CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-140

CORRESPONDENCE

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

FEB 3 2000

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

MINOR AMENDMENT
(CMC Information Enclosed)

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS CAPSULES,
1MG, 2MG, 5MG AND 10MG
ANDA #75-140
RESPONSE TO AGENCY LETTER DATED February 2, 2000

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above which is currently pending final approval and to the Agency's CMC comments pertaining to this application which were forwarded to Mylan in a facsimile dated February 2, 2000. In response to the Agency's February 2, 2000 comments, Mylan is amending this application as follows.

A. REGARDING CHEMISTRY ISSUES

Page(s) _____

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Commercial/Confidential

Information and are not

releasable.

2/3/00

... in Attachment G.

Should there be any additional issues pertaining to methods validation, Mylan commits to work with the Agency to resolve any issues, post-approval.

A copy of the Agency correspondence dated February 2, 2000 is included in Attachment H, for the convenience of the reviewer.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

cc: Ms. Ruby Yu (via facsimile)

FRS/dn

Enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

December 7, 1999

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

RE: TERAZOSIN HYDROCHLORIDE CAPSULES (ANHYDROUS)
1 MG, 2 MG, 5 MG AND 10 MG
ANDA 75-140

Dear Mr. Sporn:

As previously discussed, attached is a copy of the letter dated December 3, 1999 that was sent to the Agency by Rothwell, Figg, Ernst & Kurz. Should you have any questions, please do not hesitate to contact the undersigned.

Sincerely,

John O'Donnell/maa

John P. O'Donnell, Ph.D.
Executive Vice President

/maa
Attachment

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

NAI 2nd TA recommended 12/9/99

ORIG AMENDMENT
N/AM

November 24, 1999

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

MINOR AMENDMENT
(Request for Final ANDA Approval)

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS CAPSULES
1MG, 2MG, 5MG AND 10MG
ANDA 75-140

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application (ANDA) identified above, which was granted tentative approval on September 28, 1998, and to the patent litigation pertaining to this application which has now been resolved.

In the original ANDA for Terazosin Hydrochloride Anhydrous Capsules, 5mg, submitted on June 6, 1997 and in our amendment submitted February 6, 1998 for the 1mg, 2mg and 10mg strengths, Mylan provided paragraph IV certifications pertaining to U.S. patents 5,504,207; 5,412,095; 5,294,615; 5,212,176; and 4,251,532. In our amendments dated July 25, 1997 and April 13, 1998, Mylan provided documentation of receipt of the notices sent to the patent and NDA holder of the reference listed drug, with regard to the patent certifications provided in the original ANDA submission for the 5mg strength and subsequent amendment for the 1mg, 2mg and 10mg strengths. The amendment of April 13, 1998 also provided documentation evidencing the filing of a lawsuit by Abbott Laboratories with regard to U.S. patent 5,504,207 only. No action was brought against Mylan with regard to the other 4 patents listed in the paragraph IV patent certifications.

This current amendment provides notification to the Agency, with supporting documentation, to show that Mylan has prevailed in the United States Court of Appeals for the Federal Circuit with respect to the district court decision that the Abbott listed patent for terazosin (U.S. patent 5,504,207) is invalid. Enclosed in Attachment 1 is the Federal Circuit decision which so holds. Also enclosed for your convenience (see Attachment 2) is the decision in Abbott Laboratories v. Geneva Pharmaceuticals, Inc. and Novopharm Limited and Invamed, Inc. This decision is referred to in the Federal Circuit Order issued in the Abbott v. Mylan case.

Based upon the Federal Circuit decision, there is no legal impediment which would preclude final approval of this application, and Mylan hereby requests that such approval be granted.

Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
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Human Resources	(304) 598-5406	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
		Medical Unit	(304) 598-5445		

11-26-99

In addition, as required by the tentative approval letter, this amendment provides notification that no changes have been made to the method of manufacture for the drug product, or to any other conditions under which this application was tentatively approved. Final Printed Labeling was submitted to this application on July 16, 1998.
This amendment is submitted in duplicate. Should you require additional information or have any questions concerning this amendment, please contact the undersigned by telephone at (304) 599-2595, ext. 6600 or by facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

Enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

JUL 16 1998

BIOAVAILABILITY
ORIG AMENDMENT
NDA
FPL

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

FACSIMILE AMENDMENT
(CMC and Labeling Information)

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS CAPSULES,
1MG, 2MG, 5MG AND 10MG
ANDA #75-140
RESPONSE TO AGENCY LETTER DATED JUNE 19, 1998

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above which is currently under review, and to the comments from the Agency which were provided to Mylan in a facsimile dated June 19, 1998. In response to the Agency's June 19, 1998 facsimile comments, Mylan wishes to amended this application as follows.

