CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 76-894/S-001

Name: Torsemide Tablets, 5 mg, 10 mg, 10 mg, and 100 mg

Sponsor: Apotex Corp.

Approval Date: October 3, 2007

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-894/S-001

CONTENTS

Reviews / Information Included in this Review	
Approval Letter	X
Approvable Letter	
Labeling	
Labeling Reviews	
Medical Review	
Chemistry Reviews	X
Bioequivalence Review	
Statistical Reviews	
Microbiology Review	
Administrative and Correspondence Documents	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-894/S-001

APPROVAL LETTER

ANDA 76-894/S-001

Apotex Corp.
Attn: Kiran Krishnan
2400 N. Commerce Parkway Suite 400
Weston, FL 33326

Dear Sir:

This is in reference to your supplemental new drug application dated June 30, 2005, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for Torsemide USP, 5 mg, 10 mg, 20 mg, and 100 mg.

Reference is also made to your amendments dated May 16 and August 28, 2007.

This supplemental application, submitted as a "Prior Approval Supplement", provides for the addition of an alternate drug substance manufacturer:

Apotex Pharmachem Inc. (formerly Brantford Chemicals Inc,)
34 Spaulding Drive
Brantford, Ontario
N3T 6B8 Canada

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 abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 76-894/S-001
Division File
Field Copy

Endorsements:

HFD-620/K.Woodland/
HFD-620/R.Bykadi, Ph.D./ September 10, 2007
HFD-617/B.Danso, Pharm.D./
V:\CHEMISTRY DIVISION I\TEAM 5\PM FOLDER\76894S01.RV2.DOC
F/T by:
APPROVABLE

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

/s/

Kathy P. Woodland
9/11/2007 08:44:46 AM
CHEMIST

Gururaj Bykadi
9/12/2007 10:14:31 AM
CHEMIST

Benjamin Danso
10/3/2007 02:27:26 PM
CSO

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

/s/

Paul Schwartz
10/3/2007 02:58:00 PM
Signed for R. Patel

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-894/S-001

CHEMISTRY REVIEWS

Office of Generic Drugs
Chemistry, Manufacturing, and Control Review
Chemistry Review No. 1

ANDA 76-894/S-001

NAME AND ADDRESS OF APPLICANT:

Apotex, Inc.
50 Steinway Boulevard
Etobicoke, ON M9W 6Y3 Canada

US Agent:
Apotex Corp.
Heathrow Drive
Lincolnshire, IL USA 60069

Tel no.: (847) 821-8005
Fax: (847) 353-2982

PURPOSE OF AMENDMENT/SUPPLEMENT:

Prior Approval Supplement
Alternate drug substance manufacturer: Apotex Pharmachem Inc.

AMENDMENTS AND OTHER DATES:

Original supplement submission June 30, 2005

PHARMACOLOGICAL CATEGORY:

Treatment of adema associated with congestive heart failure, renal disease, or hepatic disease.
Treatment of hypertension alone or in combination with other antihypertensive agents.

NONPROPRIETARY NAME: Torsemide USP

DOSAGE FORM:	**STRENGTH:**	**R_x/OTC:**	**RECALLS**
Tablets	5 mg, 10 mg, 20 mg 100 mg	Rx	None

TRADE NAME N/A **ESTABLISHMENT INSPECTION** Pending

RELATED IND/NDA/DMF(s): N/A

STERILIZATION N/A **LABELING** N/A **SAMPLES** N/A

BIOEQUIVALENCY STATUS N/A

ORDER OF REVIEW: The application submission(s) covered by this review was taken in the date order of receipt

Yes _x____ No _____

If no, explain reason(s) below:

COMPONENTS, COMPOSITION, MANUFACTRUING, CONTROLS see next pages

REMARKS AND CONCLUSION: Not Approvable

REVIEWER:
Kathy P. Woodland

DATE COMPLETED:
March 28, 2006

APPEARS THIS WAY
ON ORIGINAL

Redacted 3 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #1

DMF CHECKLIST FOR ANDA# 76-894/S-001 REVIEW # 1

DMF #	DMF TYPE/SUBJECT/HOLDER	ACTION CODE	RESULT OF REVIEW	DATE REVIEW COMPLETED
18466	II/Torsemide/Apotex Pharmachem	1	I	2/28/06

Comments: Reviewed by K.Woodland

ACTION CODES: (1) DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows:

(2) Type 1 DMF;
(3) Reviewed previously and no revision since last review;
(4) Sufficient information in application;
(5) Authority to reference not granted;
(6) DMF not available;
(7) Other (explain under"Comments").

