

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

75491

ADMINISTRATIVE DOCUMENTS

Telephone Conversation Memorandum

ANDA: 75-491
DRUG: Bupropion Hydrochloride Tablets, 75 mg and 100 mg
FIRM: Mylan Pharmaceuticals Inc.
PERSONS INVOLVED: Mylan: John Odonnell, Bill Addictson, Frank Sisto, Marilyn Friedly,
FDA: Ubrani Venkataram, Tim Ames
PHONE NUMBER: 1-800-848-0461
DATE: March 20, 2000

Background:

Firm had been issued a FAX deficiency February 25, 2000 which contained the comment:

2. Please include a test and provide specifications for moisture content of the coated tablets as an in-process control.

Previous clarification of this request was unsatisfactory to the firm and they requested a telephone conference to discuss this issue.

Upon contacting the firm UVenkataram (UV) asked the firm to explain their coating process and what in-process controls were being used to monitor the moisture content. Mylan explained that the film coating process

The firm further explained

UV pointed out that while there was a weight gain parameter for the color coat, none appeared for the clear coat. It was suggested that the firm implement a specification for this missing parameter as an indirect method for monitoring moisture content. UV also pointed out that the finished product specification for moisture content of NMT % seemed to be high considering the data regarding this specification, and that tightening this specification seems to be appropriate as a further control for moisture content.

The firm suggested that to further control the moisture content they would

something in the range of NMT $\%$ moisture content to We indicated they should submit this in their response and it would be considered.

Timothy W. Ames, R.Ph., M.P.H.
Project Manager, Div Chem. II, Team 8, OGD

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cc: ANDA 75-491
Division file (1)

**REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 75-491 Date of Submission: October 30, 1998

Applicant's Name: Mylan Pharmaceuticals Inc.

Established Name: Bupropion Hydrochloride Tablets, 75 mg and
100 mg

Labeling Deficiencies:

1. CONTAINER 100s and 500s
 - a. Relocate the "WARNING:" statement to the main panel.
 - b. We encourage you to differentiate your product strengths by boxing, contrasting colors, or some other means.

2. INSERT
 - a. GENERAL COMMENT

Delete the word _____ except where indicated below:

 - i. DESCRIPTION (4 instances, including "Bupropion hydrochloride powder ...")
 - ii. INDICATIONS AND USAGE, first sentence ("Bupropion Hydrochloric Tablets are ...")
 - iii. WARNINGS - Seizures
 - A). First paragraph (2 instances)
 - B). Second paragraph
 - C). Recommendations for reducing the risk of seizure (first 2 instances)
 - iv. ADVERSE REACTIONS, third paragraph.
 - v. DRUG ABUSE AND DEPENDENCE, second paragraph.

vi. OVERDOSAGE

Human Overdose Experience

A). First paragraph (2 instances)

B). Second paragraph (first instance)

vii. DOSAGE AND ADMINISTRATION

A). General Dosing Considerations

1). First paragraph

2). Second paragraph (first instance
... bupropion hydrochloride tablet
...)

B). Increasing the Dosage Above 300 mg/Day
(2 instances)

viii. HOW SUPPLIED

"Bupropion Hydrochloride Tablets are ..."

b. DESCRIPTION

i. Revise the chemical name to read as follows:

(±)-1-(3 ... amino]-1-propanone hydrochloride

ii. Revise the molecular weight to be "276.2".

iii. "... methylcellulose, anhydrous lactose, ..."

c. CLINICAL PHARMACOLOGY

Last sentence - "mcg" rather than

d. INDICATIONS AND USAGE

i. First paragraph, second sentence - ...
seizures in a dose-dependent manner with ...

ii. First paragraph, last sentence - ... have
been conducted (see **WARNINGS**).

e. **CONTRAINDICATIONS**

Add the following as the second sentence:

... disorder. Bupropion is contraindicated in patients treated with ZYBAN™ (bupropion hydrochloride) Sustained-Release Tablets, or any other medications that contain bupropion because the incidence of seizure is dose dependent. Bupropion is also contraindicated ...

f. **WARNINGS**

Add the following text as the first paragraph:

Patients should be made aware that bupropion hydrochloride tablets contain the same active ingredient found in ZYBAN™, used as an aid to smoking cessation treatment, and that bupropion hydrochloride should not be used in combination with ZYBAN™, or any other medications that contain bupropion.

g. **PRECAUTIONS**

Information for Patients - Add the following text as the first paragraph:

Patients should be made aware that bupropion contains the same active ingredient found in ZYBAN™, used as an aid to smoking cessation treatment, and that bupropion hydrochloride should not be used in combination with ZYBAN™, or any other medications that contain bupropion.

h. **ADVERSE REACTIONS**

i. Fourth paragraph, last sentence - ... in the **WARNINGS** and **PRECAUTIONS** sections. (add "the")

ii. Other Events Observed During the development of Bupropion

A). Delete from the title.

B). First paragraph, last sentence - ... in the **WARNINGS** and **PRECAUTIONS** sections.

Please revise your container labels and insert labeling, as instructed above, and submit in final print.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

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Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research