A. REGARDING CHEMISTRY ISSUES

Page(s) 2

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Information and are not

releasable.

7/16/98

B. REGARDING MISCELLANEOUS ISSUES

In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

FDA COMMENT 1. We require a satisfactory methods validation prior to approval of the ANDA. We will schedule the validation with the District Office once we receive the revised test method and specifications for dissolution.

MYLAN RESPONSE: Mylan acknowledges that a satisfactory methods validation is required prior to approval of the ANDA. Mylan acknowledges that the methods validation will be scheduled with the District Office once the revised test method and specifications for dissolution are received.

FDA COMMENT 2. We remind you that the dissolution specifications identified in the Agency's facsimile transmission dated June 4, 1998 need to be incorporated into your stability and quality control program for all four strengths (1mg, 2mg, 5mg, and 10mg).

MYLAN RESPONSE: Mylan acknowledges and confirms that the dissolution specifications identified in the Agency's facsimile transmission dated June 4, 1998 have been incorporated into our stability and quality control program for all four strengths (1mg, 2mg, 5mg, and 10mg). This information has also been conveyed to the Division of Bioequivalence in our July 15,1998 response to the Division's comments dated June 4, 1998.

C. REGARDING LABELING ISSUES

MYLAN RESPONSE: -Attachment J contains twelve (12) copies of the following final printed bottle labels, package outserts and patient package inserts for Terazosin Hydrochloride Anhydrous Capsules, 1 mg, 2 mg, 5 mg and 10 mg.

BOTTLE LABELS

1 mg	100 capsules	Code - RM2260A
	1000 capsules	Code - RM2260C
2 mg	100 capsules	Code - RM2264A
	1000 capsules	Code - RM2264C
5 mg	100 capsules	Code - RM2268A
	1000 capsules	Code - RM2268C
10 mg	100 capsules	Code - RM1570A
	1000 capsules	Code - RM1570C

PACKAGE OUTSERT: Code -**TERZ:R1A**; REVISED JUNE 1998

PATIENT PACKAGE INSERT: Code - **PL:TERZ:R1A**; REVISED JUNE 1998

The enclosed labeling incorporates the revisions requested in the Agency's letter dated June 19, 1998. A copy of this letter is provided in Attachment H for the convenience of the reviewer.

In order to facilitate the review of this labeling and in accordance with 21 CFR 314.94(a)(8)(iv), Attachment I contains a side-by-side comparison of the final printed labeling to the labeling that was previously submitted. It is noted that prior to approval of this application the agency reserves the right to request further changes in the Mylan labeling based upon the changes in the approved labeling of the listed drug or upon further review of the application.

A copy of the Agency correspondence dated June 19, 1998 is included in Attachment H, for the convenience of the reviewer.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of the technical sections of this amendment, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

FOL

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

NEW CORRESP

JUL 15 1998

This submission represents an incomplete response to the FAX-NA dated 6-19-98. It should be changed to new correspondence. ~~[illegible] should NOT go to [illegible] pending list.~~ [illegible] 7-18-98

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

BIOEQUIVALENCE AMENDMENT

RE: TERAZOSIN HYDROCHLORIDE CAPSULES, 1MG, 2MG, AND 10MG
ANDA #75-140
RESPONSE TO AGENCY CORRESPONDENCE DATED JUNE 4, 1998

Dear Mr. Sporn:

Reference is made to the ANDA identified above, which is currently under review, and to the June 4, 1998 letter pertaining to this application which was forwarded to Mylan from the Office of Generic Drugs' Division of Bioequivalence. In response to the June 4 correspondence, Mylan wishes to amend the application as follows:

A. REGARDING BIOEQUIVALENCE ISSUES:

The Division of Bioequivalence has completed its review and has no further questions at this time. However, you should be informed of the following:

FDA COMMENT 1. You have conducted the dissolution testing for the test and reference products, Terazosin Hydrochloride Capsules, 1mg, 2mg and 10mg in water. The dissolution data indicated that the test product meets the FDA dissolution specification of 80% (Q) of the labeled amount dissolved in 30 minutes.

