CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-100

CORRESPONDENCE

lek

LEK USA, Inc.

333 Sylvan Avenue
Englewood Cliffs
N.J. 07632

Phone: (201) 541 9310
Fax: (201) 541 9314

FPL

NEW CORRESP

NC to FA

Food and Drug Administration
Central Document Room
Metro Park North -II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

October 20, 1998

Product: BROMOCRIPTINE MESYLATE CAPSULES USP, 5 mg (ANDA # 75 - 100): FACSIMILE AMENDMENT

Manufacturer: LEK Pharmaceutical and Chemical Company d.d.
U.S. Contact: LEK USA, Inc.
Andej Gasperlin
Director

To whom it may concern:

On behalf of Lek Pharmaceutical and Chemical Company d.d., enclosed please find our Facsimile Amendment (archival, review, and field copies) for BROMOCRIPTINE MESYLATE CAPSULES USP, 5 mg, in response to FDA's Deficency Letter of September 22, 1998.

We trust that this Facsimile Amendment satisfactorily answers FDA's subject letter.

Thank you.

Sincerely yours,

OCT 22 1998

Andrej Gasperlin
Director

Encl:

cc: M. Sopar-Urleb - LEK d.d., Ljubljana, Slovenia

lek

Pharmaceutical and Chemical Company d.d.
Verovškova 57, 1526 Ljubljana, SLOVENIA
Tel: + 386 61 188 21 11

Director Division of Labeling and Program Support

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration

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7500 Standish Place, Room 150
Rockville, MD 20855-2773
USA

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Cable: lek ljubljana si
Regulatory Affairs
Tel: + 386 61 181 41 11
+ 386 61 553 150
Facsimile: + 386 61 557 881

October 19, 1998

Dear Sir/Madam,

Re: ANDA # 75-100
on Bromocriptine Mesylate Capsules USP, 5 mg -
FACSIMILE AMENDMENT

Please refer to our Abbreviated New Drug Application (ANDA) # 75-100 dated March 25, 1997, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Bromocriptine Mesylate Capsules USP, 5 mg and to our amendment(s) dated May 15, 1997 and April 9, 1998.

Reference is also made to the Deficiency Letter concerning CMC section and labeling dated September 22, 1998.

Enclosed please find replies to all deficiencies listed in the Deficiency Letter. Each question from your letter is directly followed by our answer. The chemistry deficiencies are listed first, the labeling deficiencies follow.

The documentation is sent in three copies (review, archival and field copy). Because Lek is a foreign applicant the third (field) copy is being submittted directly to OGD as instructed under 21 CFR 314.440. Lek hereby certifies that the third (field) copy provided is a true copy of the archival and review copies of the application.

With best regards,

Lek Pharmaceutical and Chemical Company d.d.
Regulatory Affairs

Mirjan Žorž, Ph.D.
Head of Department

Mirjam Šopar-Urleb
Director

RECD

OCT 2 2 1998

lek

Pharmaceutical and Chemical Company d.d.
Verovškova 57, 1526 Ljubljana, SLOVENIA

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Food and Drug Administration
Central Document Room
Metro Park North II
7500 Standish place, Room 150

FACSIMILE MESSAGE

00 1 301 827 4337

NDA [illegible] AMENDMENT

To: ***Mrs Denise Huie***
Project manager

N/FA

From: Regulatory Affairs - Pharmaceuticals
➢ Mr Mirjan Žorž PhD

Date: October 20, 1998

No.:

No. of page(s): 1+4

cc Lek: Mr A.Gašperlin LEK USA, Inc

Subject: *ANDA 75-100 Facsimile Amendment*

Dear Mrs Huie,

Reference is made to your Facsimile Amendment dated September 22, 1998 concerning ANDA 75-100 for Bromocryptine Mesylate Capsules USP, 5 mg. We have answered and completed all the requirements stated in the mentioned facsimile. The relevant documents are being sent today to your address via courier and is planned to be at your disposal on October 22, 1998, at the latest. Please find for your information the attached copies of:

1. Official letter of our representative office in USA
2. Cover letter
3. Form FDA 356h

With best regards,

Lek Pharmaceutical and Chemical Company d.d.
Regulatory Affairs

Mirjan Žorž PhD
Head of Department

Mirjam Šopar-Urleb
Director

lek

LEK USA, Inc.