Page of . -- --

Kathy P. Woodland 4/4/06

Reviewer Signature Date

HFD 620 / R. Bykadi, Ph.D. / TL / R. Bykadi 4-20-2006

V:\Chemistry Division I\Team 5\Final Version For DFS\76894s01.rv2.doc

Office of Generic Drugs
Chemistry, Manufacturing, and Control Review
Chemistry Review No. 2

ANDA 76-894/S-001

NAME AND ADDRESS OF APPLICANT:

Apotex, Inc.
50 Steinway Boulevard
Etobicoke, ON M9W 6Y3 Canada

US Agent:
Apotex Corp.
Attn: Kiran Krishnan
2400 N. Commerce Parkway, Suite 400
Weston, FL 33326

Tel: 954-984-3986
Fax: 954-349-4233

PURPOSE OF AMENDMENT/SUPPLEMENT:

Prior Approval Supplement
Alternate drug substance manufacturer: Apotex Pharmachem Inc.

AMENDMENTS AND OTHER DATES:

Original supplement submission	June 30, 2005
Amendment	May 16, 2007
Amendment (Telephone)	August 28, 2007

PHARMACOLOGICAL CATEGORY:

Treatment of adema associated with congestive heart failure, renal disease, or hepatic disease. Treatment of hypertension alone or in combination with other antihypertensive agents.

NONPROPRIETARY NAME: Torsemide USP

DOSAGE FORM:	**STRENGTH:**	**R_x/OTC:**	**RECALLS**
Tablets	5 mg, 10 mg, 20 mg	Rx	None

100 mg

TRADE NAME N/A **ESTABLISHMENT INSPECTION** Acceptable 7/12/2005

RELATED IND/NDA/DMF(s): N/A

STERILIZATION N/A **LABELING** N/A **SAMPLES** N/A

BIOEQUIVALENCY STATUS N/A

ORDER OF REVIEW: The application submission(s) covered by this review was taken in the date order of receipt

Yes _____ No ___x___

If no, explain reason(s) below:
Minor Amendment

COMPONENTS, COMPOSITION, MANUFACTRUING, CONTROLS see next pages

REMARKS AND CONCLUSION: Approvable

REVIEWER:
Kathy P. Woodland

DATE COMPLETED:
September 7, 2007

Redacted 3 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #2

DMF CHECKLIST FOR ANDA# 76-894/S-001 REVIEW # 2

DMF #	DMF TYPE/SUBJECT/HOLDER	ACTION CODE	RESULT OF REVIEW	DATE REVIEW COMPLETED
18466	II/Torsemide/Apotex Pharmachem	1	A	7/25/2007

Comments:Reviewed by K.Woodland

ACTION CODES: (1) DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows:

(2) Type 1 DMF;
(3) Reviewed previously and no revision since last review;
(4) Sufficient information in application;
(5) Authority to reference not granted;
(6) DMF not available;
(7) Other (explain under"Comments").

Page of . -- --

---------- ---------- -------
Reviewer Signature Date

APPEARS THIS WAY ON ORIGINAL

cc:ANDA
Field Copy
Division File
Endorsements:

HFD-620/K.Woodland/
HFD-620/R.Bykadi,Ph.D./ September 10, 2007
V:\CHEMISTRY DIVISION I\TEAM 5\PM FOLDER\76894S01.RV2.DOC
F/t by:

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-894/S-001

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

APOTEX INC.

NDA NO. 76-894 REF NO. Scc-001
NDA SUPPL. FOR Supplier Add.