MYLAN RESPONSE: Mylan acknowledges that the dissolution data obtained from the testing of Terazosin Hydrochloride Capsules, 1mg, 2mg and 10mg in water meets the FDA dissolution specification of 80% (Q) of the labeled amount dissolved in 30 minutes.

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JUL 16 1998
GENERIC DRUGS

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Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Business Development	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Human Resources	(304) 598-5406	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
		Medical Unit	(304) 598-5445		

FDA COMMENT 2. As the test product meets the Tier I dissolution (in water), your request to use the Tier II dissolution method as published in the USP 23, Twentieth Interim Revision, page 4 for hard gelatin capsules is denied. Therefore, the dissolution testing conducted on the test and reference products using 0.1 N HCl plus pepsin as dissolution medium is not acceptable, and consequently, these dissolution data submitted to the Division of Bioequivalence will not be reviewed.

MYLAN RESPONSE: As the test product meets the Tier I dissolution (in water), Mylan acknowledges that our request to use the Tier II dissolution method as published in the USP 23, Twentieth Interim Revision, page 4 for hard gelatin capsules is denied. Based on this, Mylan also acknowledges that the dissolution testing conducted on the test and reference products using 0.1 N HCl plus pepsin as the dissolution medium is not considered acceptable to the Division of Bioequivalence and will, therefore, not be reviewed.

FDA COMMENT 3. The Agency has recently revised the dissolution specification for Terazosin HCl Capsules. The modified dissolution specification for this product is the following:

Medium: water, 900 mL
Apparatus: USP 23, paddle
Speed: 50 rpm
Dissolution Specification: NLT 80% in 60 min.

MYLAN RESPONSE: Mylan acknowledges that the Agency has recently revised the dissolution specification for Terazosin HCl Capsules and hereby commits to incorporate the following dissolution testing and revised specification into its stability and quality control programs for all strengths of Terazosin HCl Anhydrous Capsules (1mg, 2mg, 5mg and 10mg):

Medium: water, 900 mL
Apparatus: USP 23, paddle
Speed: 50 rpm
Dissolution Specification:

Revised finished product specifications, post-approval stability protocols and dissolution procedure reflecting this change are provided in Attachments A, B, and C, respectively.

As indicated in the Amendment to the 5mg application providing for the additional strengths (1mg, 2mg, and 10mg) and in the response to the Agency's telephone request dated 02/12/98, it was noted that Mylan observes significant variability with both the samples and standards when the dissolution is performed in water, especially for the 1mg and 2mg dosage strengths. Upon further investigation, Mylan found that when the method of analysis is changed from detection to analysis at the variability is reduced. The rate of dissolution obtained by analysis is essentially the same as that obtained by the previously submitted

FDA COMMENT 4. The comparative dissolution testing data of the test and reference capsules of 1mg, 2mg and 10mg strengths meet the currently revised dissolution specification, and therefore, the waiver of in vivo bioequivalence study on 1mg, 2mg and 10mg strengths of the test product is granted.

The following dissolution testing will need to be incorporated into your stability and quality control programs:

> The dissolution testing should be conducted in 900mL of water at 37°C using USP Apparatus 2 (paddle) at 50rpm. The test product should meet the following specifications:

MYLAN RESPONSE: Mylan acknowledges that the comparative dissolution testing data of the test and reference capsules of 1mg, 2mg and 10mg strengths meet the currently revised dissolution specification, and therefore, the waiver of in vivo bioequivalence study on 1mg, 2mg and 10mg strengths of the test product is granted.

The dissolution testing requested by the Division of Bioequivalence will be incorporated into Mylan's stability and quality control programs as of the date of this amendment. Mylan has revised the finished product specifications, dissolution procedure, and post-approval stability protocols for Terazosin Hydrochloride Capsules, 1mg, 2mg, 5mg and 10mg to incorporate the requested changes in the procedure and specifications for dissolution. These revised documents are provided in Attachments A, C, and B, respectively.