333 Sylvan Avenue
Englewood Cliffs
N.J. 07632

Phone: (201) 541 9310
Fax: (201) 541 9314

Food and Drug Administration
CDER / Office of Generic Drugs
Document Control Room
MPN II
7500 Standish Place
Rockville, MD, 20855

ORIG AMENDMENT

April 9, 1998

RE :	ANDA 75-100
Product :	BROMOCRIPTINE Mesylate Capsules, USP 5.0 mg
Manufacturer:	LEK Pharmaceutical and Chemical Company d.d. Ljubljana, Slovenia
U.S. Agent :	LEK USA, Inc. Andrej Gasperlin Vice President, Sales & Marketing

Major Amendment Reply

Dear Sir / Madam :

On behalf of LEK Pharmaceutical and Chemical Company d.d., please find herewith enclosed the replies to the FDA Major Amendment letter dated September 25, 1997.

To facilitate the review of the information submitted a copy of FDA's September 25, 1997 letter and Lek d.d.'s letter dated April 2, 1998 are attached.

Thanks for your attention.

Sincerely,

Andrej Gasperlin
Vice President, Sales & Marketing

APR 10 1998

GENERIC DRUGS

Encl.
CC.: Mrs. Mirjam - Šopar Urleb, Product Registration

brcp09ap8

lek

Lek Pharmaceutical and Chemical Company d.d.

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Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration

Document Control Room
MPN II
7500 Standish Place
Rockville, MD 20855
USA

April 2, 1998

Dear Sir/Madam,

RE: ANDA # 75-100 on
Bromocriptine Mesylate Capsules USP, 5 mg -
MAJOR AMENDMENT

Please refer to our Abbreviated New Drug Application (ANDA) dated March 25, 1997, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Bromocriptine Mesylate Capsules USP, 5 mg and to our amendment dated May 15, 1997.

Reference is also made to the Deficiency Letter concerning CMC section and labeling dated September 25, 1997.

Enclosed please find replies to all deficiencies listed in the above mentioned Deficiency Letter. Each question from your letter is directly followed by our answer. The chemistry deficiencies are listed first, the labeling deficiencies follow.

The documentation is sent in three copies (review, archival and field copy). Because Lek is a foreign applicant the third (field) copy is being submitted directly to OGD as instructed under 21 CFR 314.440. Lek

APR 10 1998

GENERIC DRUGS

hereby certifies that the third (field) copy provided is a true copy of the archival and review copies of the application.

We hope we have completely replied to all deficiencies listed in your letter and we do hope that the review clock will be reactivated.

We appreciate your consideration.

Sincerely yours,

Dr. V. Gabrijelčič
Project Manager

M. Šopar-Urleb
Director Regulatory Affairs

lek

505(j)(2)(A)(ok)
Anna Marie T. Weiler
5/21/97

LEK USA, Inc.

333 Sylvan Avenue
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N.J. 07632

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Fax: (201) 541 9314

Mr. Jerry Phillips
Director, Division of Labeling and Program Support
Food and Drug Administration
CDER / Office of Generic Drugs
MPN 2 - HFD - 600
7500 Standish Place
Rockville, MD, 20855

N/A AMENDMENT

May 15, 1997

RE :	ANDA 75-100
Product :	BROMOCRIPTINE Mesylate Capsules, USP 5.0 mg
Manufacturer:	LEK Pharmaceutical and Chemical Company d.d. Ljubljana, Slovenia
U.S. Agent :	LEK USA, Inc. Andrej Gasperlin Vice President, Sales & Marketing

Reply to Refuse to file letter, May 08, 1997

Dear Mr. Phillips :

On behalf of LEK Pharmaceutical and Chemical Company d.d., please find herewith enclosed the replies to the Refuse to file letter dated May 08, 1997.

To facilitate the review of the information submitted a copy of FDA's May 08, 1997 letter and Lek d.d.'s letter dated May 12, 1997 are attached.

Thanks for your attention.

Sincerely,

Andrej Gasperlin
Vice President, Sales & Marketing

RECEIVED
MAY 16 1997

Encl.
CC.: Mrs. Mirjam - Šopar Urleb, Head of Product Registration
Mr. Janko Žmitek, Ph.D. , Director R&D

brcp15m7

lek

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Telefax: +386 61/159 51 25

Mr. Jerry Phillips
Director Division of Labeling and
Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration

MPN II, HFD - 600
7500 Standish Place
Rockville, MD 20855
USA

May 12, 1997

RE: ANDA 75-100

Dear Mr. Phillips,

Please refer to our Abbreviated New Drug Application (ANDA) dated March 25, 1997, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Bromocriptine Mesylate Capsules, USP 5 mg, and to FDA refuse to file letter dated May 8, 1997.

