Rx	--
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 the addition of the [redacted] as an additional site for the [redacted] of the drug substance, pioglitazone hydrochloride. The [redacted], in the new/additional facility does not differ substantially from that in the former approved facilities. *Drug substance [redacted] in the [redacted] facility does not differ (profile and stability) from the one [redacted] at the currently approved sites.* The facility was inspected on January 24 (initiated) to 24 (finalized), 2002. The Office of Compliance on January 25, 2002 issued an acceptable recommendation. *Acceptable, all regulatory requirements are fulfilled.*

Conclusions and Recommendations: The [redacted] is acceptable for the [redacted] of the drug substance pioglitazone. From the CMC point of view, this supplement can be approved.
Issue Approval Letter.

Reviewer Name (and signature) **Date Completed:** 04-FEB-2002

Xavier Ysern, PhD
Review Chemist

R/D Init.
Stephen Moore, PhD
Chemist Team Leader

filename: /nda/21073s15.doc

SS-CBE 30 days
AP

00 Page(s) Withheld

X § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 21-073
S015

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21073/015
Stamp: 05-OCT-2001 Regulatory Due: 05-FEB-2002
Applicant: TAKEDA PHARMS
475 HALF DAY RD STE 500
LINCOLNSHIRE, IL 60069

Priority: 1P Org Code: 510
Action Goal: District Goal: 01-MAR-2002
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 25-JAN-2002 by M. GARCIA (HFD-322) 301-594-0095

Establishment: [redacted]
DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 25-JAN-2002
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: [redacted]

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/s/

Xavier Ysern
2/26/02 08:20:24 AM
CHEMIST

Stephen Moore
2/26/02 10:06:12 AM
CHEMIST

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APPLICATION NUMBER:

NDA 21-073/S015

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-073/S-015

PRIOR APPROVAL SUPPLEMENT

Takeda Pharmaceuticals North America, Inc.
Attention: Robert M. Pilson, R.Ph., J.D.
475 Half Day Road, Suite 500
Lincolnshire, IL 60069

Dear Dr. Pilson

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Actos® (pioglitazone HCl) Tablets

NDA Number: 21-073

Supplement Number: S-015

Date of Supplement: October 4, 2001

Date of Receipt: October 5, 2001

This supplement proposes to add [redacted] as a [redacted] of the pioglitazone hydrochloride drug substance.

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on December 5, 2001, in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be February 5, 2002.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room 14B-19
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, please call me at (301) 827-6422.

Sincerely,

{See appended electronic signature page}

Jena Weber
Regulatory Project Manager
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Jena Weber
10/12/01 12:18:27 PM