MISC. COMMENT. Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

MYLAN RESPONSE: Mylan acknowledges and understands that the bioequivalency comments expressed in the letter dated June 4, 1998 are preliminary and may be revised after review of the entire application.

For your reference, a copy of the Agency correspondence dated June 4, 1998 is enclosed. All information and data in this response pertaining to dissolution will also be provided in our response to the June 19, 1998 facsimile correspondence from the Office of Generic Drugs which contained comments regarding the CMC sections of the subject application.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

enclosures

NAI

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

NEW CORR
NC

Proof of Notification and Copy of civil actio
Dt 5/5/98

APR 13 1998

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

PATENT AMENDMENT

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS CAPSULES
1MG, 2MG, 5MG, AND 10MG
ANDA #75-140

Dear Mr. Sporn:

This amendment to the ANDA identified above provides documentation of receipt of the notice required by 21 CFR 314.95(a), as it pertains to the Paragraph IV patent certification submitted in our amended application, dated February 6, 1998. The enclosed information also provides documentation of the notifications of patent infringement filed against Mylan. The attached letter from our Legal Department provides the specifics regarding the enclosed information.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this submission, please contact the undersigned by phone at (304) 599-2595, ext. 6600 or by facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

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APR 14 1998
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Nadine 4/14/98

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Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
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		Medical Unit	(304) 598-5445		

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

APR 13 1998

Offices of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS
CAPSULES, 1 MG, 2 MG, 5 MG AND 10 MG
ANDA NO. 75-140
PATENT AMENDMENT

Dear Mr. Sporn:

Pursuant to 21 CFR 314.95(e), Mylan hereby amends the above referenced application with documentation of receipt of the notice required by 21 CFR 314.95(a). With respect to the 1 mg, 2 mg and 10 mg strengths, I have enclosed documentation of receipt by the owner of the patents, and the holder of the application for the listed drug claimed by said patents. Proof of delivery by Registered Mail, Return Receipt evidences receipt by Abbott Laboratories on February 11, 1998. With respect to the 5 mg strength, this application was previously amended on July 25, 1997, and documentation was provided relative to the required notice.

FDA has also requested a copy of the notification that a lawsuit has been filed within the 45 day period provided for in Section 505(j)(4)(B)(iii) of the Federal Food, Drug and Cosmetic Act. Relative to the 5 mg strength, enclosed is a copy of the Complaint which was filed by Abbott Laboratories on August 1, 1997. Relative to the 1 mg, 2 mg and 10 mg strengths, enclosed is a copy of the Complaint filed by Abbott Laboratories on March 2, 1998.

Sincerely,

Dawn J. Beto, Esq.
Corporate Counsel

DJB/dc

Enclosures

Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
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		Medical Unit	(304) 598-5445		

ABBOTT

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-3500

NDA 3/26/98

NEW CORRESP

NC

March 3, 1998

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs, HFD-600
7500 Standish Place, Rm. 150
Rockville, Maryland 20855

RE: Abbott Laboratories v. Mylan Pharmaceuticals, Inc., and Mylan Pharmaceuticals, Inc. ANDA 75-140

Gentlemen:

ANDA 75-140 filed by Mylan Pharmaceuticals, Inc. ("Mylan") contains certifications under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) asserting that the manufacture, use and sale of its terazosin hydrochloride capsules* does not infringe five United States patents owned by Abbott Laboratories ("Abbott"). Specifically, the certifications are as to U.S. Patent Nos. 4,251,532, 5,212,176, 5,294,615, 5,412,095, and 5,504,207. Notice of these certifications was received by Abbott on February 11, 1998.

This letter is to advise FDA that on March 2, 1998, Abbott filed a lawsuit against Mylan in federal district court in Chicago, Illinois, alleging infringement of one of the above-referenced patents (U.S. Patent No. 5,504,207). A copy of the lawsuit is enclosed. (No. 98C 1280 (N.D. Ill. filed March 2, 1998).)

Because Abbott has filed its action within 45 days of receipt of notice of the certifications, pursuant to the Federal Food, Drug and Cosmetic Act, §505(j)(4)(B)(iii), **the agency cannot approve ANDA 75-140 until "the expiration of the thirty-month period beginning on the date of the receipt of the notice...**or such shorter or longer period as the court may order..."