Please find as follows:

Comparative *in vitro* dissolution data between our proposed drug product and the reference listed drug **are included** in the ANDA on **pages 721-731**. They are part of the Section VI: Bioavailability/ Bioequivalence.
Please accept our apology since this was not indicated in the table of contents. The properly revised table of contents (indicating where in the ANDA the comparative *in vitro* dissolution testing data are presented as well as where the Certificates of Analysis of our and reference listed product are included) is enclosed.

While we regret that we did not include the comparative dissolution data in the table of contents the data were actually contained in the submission and we request that the Refuse to file letter be resented and that the filing date be considered the receipt date of the application in the Office of Generic Drugs.

We appreciate your consideration.

Looking forward to hearing from you soon.

Sincerely yours,

M. Šopar-Urleb
Head of Product Registration

Dr. J. Žmitek
R&D Director

Enclosures:

- Revised table of contents
- Additional copies of comparative *in vitro* dissolution data (pages 721-731) for your convenience

ANDA 75-100

Lek USA Inc.
Attention: Andrej Gasperlin
U.S. Agent for: Lek Pharmaceutical and Chemical Company d.d.
333 Sylvan Avenue, 2nd Floor
Engelwood Cliffs, NJ 07632

Dear Sir:

This letter is a correction to our "Refuse to File" letter dated May 8, 1997. In addition, we refer to your correspondence dated May 15, 1997.

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: Bromocriptine Mesylate Capsules USP, 5 mg

DATE OF APPLICATION: March 25, 1997

DATE OF RECEIPT: March 28, 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:

Sheila O'Keefe
Project Manager
(301) 827-5848

Sincerely yours,

/S/

Jerry Phillips 5/27/97
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-100

Lek USA Inc.
Attention: Andrej Gasperlin
U.S. Agent for: Lek Pharmaceutical and Chemical Company d.d.
333 Sylvan Avenue, 2nd Floor
Engelwood Cliffs, NJ 07632

MAY 8 1997

Dear Sir:

Please refer to your abbreviated new drug application (ANDA) dated March 25, 1997, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Bromocriptine Mesylate Capsules USP, 5 mg.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

> You have failed to submit comparative *in vitro* dissolution data between your proposed drug product and the reference listed drug. Comparative dissolution data profiles should include individual tablet data as well as the mean, range, and standard deviation at each point for twelve tablets. The lot numbers of the tablets tested should also be identified.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3)If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Anna Marie H. Weikel
Project Manager
(301) 827-5862

Sincerely yours,

/S/

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

ANDA 75-100
cc:

Endorsement:

/S/

Release to File
5/5/97
Ana Marie H. Weidel

lek

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FDA
Center for drug evaluation and research
Office of generic drugs

MPN II, HFD - 632
7500 Standish Place
Rockville, MD 20855

March 25, 1997

Dear Sirs,

Enclosed please find original Abbreviated New Drug Application submission for Bromocriptine Mesylate Capsules, USP 5 mg.

This ANDA is submitted pursuant to the Section 505(j) of the Food, Drug and Cosmetics Act and regulations implementing that Act (Title 21 of the Code of Federal Regulations), and contains in Lek's opinion and to the best of our knowledge all information required.

Please note the following identifying data:

Type of submission: ANDA - original

Name, title, signature, and address of the applicant:
Lek
Pharmaceutical and Chemical Company d.d.
Verovškova 57
1526 Ljubljana
Slovenia

RECEIVED
1997

Responsible Official:
Dr. J. Žmitek, Director of Research and Development Division

Established name of the drug product:
Bromocriptine Mesylate Capsules, USP 5 mg

Number of volumes submitted:

- 1 archival copy (6 volumes)
- 1 review copy (7 volumes)
- 1 third copy (6 volumes)

Should you have any questions concerning this ANDA, please contact:

Lek USA, Inc.
Mr. A.Gašperlin, Vice President Sales&Marketing
333 Sylvan Avenue
Englewood Cliffs, New Jersey 07632
Phone: 201 541-9310
Fax: 201 541-9314

or directly Headquaters in Ljubljana:

Research and Development Division
Mrs. M.Šopar-Urleb, Head of Product Registration
Phone: + 386 61 553 150
Fax: + 386 61 159 51 25

Sincerely yours,

Dr. Janko Žmitek
R&D Director

CC: Mr. A. Gašperlin, Lek USA, Inc.