

\* CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-100

CORRESPONDENCE



LEK USA, Inc.

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

333 Sylvan Avenue  
Englewood Cliffs  
N.J. 07632

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

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 Deficiency Letter of September 22, 1998.

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

Thank you.

Sincerely yours,

Andrej Gasperlin  
Director

Encl.

OCT 22 1998

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

Director Division of Labeling and Program Support

**Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration****MPN II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773  
USA**

Facsimile: + 386 61 168 35 17

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**

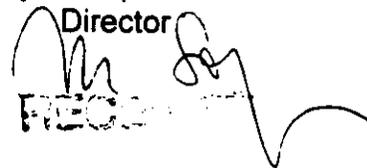
Please refer to our Abbreviated New Drug Application (ANDA) # 75-100 dated March 25, 1997, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Bromocriptine Mesylate Capsules USP, 5 mg and to our amendment(s) dated May 15, 1997 and April 9, 1998.

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 submitted 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.o.**  
**Regulatory Affairs****Mirjan Žorž, Ph.D.**  
Head of Department**Mirjam Šopar-Urleb**  
Director  
RECEIVED

OCT 22 1998



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

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

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 Facsimile: + 386 61 168 35 17  
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**FACSIMILE MESSAGE**

**00 1 301 827 4337**

**NDA 75-100 AMENDMENT**

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

From: Regulatory Affairs - Pharmaceuticals  
 > Mr Mirjan Žorž PhD

Date: October 20, 1998

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 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**

*N/A*

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

*Recd...  
4/21/98*

**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*  
Andrej Gasperlin  
Vice President, Sales & Marketing

**REC'D**

**APR 10 1998**

**GENERIC DRUGS**

brcp09ap8

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



**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**

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**Research and Development**  
Telephone: +386 61/181 41 11  
Telefax: +386 61/159 51 25

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.

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APR 10 1998

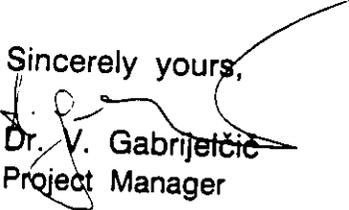
**GENERIC DRUGS**

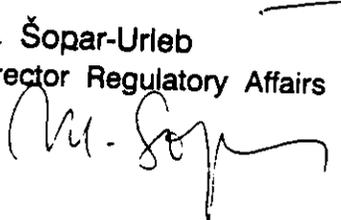
hereby certifies that the third (field) copy provided is a true copy of the archival and review copies of the application.

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. Gabriječić  
Project Manager

  
M. Šopar-Urleb  
Director Regulatory Affairs



505(j)(2)(a)(ok)  
Annamarie N. Weiler  
5/2/97

LEK USA, Inc.

333 Syvan Avenue  
Englewood Cliffs  
N.J. 07632

Phone: (201) 541 9310  
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*  
Andrej Gasperlin  
Vice President, Sales & Marketing

RECEIVED

MAY 16 1997

GENERO DIVISION

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



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

**Lek Pharmaceutical and  
Chemical Company d.d.**

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Telephone: +386 61/181 41 11  
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**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.

MAY 10 1997

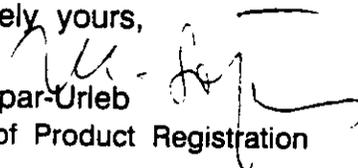
ORIGINAL FILED

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. 27  
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 *J* 5/27/97  
Director  
Division of Labeling and Program Support  
Office of Generic Drugs  
Center for Drug Evaluation and Research

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

-----  
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----- 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/*



*Refuse to File  
5/5/97  
Ana Marie H. Weibel*

**FDA  
Center for drug evaluation and  
research  
Office of generic drugs**

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

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Telefax: +386 61/159 51 25

*used in  
computer  
C. Hedger  
7-19-9*

**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**

8 1997

**Responsible Official:**

Dr. J. Žmitek, Director of Research and Development Division

*65-1000-1000*

**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 Headquarters in Ljubljana:

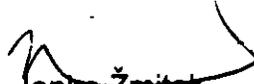
Research and Development Division

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.