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MAR 09 1998
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Modified 3-11-98

Should you have any questions concerning this matter, please feel free to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844

cc: Division of Cardio-Renal Drug Products, HFD-110
Central Document Room, Park Bldg., Rm. 2-14
Drug Information Services Branch, HFD-84

*The 1 mg, 2 mg and 10 mg capsules are a generic versions of Abbott's Hytrin® capsules. Previously, Mylan had filed a similar certification with respect to its 5 mg capsule and Abbott filed suit against Mylan. See my letter to you dated August 5, 1997 (copy enclosed).

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

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

N/AB

FEB 24 1998

TELEPHONE AMENDMENT

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS CAPSULES
1MG, 2MG, 5MG, AND 10MG
ANDA #75-140
RESPONSE TO FEBRUARY 12, 1998 TELEPHONE REQUEST

Dear Mr. Sporn:

Reference is made to the pending ANDA identified above which is currently under review and to a February 12, 1998 telephone request for additional information which was received from the Division of Bioequivalence. Enclosed, as requested in the February 12 telephone conversation, please find dissolution profile data for Mylan's Terazosin Hydrochloride Anhydrous Capsules, 1mg, 2mg, 5mg, and 10mg and the reference listed drug (Hytrin® Capsules) using water as the dissolution medium. This data is included in the attached report which provides dissolution data for both Mylan's Terazosin Hydrochloride Anhydrous Capsules and Hytrin® Capsules using either water, 0.01N HCl, or 0.1N HCl with pepsin as the dissolution medium. This report provides Mylan's rationale for using 0.1N HCl with pepsin as the proposed dissolution medium for this product.

Pursuant to 21 CFR 314.96(b) we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office.

This amendment is submitted in duplicate. Should you have any questions regarding this submission or require additional information, please contact the undersigned by phone at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

cc: Dr. Lizzie Sanchez (via facsimile)

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FEB 25 1998
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[RDLIB.ANDA.TERAZOSIN-CAP-5MG]TELEPHONE-AMENDMENT-021298.WPD

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
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MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

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

FEB 12 1998

NC

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS CAPSULES, 5 MG
ANDA #75-140
AMENDMENT TO PROVIDE FOR THE ADDITION
OF 1 MG, 2 MG, AND 10 MG CAPSULES

Dear Mr. Sporn:

Mylan wishes to amend the above referenced amendment for ANDA #75-140 which was submitted to the Agency on February 6, 1998. Subsequent to its submission to the Agency, we found that page 401, page 2 of 3 of the Table of Contents for Section VIII entitled Raw Materials Controls was inadvertently not paginated.

Attached please find a replacement for page 401 of the application (labeled as page 401(a)) which contains a paginated copy of page 2 of 3 of the Table of Contents.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment as submitted to the Office of Generic Drugs has been forwarded to the FDA's Baltimore District Office.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

RECEIVED
FEB 13 1998
GENERIC DRUGS

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

BIOAVAILABILITY

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

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

FEB 6 1998

ORIG AMENDMENT

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS CAPSULES, 5 MG
ANDA #75-140
AMENDMENT TO PROVIDE FOR THE ADDITION
OF 1 MG, 2 MG, AND 10 MG CAPSULES

change to 10 mg 4/6/98

Dear Mr. Sporn:

The enclosed amendment to the pending application referenced above for Terazosin Hydrochloride Anhydrous Capsules, 5mg, provides for the inclusion of three additional dosage strengths (1 mg, 2 mg and 10 mg capsules).

Terazosin Hydrochloride Anhydrous Capsules, 1 mg, 2 mg and 10 mg will be manufactured, tested, packaged and labeled by Mylan Pharmaceuticals Inc. in Morgantown, WV following the procedures for the 5 mg capsules, as currently provided in the ANDA. All four dosage strengths of Terazosin Hydrochloride Anhydrous Capsules are compositionally proportional. Based on the compositional proportionality of these products and the bioequivalence of the 5 mg capsule versus the reference listed drug (Hytrin® Capsules, 5 mg), as demonstrated in the data provided in the original application, this amendment contains an *in vivo* biowaiver request for the 1 mg, 2 mg, and 10 mg dosage strengths.

This amendment consists of a total of 9 volumes.
- Archival Copy - 3 volumes.
- Review Copy - 4 volumes.
  - Technical Section For Chemistry - 3 volumes.
  - Technical Section For Pharmacokinetics - 1 volume.
- Analytical Methods - 2 extra copies; 1 volume each.