June 30, 2005

Office of Generic Drugs
CDER, Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

RECEIVED
JUL 0 1 2005
OGD/CDER

submitted
7-11-05

To Whom It May Concern:

Re: PRIOR APPROVAL SUPPLEMENT
Alternate Drug Substance Manufacturer: Apotex Pharmachem Inc.
Torsemide Tablets 5 mg, 10 mg, 20 mg and 100 mg
ANDA No. 76-894

Apotex Inc. is hereby submitting a Prior Approval Supplement to ANDA No. 76-894 for Torsemide Tablets 5 mg, 10 mg, 20 mg and 100 mg. This Supplement is being submitted in triplicate (Archival, Review and Field copies), and the required Field Copy Certification can be found in the last section. The Supplement consists of one volume and contains chemistry and bioequivalence information.

This Prior Approval Supplement is being submitted in accordance with 21 CFR 70(b)(1)(iv) and Guide No. 22-90: OGD Policy and Procedure Guide, as well as Guidance to Industry: Changes to an Approved NDA or ANDA (Revision 1), to seek FDA approval for Apotex Inc. to use an alternate manufacturer, Apotex Pharmachem Inc., for the drug substance, torsemide USP.

We are also requesting the

[redacted]

is a future consideration.

In addition, some minor revisions have been made to the drug substance specification for the material made by the proposed alternate manufacturer. The limit for [redacted] been revised from [redacted] % to [redacted]% in order to comply with the API's specification. Please note that the revised limit of [redacted]% is still in compliance with the USP monograph.

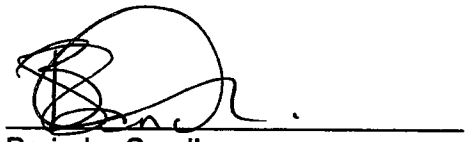
50 Steinway Blvd., Etobicoke, Ontario, Canada M9W 6Y3
Tel. 416.675.0338 Fax. 416.675.0340 www.apotex.com

APOTEX INC.

Furthermore, the tests for [redacted] have been removed from Apotex Inc.'s drug substance specification for the material made by API, to not only be consistent with the API's specification but also due to the fact that this is a highly soluble and rapidly dissolving drug substance.

Should you have any questions or concerns regarding the enclosed, please do not hesitate to contact me by telephone at (416) 675-0338, extension 4207, by fax at (416) 675-0340 or by e-mail at bsandhu@apotex.com.

Best Regards,



Barinder Sandhu
Project Leader, Regulatory Affairs – Solid Dose US

cc: Bernice Tao, Associate Director, Regulatory Affairs – Solid Dose US, Apotex Inc.
Kalpesh Shroff, Project Leader, Regulatory Affairs – Parenterals & US Office, Apotex Corp.

ANDA 76-894/S-001

Apotex Corp.
US Agent for Apotex Inc.
Attention: Tammy McIntire
2400 North Commerce Parkway, Suite 400
Weston, FL 33326

APR 10 2006

Dear Madam:

This is in reference to your supplemental new drug application dated June 30, 2005, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for Torsemide Tablets, 5 mg, 10 mg, 20 mg, and 100 mg.

This supplemental application, submitted as a "Prior Approval Supplement", provides for the addition of an alternate drug substance manufacturer:

Apotex Pharmachem Inc.
(formerly Brantford Chemicals Inc.)
34 Spalding Drive
Brantford, Ontario
N3T 6B8 Canada

The supplemental application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

1. The DMF #18466, Torsemide USP, is currently inadequate. The DMF holder has been notified. Please do not respond to this letter until the DMF holder has informed you that a complete response to the DMF deficiencies has been submitted to the agency.

2. [redacted] Please submit a batch using drug substance that has met all specifications.

3. Page 170 of the supplement refers to "[redacted] Tablets". Please explain.

4. Please note that per current USP 29 monograph for Torsemide, you should have a listing for 'Residual Solvents' test for Torsemide drug substance. However, you [redacted]

The file on this supplemental application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw this supplemental application. Your amendment should respond to all the deficiencies listed. Partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The responses to this letter will be considered as a MINOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this supplemental application, you may request an opportunity for a hearing.