As required by 21 CFR 314.96(b) we certify that a true copy of the technical sections of this amendment, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office. The following Table of Contents and Reader's Guide detail the documentation submitted in support of this amendment.

This amendment is submitted in duplicate. All correspondence regarding this amendment should be directed to the attention of the undersigned at Mylan Pharmaceuticals Inc., P.O. Box 4310, 781 Chestnut Ridge Road, Morgantown WV, 26504-4310, or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

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FEB 0 9 1998
GENERIC DRUGS

Madam 2/17

Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
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Human Resources	(304) 598-5406	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
		Medical Unit	(304) 598-5445		

[RDLIB.ANDA TERAZOSIN]SECTIONS-01THRU07

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

JAN 30 1998

AMENDMENT
N/A m

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

MINOR AMENDMENT

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS CAPSULES, 5 MG
ANDA #75-140
RESPONSE TO AGENCY LETTER DATED NOVEMBER 12, 1997

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above which is currently under review, and to the comments from the Agency regarding this application which were forwarded to Mylan by facsimile on November 12, 1997. With regard to the November 12 comments, Mylan wishes to amend this application with the following:

REGARDING CHEMISTRY ISSUES:

Page(s) 3

Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

11/30/98

In summary, Mylan has taken all possible manufacturing precautions to maintain an "anhydrous" drug substance throughout the processing and packaging of this product. In addition, available drug substance stability data (*i.e.*, loss on drying) demonstrates that two years of room temperature storage in fiber drums, without dessication, does not yield a hydrated form. These data strongly suggest that

the anhydrous drug substance is not hygroscopic. Based upon these data, Mylan will maintain the term "anhydrous" in the product description in order to differentiate this drug substance and drug product from those manufactured using a hydrated form of the drug substance.

FDA COMMENTS 2/3: Container (100's and 1000's) and Insert labeling deficiencies:

MYLAN RESPONSE: Attachment O contains four (4) copies of the draft outsert, patient package insert and bottle labels for Terazosin Hydrochloride Capsules, 5 mg. The enclosed labeling incorporates the revisions requested in the Agency's correspondence of November 12, 1997. A copy of this correspondence is provided in Attachment N for the convenience of the reviewer.

Mylan acknowledges that the Agency requested final printed labeling instead of draft labeling. However, Mylan plans to amend the referenced ANDA (ANDA n the near future to provide for the 1 mg, 2 mg, and 10 mg strengths. The addition of the 1 mg, 2 mg, and 10 mg strengths will require that the labeling be revised to include information regarding the new strengths. Accordingly, the labeling for the 5 mg strength remains in draft format.

In order to facilitate the review of this labeling, Attachment P contains a side-by-side comparison of the revised draft bottle labels and outsert/patient package insert (TERZ:R1) to the draft labeling that was previously submitted. It is noted that prior to approval of this application the agency reserves the right to request further changes in the Mylan labeling based upon changes in the approved labeling of the listed drug or upon further review of the application.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office.

For your reference, a copy of the Agency letter dated November 12, 1997, is enclosed in Attachment N.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned by phone at (304) 599-2595, ext. 6600 or by facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

ANDA 75-140

OCT 23 1997

Mylan Pharmaceuticals Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, West Virginia 26504-4310

Dear Sir:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Terazosin Hydrochloride Capsules 5 mg.

1. The Division of Bioequivalence has completed its review and has no further questions at this time.

2. The following dissolution testing will need to be incorporated into your stability and quality control programs. The dissolution testing should be conducted in 900 mL of water at 37°C using USP XXIII apparatus II (paddle) at 50 rpm. The test product should meet the following specification:

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,

/S/

Rabindra N. Patnaik, Ph.D.
Acting Director,
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

WORKING AMENDMENT

SEP 3 1997

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

TELEPHONE AMENDMENT

RE: TERAZOSIN HYDROCHLORIDE CAPSULES, 5MG
ANDA #75-140

Dear Mr. Sporn:

Reference is made to the pending ANDA identified above and to a September 3, 1997 telephone call from Dr. Lizzie Sanchez regarding this application.

Enclosed, as requested by Dr. Sanchez, is a copy of the analytical procedure for evaluating the dissolution of Terazosin Hydrochloride Capsules (Anhydrous), 5mg. This procedure was used to generate the dissolution data for the exhibit batch (Lot 2C012N), the results of which appear on page 412 (certificate of analysis) and page 414 (dissolution profile) of the original application.

Should you have any further questions regarding this amendment, please contact the undersigned by phone at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

cc: Dr. Lizzie Sanchez via facsimile

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SEP 4 - 1997
GENERIC DRUGS

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Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
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Information Systems (304) 285-6404
Label Control (800) 848-0463
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Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P.O. BOX 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

NAI
8/4/97

July 25, 1997

NEW CORRESP

Offices of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: TERAZOSIN HYDROCHLORIDE ANHYDROUS
CAPSULES, 5 MG
ANDA NO. 75-140

Dear Mr. Sporn:

Pursuant to 21 CFR 314.95(e), Mylan hereby amends the above referenced application with documentation of receipt of the notice required by 21 CFR 314.95(a). I have enclosed documentation of receipt by the owner of the patents, and the holder of the application for the listed drug claimed by said patents. Proof of delivery by Registered Mail, Return Receipt evidences receipt by Abbott Laboratories on July 15, 1997.

Sincerely,

Dawn J. Beto, Esq.
Senior Counsel

DJB/dc

Enclosures

RECEIVED

8-1-97

Department - Fax Numbers
Administration (304) 599-7284
Human Resources (304) 598-5406
Purchasing (304) 598-5401
Sales & Marketing (304) 598-3232

Label Control (304) 599-2595 Ext. 330
Accounting (304) 598-5403
Legal Services (304) 598-5408
Quality Control (304) 598-5407
Research & Development (304) 598-5409

Penicillin Plant (304) 599-2595 Ext. 273
Purchasing & Medical Unit (304) 598-5401
Business Development (304) 599-7284
Information Services (304) 598-5404
Maintenance & Engineering (304) 598-5411

ANDA 75-140

Mylan Pharmaceuticals Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, West Virginia 26504-4310

JUL 7 1997

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Terazosin Hydrochloride Capsules 5 mg

DATE OF APPLICATION: June 6, 1997

DATE OF RECEIPT: June 9, 1997

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Jim Wilson
Project Manager
(301) 827-5848

Sincerely yours,

/S/

Jerry Phillips 7/2/97
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

JUN 6 97

ELECTRONIC DATA ENCLOSED
BIOEQUIVALENCE DATA ENCLOSED

505(j)(2)(A)(ok)
Anne Marie T. Weibel
6/13/97

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

RE: TERAZOSIN HYDROCHLORIDE CAPSULES, 5 MG

Dear Mr. Sporn:

Pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act and 21 CFR § 314.92 and 314.94, we submit the enclosed abbreviated new drug application for:

Proprietary Name: None
Established Name: Terazosin Hydrochloride Capsules
This application consists of a total of 17 volumes.
- Archival Copy - 7 volumes.
- Review Copy - 8 volumes.
  - Technical Section For Chemistry - 3 volumes.
  - Technical Section For Pharmacokinetics - 5 volumes.
- Analytical Methods - 2 extra copies; 1 volume each.

NOTE: The Technical Section for Pharmacokinetics of the review copy and the archival copy each contain a data diskette for the bioequivalence studies conducted in support of this application. An electronic data set, using the Office of Generic Drug's new EVA software program, is currently being prepared and will be submitted as an amendment to this application as soon as it becomes available.

This application provides for the manufacture of Terazosin Hydrochloride Capsules, 5 mg. All operations in the manufacture, packaging, and labeling of the drug product are performed by Mylan Pharmaceuticals Inc., 781 Chestnut Ridge Road, Morgantown, WV 26505-2730.

As required by 21 CFR 314.94(d)(5) we certify that a true copy of the technical sections of this application, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office. The following Table of Contents and Reader's Guide detail the documentation submitted in support of this application.

All correspondence regarding this application should be directed to the attention of the undersigned at Mylan Pharmaceuticals Inc., P.O. Box 4310, 781 Chestnut Ridge Road, Morgantown WV, 26504-4310, or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

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JUN 0 9 1997
GENERIC DRUGS

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Accounting	(304) 285-6403
Administration	(304) 599-7284
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