Sincerely yours,

G. Baykadi

for Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 76-894/S-001
Division File
Field Copy

Endorsements:

HFD-620/K.Woodland/4-4-06 K Woodland 4/7/06
HFD-620/R.Bykadi, Ph.D./4-4-06 R. Bykadi 4-7-2006
HFD-617/B.Danso, Pharm.D./4-5-06 4/7/06

V:\FIRMSAM\APOTEX\LTRS&REV\76894S01.RV1.DOC

F/T by: gp/4-6-06

NOT APPROVABLE

APOTEX INC.
CANADA'S PHARMACEUTICAL COMPANY
SOCIÉTÉ PHARMACEUTIQUE ENTIÈREMENT CANADIENNE

October 5, 2006

SUPPLEMENT AMENDMENT
SCC-001/AM.

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

To whom it may concern:

Re: Intent to File Amendment in Response to Minor Deficiency Letter dated April 10, 2006 for Prior Approval Supplement: Addition of Alternate Drug Substance Manufacturer
Torsemide Tablets 5 mg, 10 mg, 20 mg and 100 mg
ANDA No. 76-894/S-001

In reference to the minor deficiency letter dated April 10, 2006 to the Prior Approval Supplement for the addition of an alternate drug substance manufacturer for Torsemide Tablets, ANDA No. 76-894/S-001, and in accordance with 21 CFR 314.120, we are providing notification that we have to delay our amendment in response to the deficiency letter, and expect to respond in six months time before the end of March 2007.

In addition, we would like to notify the Office of Generic Drugs of a change in the contact information of our US Agent at Apotex Corp., effective immediately.

The new contact information is as follows:

John G. Lay
Director, Regulatory Affairs
Apotex Corp.
Tel: (954) 384-3987
Fax: (954) 349-4233

A signed Form FDA 356h is provided.

Should you have any questions or concerns, please do not hesitate to contact me at (416) 401-7889, by fax at (416) 401-3809 or by e-mail at btao@apotex.com.

Sincerely,

Bernice Tao
Director
Regulatory Affairs – Solid Dose US

RECEIVED
OCT 10 2006
OGD / CDER

50 Steinway Blvd., Etobicoke, Ontario, Canada M9W 6Y3
Tel. 416.675.0338 Fax. 416.675.0340 www.apotex.com

Proudly Canadian

ORIGINAL

APOTEX INC.
CANADA'S PHARMACEUTICAL COMPANY
SOCIÉTÉ PHARMACEUTIQUE ENTIÈREMENT CANADIENNE

SUPPLEMENT AMENDMENT
SCC-001-AM

August 28, 2007

By fax to Gururaj Baykadi

Fax: 301-594-0180

10 pages (including this one)

Hard Copy (in triplicate) to follow

Office of Generic Drugs
CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

To Whom It May Concern,

Re: Telephone Amendment in Response to FDA Telephone Deficiency received on August 21, 2007
Torsemide Tablets, 5 mg, 10 mg, 20 mg and 100 mg
ANDA 76-894/S-001

Apotex Inc. is hereby submitting a telephone amendment in response to the telephone deficiency for **Torsemide Tablets, 5 mg, 10 mg, 20 mg and 100 mg ANDA 76-894/S-001**, received from Gururaj Baykadi on August 21, 2007.

Deficiencies:

1 *On page 10, Apotex mentions the use of a* [redacted]

Response:

[redacted]

2. [redacted]

Response: We acknowledge your comment. [redacted] two batches are as follows:

GP0349: [redacted]
GP0350:

This complete response is submitted by fax, and will be followed by hard copy in triplicate (archive, review and field copies).

Please direct any communications regarding this application to Kiran Krishnan at Apotex Corp., the authorized US agent for Apotex Inc., at (954) 984-3986 by fax at (954) 349-4233, or alternatively please do not hesitate to contact me at (416) 401-7889, by fax at (416) 401-3809 or via email at btao@apotex.com.

Sincerely,

Bernice Tao
Director, Regulatory Affairs – US